Science Shop

Hereditary disorders in pedigree dogs and look-a-likes

C.W.M. Van Zeeland BSc, Dr. B. Beerda (editor)

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Hereditary disorders in pedigree dogs and look-a-likes

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Stichting Dier&Recht

Stichting Dier&Recht beoogd dieren meer rechten te geven en bestaat uit een team van juristen, onderzoekers en beleidsmedewerkers, met steun van diverse vrijwilligers en stagiaires.
Door middel van rechtszaken wil Dier&Recht de rechtspositie van het dier verbeteren, en met voorlichting en spraakmakende campagnes probeert de stichting het denken over dieren te veranderen.

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Het Departement Dierwetenschappen is betrokken bij onderzoek en onderwijs gericht op de gezondheid en het welzijn van dieren en mensen. De nadruk ligt op het functioneren van de dieren, zowel vanuit nieuwsgierigheid, maar ook in relatie tot de verscheidende functies die dieren hebben voor mensen.

Content

Preface

This thesis is part of a project of the Wageningen UR Science shop. The Science shop helps non-profit companies and organisations in finding answers to questions and issues by helping set up a research. It is a part of Wageningen University and Research Centre and it is interdisciplinary, including students on the projects. The advisory committee serves as a device to give all parties a voice and to make sure everybody gets what they want out of the project.
This project is focussed on three hereditary disorders in dogs to investigate the difference between pedigree dogs and look-a-likes, concerning the prevalence of hereditary disorders. It also looks at the implications of the hereditary disorders on the dog and the owner, according to the owner. Furthermore it looks at what the breeders think of taking hereditary disorders into account when breeding. Are they prepared to put effort into lowering the prevalence of certain hereditary disorders in their pups and to what extend does that effort go?
This thesis is a part of my master in Animal Sciences. The subject fits in both specialisations: Animal Health and Behaviour and Animal Breeding and Genetics, since I will look at hereditary disorders and the effect of them on the welfare of the dog and its owner.

List of abbreviations
CA=Cataract
ED=Elbow dysplasia
FCI=Fédération Cynologique Internationale
HD=Hip dysplasia

Important definitions
Purebred: dog of a certain breed, without specification whether the dog has a FCI approved pedigree certificate or not
Mixed breed: dog with ancestors of different breeds
Pedigree dog: dog of a certain breed with a FCI approved pedigree certificate
Look-a-like: dog of a certain breed without a FCI approved pedigree certificate

Summary

Dogs are an important source of companionship for humans and with an estimated number of 1.5 to 1.8 million, on a human population of about 17 million, have a significant role in Dutch society. There are 343 Fédération Cynologique Internationale (FCI) acknowledged breeds, divided in ten breed groups, with each breed have its own set of traits. To maintain these, pedigree dogs used for breeding are selected for uniform breed specific traits with the risk of inbreeding and associated risks of disease susceptibility and hereditary disorders. There is good scientific evidence that purebred dogs are at increased risk of a specific set of hereditary disorders relative to mixed breeds, though some hereditary disorders occur at a similar prevalence in purebred dogs and mixed breeds. Here, we define 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. It has been speculated that 40% of the purebred dogs has a hereditary disorder, which raises questions about the validity of the claim and if certified pedigree dogs and look-a-likes are equally affected by hereditary disorders. In theory, look-a-likes may suffer the consequences of sharing allelic distribution patterns with pedigree dogs, benefit from outbreeding and / or miss out on health screening programs for pedigree dogs. This study addresses if there is a difference in prevalence of hereditary disorders between dogs with a FCI approved pedigree (hereafter referred to as pedigree dog) and without (look-a-like). Often, disorders are diagnosed with early stage detection methods, meaning prevalence does not refer to clinical symptoms per se and includes dogs that show early signs of a disorder without developing its overt manifestations. This implies that prevalences reported here allow to detect effects and trends, but overestimate the absolute numbers of dogs that suffer from the consequences of a disorder.
As a study model we focussed on 2 dog breeds, German shepherds and Rottweilers, and three hereditary disorders, hip dysplasia (HD), elbow dysplasia (ED) and cataract (CA). Multiple sources were used to gain information on breed dependent hereditary disorders, especially the prevalences of HD, ED and CA. Relevant scientific literature was reviewed and databases with dog health records and breed information were analysed, namely the records of a questionnaire primarily designed to asses owner-satisfaction of owning a dog (n=1,020 records), the records of a questionnaire developed and managed by Dier&Recht (n=1,074 records, of which 63 on German shepherds and 23 on Rottweilers) and a database with HD scores in German shepherds with an FCI approved pedigree in the Netherlands and Germany (n=704,337 records). Also, we developed a questionnaire to collect new information and test if the required information can be obtained by means of using an internet-based survey. The count (categorical) data was analysed with Chi-square tests and continuous data with ANOVA.
A literature review revealed significant differences between countries in the prevalence of HD and ED, based on screening results, in purebred German shepherds and Rottweilers. The period of data collection, age of the dogs included in the studies and the diagnostic methods and classification systems used, differed between studies (read countries), causing variation in the outcomes. The database on owner-satisfaction of owning a dog revealed no significant differences in the prevalence of disorders in dogs with and without a FCI approved pedigree. Owners of dogs with a FCI approved pedigree were more satisfied with their dog than owners of dogs without a FCI approved pedigree, and reported more often to in the future purchase a dog of the same breed. The questionnaire of Dier&Recht revealed a significant lower prevalence of hereditary disorders in look-a-likes than pedigree dogs, i.e. for all breeds taken together. In more detail, for German shepherds and Rottweilers, there was no significant difference in health status between pedigree dogs and look-a-likes, but here the number of records in the analyses was low. The HD database of the German shepherd association, based on screening results, showed that the prevalence of HD, both mild and severe forms, has decreased significantly from 1985 to 2010. The self-developed questionnaire showed no significant difference in prevalence of disorders between pedigree dogs and look-a-likes, but the number of useful records was low. Results from this survey confirmed that according to dog-owners disorders in their dog affected overall movability and vitality and decrease the quality of the dog's life.
Owner-reports, as collected with our own surveys, did not indicate that pedigree dogs suffer more health disorders than look-a-likes or mixed breeds and owners of pedigree dogs seemed relatively

satisfied with their dog. Likely, other factors than the actual health of a dog determined the owner's view on their dogs. For example, owners may accept that HD and ED are a problem in some types of purebred dogs and do not take these disorders into account when expressing their satisfaction with their dog. Earlier studies that compared the health of purebred dogs to that of mixed breeds demonstrated that specific hereditary disorders (not all) have a higher prevalence (1.27 to 3.45 times) in purebred dogs than mixed breeds. However, claiming a precise percentage of purebred dogs with hereditary disorder remains unsubstantiated, for example because of the variation in prevalences of different disorders across populations. Environmental influences on disorders add to the variation in prevalence, especially in those disorders with relatively low heritability coefficients. For HD and ED, the latter are substantial (i.e. the heritability of HD is 0.35 in German shepherds and 0.39 in Rottweilers, for ED this is 0.18 in German shepherds and 0.14 in Rottweilers), allowing to select against these disorders. The presently found decreasing prevalence of HD in German shepherds illustrates how health promoting breeding policies can be effective. Comparing certified pedigree dogs to look-a-likes proved impossible, because of a lack of reliable information on the prevalence of hereditary disorders in look-a-likes as a specific group. In the Dier&Recht data base, there was a significantly higher prevalence of (any) hereditary disorders in pedigree dogs than look-a-likes, for all breeds taken together. However, this outcome was based on owner-reports, and we experienced with our newly developed questionnaire that dog owners, who fill out internet questionnaires, may have strong and coloured views on matters relating to pedigree dogs. Earlier studies based on veterinarian conducted health measurements generated different results regarding dog (hereditary) disorder prevalence than those based on owner reports. Where the former typically find increased health risk for purebreds compared to mixed breeds, the latter may fail to register this and the validity of owner reports in recording dog health seems limited. A veterinarian conducted dog health monitoring approach is needed for establishing to what degree pedigree dogs and look-a-likes are differently at risk of hereditary disorders.

Thus, earlier studies demonstrated clearly how purebred dogs are at increased risk of hereditary disorders compared to mixed breeds, though present findings on German Shepherds, for example, suggest recent health promoting breeding policies can improve matters. To what degree look-a-likes still suffer the from the consequences of the former whilst missing out on the benefits of the latter remains yet to be determined. Owner reports in an internet database of Dier&Recht indicate that pedigree dogs are at increased risk of hereditary disorders compared to look-a-likes. However, establishing the health status of dogs in this relatively easy way, that is by means of owner reports, does not seem to produce valid results and a laborious systematic recording of reliable health records on pedigree dogs and look-a-likes is required. Given the variety in diagnostic methods used and the variation in prevalences across dog populations breeds and disorders, any general figure on the prevalence of hereditary disorders in pedigree dogs, look-a-likes or mixed breeds may be readily criticized. As such, the value of generalized prevalence estimates is in the detection of trends and effects, i.e. making relative comparisons, more than in its absolute level.

1 Introduction

Dogs are an important source of companionship for humans and are a significant part of human societies, for example as indicated by their numbers. Worldwide there are an estimated 30 dogs per 1000 inhabitants, with in Europe 112 dogs per 1000 inhabitants. For the Netherlands, estimates have been made of 109 dogs per 1000 inhabitants (Leenstra & Vellinga, 2011), meaning there are over 1.5 million dogs in the Netherlands (FCI, 20101). Thirty-five per cent of these dogs is registered as a pedigree dog (Raad van Beheer, 20101). In the following, we refer to 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. The dog population is composed of over 343 Fédération Cynologique Internationale (FCI) acknowledged breeds (FCI, 20102) divided in ten breed groups. These breed groups were defined based on appearance, character or the initial purpose of the breed (Raad van Beheer, 20102). Dog breeds may be grouped into four genetic clusters with similar terrestrial origin, morphology or purpose for humans (Parker et al., 2004). Originally dogs underwent a process of self-domestication, but over the last centuries humans started to strongly select dogs for different traits, which rapidly resulted in over 400 different breeds (Parker et al., 2004). Due to breed splits, the effective breeding population sizes in dogs have become relatively small, resulting in an increased risk of inbreeding. When inbreeding takes place, the chances of homozygote loci increases and with that the manifestation of recessive alleles based health disorders. There is a confirmed association between inbreeding and increased disease risk in purebred dogs (Rooney, 2009). Due to reduced genetic diversity purebreds suffer a higher prevalence of hereditary disorders. Breeders select regions of the genome that contain a desired trait and thereby also select for a disorder in that same region, which has led to breeds becoming particularly predisposed to certain hereditary disorders. Genetic disorders can seriously compromise the welfare of an animal (Wade, 2011). Hereditary disorders may results from having two unfavourable alleles, of which the risk is relatively high when parents are closely related, which facilitates the offspring to be homozygous for genes. A hereditary disorder can be monogenic or polygenic. Monogenic disorders are influenced primarily by only one gene, a polygenic disorder by multiple (Griffiths et al., 2008) and the more mutations with negative effects are involved, the more the dog is affected by the disorder. Hip dysplasia is an example of such a polygenic hereditary disorder, where more than 9 genes are involved (Marschall and Distl, 2007). This shows in the appearance of the disorder, which manifests to different degrees of severity. Since the different degrees of severity in hip dysplasia can also be influenced by environmental factors, like nutrition and exercise, the mode of inheritance is therefore also classified as multifactorial. The heritability of hip dysplasia has been estimated in the range of 0.25 to 0.40 (OMIA; 2014). To what degree pedigree dogs are more at risk of (genetic) health disorders than non-pedigrees is a point of on-going discussion, and it is unknown for example if look-a-likes with similar phenotypes as their pedigree counterparts share similar health risks. There is controversy regarding when a dog is a purebred, look-a-like or mixed breed. Purebreds could be identified as a certain breed by a veterinarian, with dogs that are a mix of multiple breeds labelled as mixed breed (Bellumori et al., 2013). Alternatively, purebred dogs could be defined as dogs that conform to the written breed standards, which mixed breed dogs do not (Rooney and Sargan, 2010). In many studies with purebred dogs the difference between a pedigree dog and a look-a-like is not mentioned. In the present study, a purebred dog is considered a pedigree dog when it has a FCI approved pedigree certificate. When a dog is characterised as being from a certain breed, but not having a FCI approved pedigree certificate, it is called a look-a-like. The FCI is the World Canine Organisation that holds records of the breed standards, written by the country from which the breed originates. It also updates and translates the various international regulations. The FCI trains judges that judge dogs in shows according to the regulations and breed standards, which assist the breeders in their attempt to produce top-quality dogs (FCI, 2010[2,3]). Selective dog breeding is typically based strongly on selection for desirable morphology or personality, which as an unwanted side-effect may increase the risk of disorders. For example, selecting dogs for an elongated body conformation makes the dog more susceptible for hip dysplasia (Roberts & McGreevy, 2010). The average length/height (L/H) ratio of 30 breeds was calculated and compared to the percentage of dysplastic dogs in that breed. A strong correlation was found between the L/H ratio and the percentage of dysplastic dogs (Spearman $r=0.727$, $P<0.001$), with longer dog breeds being more susceptible to HD than tall or square dog

breeds. Where some heritable disorders are breed specific others are not, like hypothyroidism; one of 312 inherited disorders that have been identified as not being breed specific (Collins *et al*., 2010; Summers *et al*., 2010). The breeding for a specific conformation can be taken to the extreme, in which case the quality of life of the dog is diminished (Rooney, 2009). In practice, it is impossible to select against all hereditary disorders at once, for example as this would substantially decrease the effective breeding population size.
In the US, hereditary disorders were established in 65,952 purebred dogs and 22,683 mixed breed dogs over the period from 1995 to 2010 (Bellumori *et al.*, 2013). Dogs were identified as from a certain breed by a veterinarian. Twenty-eight disorders and injuries were examined and the results indicated that for 10 disorders and injuries, including elbow dysplasia and cataract, purebred dogs had a 1.27 to 3.45 times higher probability (depending on the type of disorder) of expressing the disorder than mixed breed dogs. Particularly, they reported that the purebred dog population of Rottweiler's have a higher probability of 6.3% for elbow dysphasia. For a specific set of 16 disorders and injuries, including hip dysplasia, purebred dogs had a range of values for different disorders of a 0.85 to 2.04 times higher probability of expressing the disorder/injury. The prevalence of hip dysplasia in purebred dogs and mixed breed dogs were similar and also Rettenmaier et al. 2002 found no significant differences of hip dysplasia between purebred and mixed breed dogs. For ruptured cranial cruciate ligament, and being hit by a car, the mixed breeds had a 1.27 to 1.69 times higher risk (Bellumori *et al.*, 2013). At least part of the hereditary disorders dogs from a certain breed have a significantly higher probability for expressing it than dogs of multiple breeds. However, it also shows that some causes of death are higher for mixed breeds than for purebred dogs.

It has been suggested that 40% of all purebred dogs have a hereditary disorder, based on population health surveys (Gubbels & Scholten, 2005). This would mean that out of roughly 500,000 purebred dogs, 200,000 dogs are affected by a hereditary disorder. The literature underlying this assumption included studies of 20 to 30 years ago, and methods and outcomes differ substantially across studies. For example, the scores for hip dysplasia were in one article given on the basis of X-rays Coopman *et al.* (2008) whereas for another study it remains obscure what exactly has been scored (Janutta *et al.*, 2006). Since the prevalence of hereditary disorders varies, for example over time, possibly in response to changes in breeding strategies, an update of the current status is desirable. The prevalence of a disorder is the total number of cases in the population at a given time, typically divided by the population size. Incidence is a measure of the risk of developing new cases within a specified period of time. Hereditary disorders, usually have a long time span, making prevalence the preferred risk indicator and the one that is used here. Disorders may be diagnosed with early stage detection methods, meaning that reported "prevalences" does not refer to clinical symptoms per se and include cases of early signs of a disorder without further development into overt manifestations. This implies that prevalences reported, do allow to detect effects and trends, but will overestimate the absolute numbers of dogs that suffer from the consequences of a disorder.
Earlier studies that looked at hereditary disorders in a certain breed of dogs did not differentiate between pedigree dogs and look-a-likes within the group of purebred dogs. The two subgroups may, however, differ as some breed clubs make increasing efforts to breed healthy dogs. This study aims to find out whether the prevalence of hereditary disorders differs between certified pedigree dogs and look-a-likes. The answers to our research questions likely vary with factors like dog breed and type of disorder. Given time constraints, data analyses are focused, for example on specific breed-disorder cases, representing small scale models of the actual situation. Findings from earlier studies are used as a major source of information for answering research questions. The hereditary disorders that we studied in two dog breeds, are two bone disorders; hip dysplasia (HD) and elbow dysplasia (ED), and the eye disorder cataract (CA). Both types of dysplasia (HD and ED) are malformations of the joint. The diagnosis of hip and elbow dysplasia is established by means of radiographic examinations according to the FCI standards, which can be sensitively diagnosed by X-ray photos. The bone disorders are polygenic and multifactorial and the severity can differ among dogs, for example according to the scoring system presented in Tables 1a and b. In this study a dog is called affected by the disorder with a score of 2 to 5 for HD and/or 1 to 3 for ED. Cataract is clouding of the lens in the eye, which impairs the vision. This clouding of the eye is easier to notice than bone abnormalities, and detectable for dog owners, though they may have difficulty in assessing the severity. A veterinarian should be consulted to ensure that the clouding of the eye is cataract and to assess its severity. In this

study, the dog is considered to be affected by cataract when the owner reports that the dog has cataract.

Table 1a. The scoring system for HD.

Score	Hip dysplasia
1	Normal (no abnormalities)
2	Almost normal
3	Mild
4	Medium
5	Severe

Table 1b. The scoring system for ED.

Score	Elbow dysplasia
0	Normal (no abnormalities)
1	Mild (<2 mm anomaly)
2	Moderate (2-5 mm anomaly)
3	Severe (>5 mm anomaly)

The studied breeds are German shepherds and Rottweilers, which are common breeds in the Netherlands in 2013 (Raad van Beheer, 2010[3]). In Table 2, the 10 dog breeds with the most pedigree registrations in 2013 (both born in the Netherlands and import) are ranked on number of registrations. The German shepherd is the third most popular dog breed in The Netherlands with 1,855 registrations in 2013. The Rottweiler is at place 19 and less common with 492 registrations (Table 2).

Table 2. The top 10 of dog breeds in the Netherlands based on the number of registrations (born in the Netherlands and import) with Raad van Beheer in 2013.

	Breed	Number of registrations
1	Labrador retriever	3105
2	Golden retriever	1932
3	German shepherd	1855
4	Bernese mountain dog	1255
5	Chihuahua	1060
6	Staffordshire bull terrier	1047
7	Border collie	868
8	French bulldog	839
9	Boxer	799
10	Dachshund rough coated	768

Summarizing, inherited disorders and their prevalence in different dog populations like purebred, look-a-likes and mixed breed dogs are the main subject of this research project. It has been suggested that a high percentage (e.g. 40%, Gubbels and Scholten 2005) of all purebred dogs are affected by genetic disorders. In contrasts, it has been put forward that contemporary breeding policies, which are in place for pedigree dogs only, promote good health. This research project aims at compiling information about genetic disorders in pedigree dogs, particularly to retrieve all data on differences in prevalence of genetic diseases between pedigree dogs, look-a-likes and mixed breed dogs. To obtain sufficient data for this short-term research project three strategies are applied to analyse and report relevant results. There are many different breeds (>400) and at the same time there are many genetic disorders in dog breeds (>350), and we decided to focus on two popular dog breeds, the German Sheppard and the Rottweiler. The three inherited disorders which are targeted are hip dysplasia (HD), elbow disease (ED), and cataract (CA). The first strategy is to perform a systematic scientific literature study on these three genetic disorders (HD, ED, CA) and compare prevalences in pedigree dogs, look-a likes and mixed breed dogs. The second strategy is the analysis of databases, one obtained via the German Sheppard Association, another from the Dutch association Dier&Recht and a third from WUR. The third strategy entails the development of a questionnaire to collected new owner-reported records on the health of pedigree dogs, look-a-likes and mixed breeds. The latter survey is specifically designed to estimate the existing prevalence of genetic disorders in the Netherlands.

2 Material and method

This study used multiple sources to gain information on the difference in prevalence of genetic disorders, especially HD, ED and CA, in pedigree dogs, look-a-likes and mixed breeds. First of all, a scientific literature study was performed on the prevalence of genetic disorders, including in other countries than the Netherlands. Second, available databases of Dier&Recht, WUR and a database on German Shepherds were analysed to estimate the present prevalence of genetic disorders among dogs in Germany and the Netherlands. Lastly, a questionnaire was developed for monitoring the prevalence of disorders, now and possibly in the future, for example to investigate if certain kennel club policies have an influence on disorder prevalence.

2.1 Scientific literature study

Recent findings on the prevalence of genetic disorders could be compared to those reported earlier for the purpose of assessing trends over time. Also, large and extensive earlier studies may provide valuable findings that may be extrapolated for answering the present research questions. Thus, for this study, it is important to know the history of the prevalence of HD, ED and CA, so that we may compare the present prevalence of disorders to the past situation. Findings for different countries than the Netherlands may be used to estimate the Dutch situation. Examples of keywords used to search scientific literature are: *prevalence, pedigree*, *hip dysplasia*, *elbow dysplasia*, *cataract*, *Netherlands*, *dog*, *dogs*, *German shepherd*, *Rottweiler*. These words have been used in different combinations and in different searching websites (e.g. Web of Science, Pubmed).

2.2 Databases

One of the databases that was used to find a possible difference in prevalence of hereditary disorders in pedigree dogs and look-a-likes is a questionnaire that was online from April 2011 to September 2011. The survey was designed to measure the satisfaction of the dog owner about dog-ownership and their dog. Some of the questions were about health disorders in the dogs and since the owners reported on their dog having a pedigree certificate, the records were suitable to use in this study. From this database with 1020 records the following data was used: Whether or not the dog had a pedigree certificate of Raad van Beheer; how satisfied the owner was with the dog; whether the dog had a health disorder at the moment the questionnaire was filled in; whether the dog had a history of having a health disorder; and if the next dog of the owner would likely be of the same breed as the dog they had at the time (i.e. how satisfied were owners with the chosen breed of dog). The questionnaire was filled in for multiple dog breeds and data were analysed across breeds.
Another database that was used to assess prevalences of hereditary disorders in pedigree dogs and look-a-likes, was a database of Dier&Recht (see Appendix A). The questionnaire started half way 2012. The Dier&Recht survey addressed different disorders, as listed in Appendix B. The associations between having a pedigree and the risk of genetic health disorders were assessed for specific disorders, i.e. HD, ED and CA, as well as across different types of disorders. The numbers of dogs in which we were interested mainly (German shepherds and Rottweilers) were relatively low in the database, with 63 records on German shepherds (51 with an FCI approved pedigree and 12 without an FCI approved pedigree) and 23 on Rottweilers (12 with an FCI approved pedigree and 11 without an FCI approved pedigree). In total, 1,074 useful records across dog types were available.
For further investigation of the prevalence of HD, based on screening results, we used a database of 704,337 pedigree German Shepherds living in the Netherlands and Germany of which the breeders are members of the "Vereniging van Fokkers en Liefhebbers van Duitse herdershonden", the only German shepherd association in the Netherlands acknowledged by Raad van Beheer. This database provided information on whether a dog had HD or not and how severe the HD was, based on a screening by professionals. When a pedigree dog reserved for breeding is 1 year of age or older, it is evaluated for HD; X-rays are made of the hips and these X-rays are assessed by a professional, who gives a number 1 (no HD) to 5 (severe HD), depending on the severity of possible malformations. In this study, the

dog was considered to be affected by HD with a score of 2 to 5, divided in two groups with a score of 2 and 3 being mildly affected, and a score of 4 and 5 being severely affected. The database included multiple factors, which could be used for filtering records, and see Table 3 for a listing and further explanation. The HD scores from 1985 and 2010 were analysed to investigate if the prevalence of HD increased, decreased or stayed the same in that time period. The sex of the dogs was taken into account, for example to see if male and female dogs are at risk of HD differently. The database did not show whether the dog was treated for HD or not.

Table 3. The headings of the columns of the German shepherd HD database, provided by the German shepherd association. The headings are explained to show the possibilities of the database.

Name	Description
SZ-Nr	Pedigree number
Hund	The name of the dog
Sex	The sex of the dog (male/female)
DNA	Screening of the DNA of the dog
Wurftag	The date of birth of the dog
ED	Not explained
HD	The score of HD of the dog based on X-rays
ZW-n	New or current breeding value
ZW-a	Old breeding value
Haarart	Type of coat
Vater	The name of the sire of the dog
Mutter	The name of the dam of the dog

2.3 Questionnaire

A new questionnaire was designed with the goal to assess and monitor the prevalence of hereditary disorders in pedigree dogs, look-a-likes and mixed breeds. Owners were asked to identify their dog as a pedigree dog (having a Raad van Beheer/FCI approved certificate), a look-a-like or a mixed breed. The dog's identification in terms of its chip number was asked, and has the potential to be used to validate whether the dog had a FCI approved pedigree. Owners indicated whether the dog had a health disorder in one or more of the organ systems (asked per organ system yes/no) and if so what the name of the disorder was. Hereditary disorders can have different effects on the quality of life of the dog and the owner was asked whether the dog was affected by the hereditary disorder concerning movability, pain and vitality. Owners reported on the overall movability and vitality of the dog, regardless whether it had a hereditary disorder. The quality of life overall and the veterinarian costs were examined as well. The questions asked in the questionnaire are shown in Appendix C. Records were in part filtered for erroneous or even false entries, for example by removing multiple "suspect" (inconsistencies in reporting or funny names) entries from a same IP-address. Multiple entries from a same IP-address that did seem credible, assuming that the voter indeed owned multiple dogs, were restricted to a maximum of three records per IP-address. With these filters, 99 credible records were analysed. Due to the small total number of records, no analysis was done per breed. Findings were compared to those from other databases and to findings in earlier studies as reported in scientific literature.
The questionnaire was brought under the attention and/or promoted by the breed association for German shepherds, 'Vereniging van Fokkers en Liefhebbers van Duitse Herdershonden' (V.D.H.), and the breed association for Rottweilers, Nederlandse Rottweiler Club (NRC). Prins petfoods was asked to promote this questionnaire via their social media, as to recruit owners of look-a-likes.

2.4 Data analysis

To analyse the data, different statistical methods were used. The Chi-square test and a comparison of fractions were used to analyse count data and find differences in prevalence of HD, ED and CA, based

on screening results, between pedigree dogs, look-a-likes and mixed breeds. Continuous data was analysed with an ANOVA.

2.4.1 Chi-square test

The Chi-square test was used for analysing the questionnaire records on the owners' satisfaction with their dog, the questionnaire of Dier&Recht, for the HD database of the German shepherd association and for the first results of the questionnaire that has been developed for future research. The Chi-square test was done with the program Matman 1.1. The results showed whether there was a difference in prevalence of hereditary disorders (e.g. HD, ED and CA) between pedigree dogs, look-a-likes and mixed breeds.

The formula of the Chi-square test is as follows:

$$X^2 = \sum \frac{(observed\ number - expected\ number)^2}{expected\ number}$$

Where the expected number can be calculated as :

$$\text{expected number} = \frac{row\ total\ x\ column\ total}{n}$$

If the test statistic X^2 (Chi-square) is larger than the critical value, which depends on the degrees of freedom the interaction between row and column variables significantly determine the count scores. As a rule of thumb for small data sets, when effects are significant, residuals ($\frac{observed\ number - expected\ number}{\sqrt{expected\ number}}$) over |2| identify cells (counts) that deviate from expectations and are significant. More precisely, z-values can be calculated that when > |1.96| identify cells that deviate significantly from expectations;

$z = \left(\frac{observed\ number - expected\ number}{\sqrt{expected\ number} * (1 - row_p) * (1 - column_p)}\right)$,

with the p indicating proportion (so row or column totals divided by the total count). Interpretations of the Chi-square test outcomes should involve both factors, column and row variables.

2.4.2 Comparison of two fractions

To test for a possible change in prevalence of HD in German shepherds with an FCI approved pedigree over the years, a comparison was made of two fractions (i.e. proportions of animals affected) following the procedures described by Moore & McCabe (2008). The statistical test allows the comparison of two population fractions, in this case the fraction of German shepherds with an FCI approved pedigree with a certain score for HD in 1985 and the fraction of German shepherds with an FCI approved pedigree with the same score for HD in 2010. The steps involved in comparing fractions are described with the formulas presented below. The same procedure was used to compare results reported in scientific literature to results from other sources.
First determined is the difference between fractions of interest for two populations:

$$D = \hat{p}_1 - \hat{p}_2$$

The standard error of D is:

$$SE_D = \sqrt{\frac{\hat{p}_1(1 - \hat{p}_1)}{n_1} + \frac{\hat{p}_2(1 - \hat{p}_2)}{n_2}}$$

The margin of error for the confidence interval of $p_1 - p_2$ is:

$$m = z \times SE_D$$

with z being 1.96 for a 95% confidence interval. The confidence interval itself is calculated as

$$D \pm m.$$

When 0 is within the confidence interval, there is no significant difference between the two fractions, otherwise there is.

2.4.3 ANOVA test

The first results of the continuous data of the self-developed questionnaire were analysed with the analysis of variance (ANOVA) test. Statistical models included the independent variables dog type, owner reported disorder and veterinarian diagnosed disorder, and the dependent variables overall movability and vitality of the dog. Thus the influence of disorders on the movability, pain, vitality and quality of life of the dog was tested. The ANOVA test evaluates the hypothesis that the response variate *y* (e.g. quality of life) does not linearly relate to the independent variable *x* (e.g. the most severe disorder the dog has). A null-hypothesis (H_0: $\beta 1=0$) of no effect (relationship) is rejected in favour of an alternative hypothesis (H_a: $\beta 1\neq 0$) in the case of large test statistics (here the F-statistic).

$$\mathrm{F} = \frac{Variance\ between\ treatments}{Variance\ within\ treatments}$$

When F is smaller than the critical value, which depends on the degrees of freedom (number of records and levels of the independent variable(s)) and the residuals (variation), the null-hypothesis is adopted, which means that *y* is not affected by *x*. When F is larger than the critical value the null-hypothesis is rejected and the alternative hypothesis is adopted. Here, all dependent variables were one by one tested, against every independent variable without accounting for interaction effects.

3 Results

It was investigated if there is a difference in the prevalence of the hereditary disorders in pedigree dogs and look-a-likes, based on screening results, in part using a model approach by focussing on HD, ED and CA in German shepherds and Rottweilers. Information from countries other than the Netherlands is extrapolated to estimate the Dutch situation. Three different data sources were used; existing scientific literature, for example to see what the prevalence of the diseases was in past years and in different countries, databases that were made available to us (data of WUR, Dier&Recht and the German shepherd association) and records from a newly developed a questionnaire, specifically designed to estimate the present prevalence of the disorders.

3.1 Scientific literature study

Regarding scientific literature on the prevalence of the hereditary disorders hip dysplasia (HD), elbow disease (ED), and cataract (CA) nothing was found for German shepherds and Rottweilers in the Netherlands specifically. Next, we searched literature for further more general information on the three different hereditary disorders HD, ED and CA.

3.1.1 Hip dysplasia

First, the results of the literature study are described for hip dysplasia in European and non-European countries. In Belgium (period of time 2002-2006), the United Kingdom (period of time 1998-2007) and Finland (period of time 1988-2000) the prevalence of HD in German shepherds and Rottweilers with a FCI approved pedigree was assessed (Coopman *et al.*, 2008;Collins *et al.* 2010; Mäki, 2004). The scores for HD were determined by professionals with X-ray pictures obtained by the respective Kennel Clubs for screening. The data of the potential breeding dogs was made available by the Kennel Clubs of the respective countries and was a random sample of the population.

Table 4. An overview of the scientific literature on HD in German shepherds arranged by country. Presented are the number of dogs tested, the HD prevalence (total found in the article and when possible divided in mild and severe forms), the period of time in which the data was collected, whether the dogs had a FCI approved pedigree and the data source. Prevalence estimates that do not share a same letter in the superscript differ significantly. *ND=not determined. **This article did not mention the number of dogs.

	Country	# German shepherds	Prevalence (%)			Period	FCI approved pedigree (Y/N)	Source
			Total	Mild	Severe			
Within Europe								
1	Belgium	1245	23[a]	16	7	2002-2006	Yes	Coopman *et al.* (2008)
2	United Kingdom	ND*	<50**			1998-2007	Yes	Collins *et al.* (2010)
3	Finland	25308	37[b]			1988-2000	Yes	Mäki (2004)
Outside Europe								
4	Missouri	149	32.9[b]			1991-1995	Both	Rettenmaier *et al.* (2002)
5	Canada	402	46.8[c]			1970-1978	Both	Martin *et al.* (1980)

In Sweden the prevalence of HD in Rottweilers was studied by Malm *et al.* (2008). It was not determined whether the dogs had an FCI approved pedigree. The scores for HD date from 1984 to 2002 and the dogs were X-rayed to determine the score for a screening program. The a-select data was made available by the Swedish Kennel Club. In Missouri (period of time 1991-1995) and Canada (period of time 1970-1978) the prevalence of HD in German shepherds and Rottweilers, both with and

without a FCI approved pedigree, was assessed. These databases were acquired in veterinary hospitals in the respective countries, which means that this was not an a-select sample of the population. Comparing the Swedish figures with those from North America suggests that prevalence estimates about double when based on populations of dogs submitted to a veterinary clinic. Tables 4 and 5 show the prevalence of HD in German shepherds and Rottweilers respectively.

Table 5. An overview of the scientific literature on HD in Rottweilers arranged by country. Presented are the number of dogs tested, the HD prevalence (total found in the article and when possible divided in mild and severe forms), the period of time in which the data was collected, whether the dogs had a FCI approved pedigree and the data source. Prevalence estimates that do not share a same letter in the superscript differ significantly. *ND=not determined. **This article could not be compared, because the number of dogs was not determined.

	Country	# Rottweilers	Prevalence (%)			Period	FCI approved pedigree (Y/N)	Source
			Total	Mild	Severe			
Within Europe								
1	Belgium	346	10[a]	6	4	2002-2006	Yes	Coopman *et al.* (2008)
2	United Kingdom	ND*	20-25**			1998-2007	Yes	Collins *et al.* (2010)
3	Finland	11746	32[c]			1988-2000	Yes	Mäki (2004)
4	Sweden	14693	16.6[b]			1984-2002	ND	Malm *et al.* (2008)
Outside Europe								
5	Missouri	99	35.4[c]			1991-1995	Both	Rettenmaier *et al.* (2002)
6	Canada	26	30.8[c]			1970-1978	Both	Martin *et al.* (1980)

Prevalence estimates of HD in pedigree German shepherds range from about 20% up to near 50%, with the intermediate estimates being about one third of the study populations. For Rottweilers the range of HD prevalence estimates is from 10% to 35%, with intermediate values of about one-quarter. It seems that typically prevalence estimates for European countries are somewhat lower than for Northern-America. Together it seems that substantial proportions of pedigree Rottweilers and especially German shepherds are affected by HD. When comparing the prevalence of HD in study populations of dogs with pedigree dogs only to that with pedigree dogs and look-a-likes, there is no clear difference, and there is no (indirect) indication that pedigree dogs are more at risk than look-a-likes.

3.1.2 Elbow dysplasia

The prevalence of ED was assessed in Germany (period of time 1996-1999), Belgium (period of time 2002-2006), Finland (period of time 1988-2000), Sweden (period of time 1984-2002), South Africa (period of time 1999-2006) and the United States of America (period of time since 1990) for German shepherds and Rottweilers (Beuing et al. 2000; Coopman et al., 2008; Mäki, 2004; Malm et al., 2008; Kirberger & Stander, 2007). In all studies the score for ED was assessed by professionals through X-ray photos obtained by the respective Kennel Clubs for screening. Tables 6 and 7 show the prevalence of ED in German shepherds and Rottweilers respectively.

Table 6. An overview of the scientific literature on ED in German shepherds arranged by country. Presented are the number of dogs tested, the ED prevalence (total found in the article and when possible divided in mild and severe forms), the period of time in which the data was collected, whether the dogs had a FCI approved pedigree and the data source. Prevalence estimates that do not share a same letter in the superscript differ significantly. *ND=not determined.

	Country	# German shepherds	Prevalence (%)			Period	FCI approved pedigree (Y/N)	Source
			Total	Mild	Severe			
Within Europe								
1	Belgium	130	12[a]	6	6	2002-2006	Yes	Coopman *et al.* (2008)
2	Finland	5687	19[b]			1988-2000	Yes	Mäki (2004)
Outside Europe								
3	South Africa	24	20.8[ab]			1999-2006	ND*	Kirberger & Stander (2007)
4	USA	23088	19.5[b]			Since 1990	ND	Kirberger & Stander (2007)

The studies in Germany, Belgium and Finland used data of only dogs with a FCI approved pedigree; the studies in Sweden, South Africa and the United States of America did not specify whether the dogs had a FCI approved pedigree or not.

Table 7. An overview of the scientific literature on ED in Rottweilers arranged by country. Presented are the number of dogs tested, the ED prevalence (total found in the article and when possible divided in mild and severe forms), the period of time in which the data was collected, whether the dogs had a FCI approved pedigree and the data source. Prevalence estimates that do not share a same letter in the superscript differ significantly. *ND=not determined.

	Country	# Rottweilers	Prevalence			Period	FCI approved pedigree (Y/N)	Source
			Total	Mild	Severe			
Within Europe								
1	Germany	2114	54.21[d]			1996-1999	Yes	Beuing *et al.* (2000)
2	Belgium	135	33[ab]	21	12	2002-2006	Yes	Coopman *et al.* (2008)
3	Finland	8636	44[c]			1988-2000	Yes	Mäki (2004)
4	Sweden	11891	38.67[b]			1984-2002	ND*	Malm *et al.* (2008)
Outside Europe								
5	South Africa	148	54.7[d]			1999-2006	ND	Kirberger & Stander (2007)
6	USA	9407	40.9[a]			Since 1990	ND	Kirberger & Stander (2007)

When comparing the results from the larger (i.e. including thousands of subjects) European studies, the prevalence of ED in Rottweilers was the lowest in the Swedish study (where subjects did not necessarily have a pedigree); 39% (Sweden) compared to 44% (Finland) and 54% (Germany). Assuming the Swedish study population included in part Rottweiler look-a-likes, it seems these look-a-likes have a reduced risk of ED. The effect is not overly strong though, especially given the wide range of prevalence estimates across studies (countries). Also, the contribution of look-a-likes relative to

pedigrees in the Swedish study is speculative. The incidence of ED in German shepherds and Rottweilers was, respectively, 21% and 55% in South Africa and 20% and 41% in the United States of America (Kirberger and Stander 2007). Focusing again on the larger (US) study, which included thousands of subjects, the prevalence of ED in pedigree and look-a-like Rottweilers (41%) was comparable to that in the Swedish study on pedigree dogs and look-a-likes (39%), and relatively low compared to the prevalence in European pedigree Rottweiler populations. Regarding ED in German shepherds, the prevalence in the larger studies was comparable between pedigrees only (Finnish study; 19%) and a mixed study population of pedigree German shepherds and look-a-likes (US; 20%).

3.1.3 Cataract

The prevalence of cataract in German shepherds and Rottweilers in the Netherlands is not well-studied. However, there is an article on the prevalence of cataract in Labrador retrievers in the Netherlands, which can give some insight. In the Netherlands, 9,017 Labrador retrievers underwent 18,283 ophthalmic examinations during the period from 1977 to 2005. The data was provided by the Dutch Labrador Club and all dogs had a FCI approved pedigree (Nederlandse Labrador Vereniging, 2013). Dogs with hereditary retina degeneration (PRA, n=262) were excluded from this study. Of the 8,755 dogs that were not affected by PRA, 522 dogs (5.79%) were diagnosed to have cataract. Of the female dogs 5.85% were affected by cataract and of the male dogs 6.20% (Kraijer-Huver *et al.*,2008). The prevalence of cataract decreased in the last couple of years (see Figure 1, Kraijer-Huver *et al.,* 2008). When the dogs with PRA were excluded, the decrease in prevalence over the years was less noticeable. It seems that the prevalence of the combination of PRA and cataract decreased more over time than only cataract.
over time than only cataract.

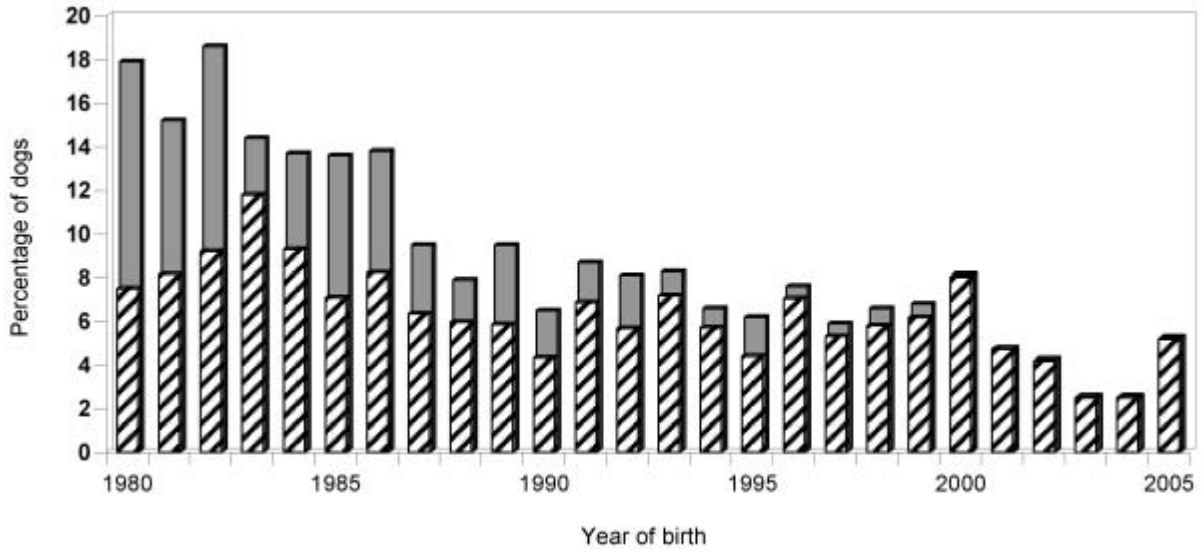

Figure 1. Percentage of cataract-affected dogs by year of birth among 9,017 Labrador Retrievers in The Netherlands (with or without PRA; gray bars), compared with the percentage among 8,755 dogs after exclusion of 262 PRA-affected animals (striped bars) that underwent ophthalmic examination as part of a pre-breeding screening program in the period 1980 through 2005 (Kraijer-Huver *et al.*, 2008).

The prevalence of CA increases with age. In purebred dogs of multiple breeds and mixed breeds, the prevalence of CA at an age below one year was 5% as compared to 100% at 16 years (Williams et al, 2004).
The Canine Inherited Disorders Database (CIDD) is a joint initiative of the Sir James Dunn Animal Welfare Centre, University of Prince Edward Island and the Canadian Veterinary Medical Association with as goal to reduce the incidence of inherited disorders in dogs by providing information (Crook *et al.*, 2011). It claims that cataract occurs in many breeds, including the German shepherd and the Rottweiler. No sources were mentioned or prevalences and, unfortunately, little information was found on CA in German shepherds and Rottweiler. In breeds where CA is a problem, the prevalence of CA increases with age.

3.2 Databases

Three databases with information on the dogs' breed, pedigree and/or health were analysed. Records of database owned by Dier&Recht and the survey on dog-ownership satisfaction are analysed with a Chi-square test to see is there is a significant difference in prevalence between pedigree dogs and look-a-likes. The database on HD scores in German shepherds with an FCI approved pedigree, owned by the German shepherd association is analysed by means of comparison of fractions of the population that are affected by disorders.

3.2.1 Questionnaire dog satisfaction

The results on the questionnaire on dog satisfaction in owners are shown below. It was tested whether owners of pedigree dogs were similarly satisfied with their dog as owners of look-a-like dogs and mixed breeds, with the latter two being referred to a non-pedigree dogs (see Table 8). Also, we tested whether owners of pedigree dogs were equally likely as owners of look-a-like dogs and mixed breeds to buy a dog of the same breed when purchasing a new dog (see Table 9).

Table 8. The scores of satisfaction of the owners with their dog. A distinction is made between dogs with and without an FCI approved pedigree. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number of dogs deviates the most from the expected numbers (residuals>|2| are considered significant).

	Not satisfied	Satisfied	Very satisfied	Total
Pedigree	22 (-1.68)	84 (-1.95)	438 (1.45)	*544*
No pedigree	36 (1.82)	108 (2.12)	317(-1.58)	*461*
Total	*58*	*192*	*755*	*1005*

The X^2-value is 19.05 (df=2), with the critical value of the X^2-distribution with 2 degrees of freedom and a P-value of 0.05 being 5.99. X^2-values > critical values imply significant effects, with residuals identifying the values that deviate most strongly from expectations. The standardized residuals identify that especially the combination of owners being satisfied with their non-pedigree dog is overrepresented. Trends for not satisfied and very satisfied are however in the opposite direction.

Table 9. The number of owners wanting the same or a different breed for the next dog they will purchase. A distinction is made between owners having a dog with an FCI approved pedigree and owners having a dog without an FCI approved pedigree. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number deviates the most from the expected numbers (residuals>|2| are considered significant).

Next dog	Owns pedigree	Owns non-pedigree	Total
Wants same breed	478 (1.95)	332 (-2.11)	*810*
Wants different breed	70 (-3.87)	135 (4.19)	*205*
Total	*548*	*467*	*1015*

Regarding whether the owner would like to have a same type of dog when purchasing one in the future, the X^2-value is 40.72 (df=1). The critical value of the X^2-distribution with 1 degree of freedom with a P-value of 0.05 is 3.84. Again, X^2-values > critical values imply significant effects, with residuals identifying the values that deviate most strongly from expectations. The standardized residuals indicate that relatively many owners of non-pedigree dogs would like to have another type of dog as their next, and that relatively few owners of a pedigree dog would choose for a different breed. Furthermore we looked at the difference in prevalence of disorders in dogs with and without an FCI approved pedigree. It should be noted that these disorders are not only hereditary disorders, but all types of disorders. First we looked at whether the dogs had a disorder at the moment the questionnaire was filled in and afterward we also looked at whether dogs have had a disorder that has been cured before the questionnaire was filled in (see Tables 10 and 11, respectively).

Table 10. The prevalence of disorders in dogs (no specific breeds) with or without an FCI approved pedigree with the assumption that a dog can have only one disorder. The disorders in this case are not limited to hereditary disorders, it can also be an infection or another disease. The disorders were present in the dog at the moment the owner filled in the questionnaire. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number of dogs deviate the most from the expected numbers (residuals>|2| are considered significant).

	Pedigree	No pedigree	Total
Disorder	125 (1.00)	87 (-1.08)	*212*
No disorder	425 (-0.51)	383 (0.55)	*808*
Total	*550*	*470*	*1020*

The X^2value is 2.74 (df=1). The critical value of the X^2-distribution with 1 degree of freedom with a P-value of 0.05 is 3.84. The X^2 value found is smaller than the critical value, which means that the observed numbers do not significantly differ from the expected numbers. From the records of the questionnaire can be concluded that there is no difference in dogs with or without an FCI approved pedigree, concerning all types of disorders between April 2011 and September 2011. The same goes for the period before April 2011 (X^2 value=1.83, df=1, see Table 11).

Table 11. The prevalence of disorders in dogs (no specific breeds) with or without an FCI approved pedigree with the assumption that a dog can have only one disorder. The disorders in this case are not limited to hereditary disorders, it can also be an infection or another disease. The disorders were already gone or controlled to the point where the dog did not notice it anymore at the moment the owner filled in the questionnaire. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number of dogs deviate the most from the expected numbers (residuals>|2| are considered significant).

	Pedigree	No pedigree	Total
Disorder	179 (-0.74)	171 (0.81)	*350*
No disorder	367 (0.54)	293 (-0.59)	*660*
Total	*546*	*464*	*1010*

Thus there seems to be no difference in prevalence of disorders in general in dogs with and without an FCI approved pedigree. However, even though there is no difference in prevalence of disorders, owners of non-pedigree dogs are more often moderately satisfied with their dog, whereas owners of pedigree dogs are more likely to buy a new dog of the same breed than owners with a dog without an FCI approved pedigree.

3.2.2 Questionnaire hereditary disorders

The records of the questionnaire on hereditary disorders, made available by Dier&Recht, have been analysed to see if there is a difference in pedigree dogs and look-a-likes concerning the prevalence of HD, ED and CA (and all disorders taken together for all breeds). Tables 12 and 13 show the observed numbers of HD, ED and CA, and all disorders, respectively, that Dier&Recht looked at taken together, with the Chi-square standardized residuals of the test in brackets. The records were dog-disorder combinations, where no distinction could be made between dogs. It was not shown whether a dog had one or more hereditary disorders. Therefore the assumption was made that all dogs could have a maximum of one hereditary disorder, overestimating the prevalence of hereditary disorders.

Table 12. The prevalence of HD, ED and CA in dogs (no specific breeds) with or without an FCI approved pedigree with the assumption that a dog can have only one hereditary disorder. Between brackets the residuals of the X2 test are found to show which number of dogs deviate the most from the expected numbers (residuals>|2| are considered significant).

	Pedigree	Look-a-like	Total
HD/ED/CA	56 (1.31)	23 (-1.59)	*79*
No	583 (-0.37)	412 (0.45)	*995*
Total	*639*	*435*	*1074*

The X^2value is 4.58 (df=1). The critical value of the X^2-distribution with 1 degree of freedom with a P-value of 0.05 is 3.84, though none of the standardized residuals are above |2|, the z-values are all ≥ |2.1|, with 1.96 being the threshold for significance. Thus, the look-a-likes have a lower risk of having HD, ED or CA than dogs with an FCI approved pedigree.

Table 13. The prevalence of the disorders mentioned in Appendix B in dogs (no specific breeds) with or without an FCI approved pedigree with the assumption that a dog can have only one disorder. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number of dogs deviate the most from the expected numbers (residuals>|2| are considered significant).

	Pedigree	Look-a-like	Total
Disorder	257 (1.60)	134 (-1.94)	*391*
No	382 (-1.21)	301 (1.46)	*683*
Total	*639*	*435*	*1074*

The same analysis on hereditary disorders in general produced similar results with a X^2value of 9.91 (df=1, with a critical value of 3.84). The z-values for all 4 cells are ≥ |3.1|, with 1.96 being the threshold for significance, meaning all values deviate from expectations. Look-a-likes have a lower risk of having the hereditary disorders mentioned in Appendix B than dogs with an FCI approved pedigree.

Looking into detail, the analysis of the prevalences of HD, ED and CA in German shepherds and Rottweilers is shown in Table 14. A Chi-square test gives reliable results when there are at least 5 records per combination. Because there were not enough records to analyse HD, ED and CA separately, and for German shepherds and Rottweilers separately, the data was summed to see if there is a difference in prevalence of HD, ED and CA together in pedigree dogs versus look-a-likes of German shepherds and Rottweilers.

Table 14. The prevalence of HD, ED and CA in German shepherds and Rottweilers with or without an FCI approved pedigree with the assumption that a dog can have only one hereditary disorder. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number of dogs deviate the most from the expected numbers.

	Pedigree	Look-a-like	Total
HD/ED/CA	19 (0.16)	6 (-0.27)	*25*
No HD/ED/CA	44 (-0.10)	17 (0.17)	*61*
Total	*63*	*23*	*86*

The X^2value is 0.14 (df=1, critical value=3.84). There appears to be no significant difference in the prevalence of HD, ED and CA in German shepherds and Rottweilers with or without a FCI approved pedigree.
The analysis of the prevalence of all disorders in German shepherds and Rottweilers with and without a FCI approved pedigree is shown in Tables 15 and 16, respectively.

Table 15. The prevalence of all disorders Dier&Recht looked at taken together in German shepherds with or without an FCI approved pedigree with the assumption that a dog can have only one hereditary disorder. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number of dogs deviate the most from the expected numbers.

	German Shepherd	Look-a-like	Total
Disorder	36 (0.34)	6 (-0.71)	*42*
No disorder	15 (-0.49)	6 (1.00)	*21*
Total	*51*	*12*	*63*

The X^2 value is 1.85 (df=1, critical value=3.84). There seems to be no significant difference in the prevalence of disorders in German shepherds and Rottweilers with or without a FCI approved pedigree.

Table 16. The prevalence of all disorders Dier&Recht looked at taken together in Rottweilers with or without an FCI approved pedigree with the assumption that a dog can have only one hereditary disorder. Between brackets the residuals of the $\mathbf{X}^2$ test are found to show which number of dogs deviate the most from the expected numbers.

	Rottweiler	No pedigree	Total
Disorder	6 (0.11)	5 (-0.11)	*11*
No disorder	6 (-0.11)	6 (0.11)	*12*
Total	*12*	*11*	*23*

The X^2 value is 0.05 (df=1, critical value=3.84). There appears to be no significant difference Rottweilers with and without a FCI approved pedigree, concerning the prevalence of all disorders mentioned in Appendix B.
The findings indicate that there is a significant difference between purebreds with and without (i.e. look-a-likes) a FCI approved pedigree in prevalence for HD, ED and CA taken together and for all hereditary disorders, with dogs with an FCI approved pedigree being at increased risk of having a hereditary disorder. When looking more specifically at German shepherds and Rottweilers, there is no significant difference between the prevalence of hereditary disorders in dogs with and without a FCI approved pedigree, but a lack of statistical power (read number of records) plays a role in this.

3.2.3 Database of HD in pedigree German shepherds

The database of HD in German shepherds, made available by the German shepherd association, includes records on pedigree German shepherds in the Netherlands and Germany. Data of dogs born from 1971 to January 2013 was available for analysis. In 1985, it became obligatory for all owners of a German shepherd with an FCI approved pedigree to register their dog in this database. The database shows whether a dog is screened for HD and what the score of the screening is. Dogs are screened from an age of 1 year old. This means that the usable data lies between year of birth 1985 and 2011. Figures 2 and 3 show the distributions of the screening scores in female and male German shepherds, respectively. The screening scores range from 1 to 5, with 1 being normal, 2 being almost normal, 3 being still permitted, 4 being moderately affected and 5 being severely affected. Scored abroad with a 1-3 in the database means that the dog was screened in a foreign country and had a score of 1, 2 or 3. In Germany and the Netherlands it is not allowed to breed with a pedigree dogs with a screening score of 4 or 5, and when a dog has a score of 3, it is strongly recommended to mate it with a dog with a score of 1. A distinction was made between male and female dogs to see if there is a difference in prevalence of HD between sexes, as different breeding schemes may be needed for the different sexes. Trends across time may reveal if current health and monitoring and breeding policies work in decreasing the prevalence of HD in German shepherds with an FCI approved pedigree in Germany and the Netherlands. To this purpose it is tested (using a Chi-square test) if there is a difference in German shepherds born in 1985 and in 2010 concerning the prevalence of HD. Table 17 shows the observed number of dogs with a HD score of ≤ 3 and the observed number of dogs with a HD score of ≥ 4 with the residuals of the test in brackets.

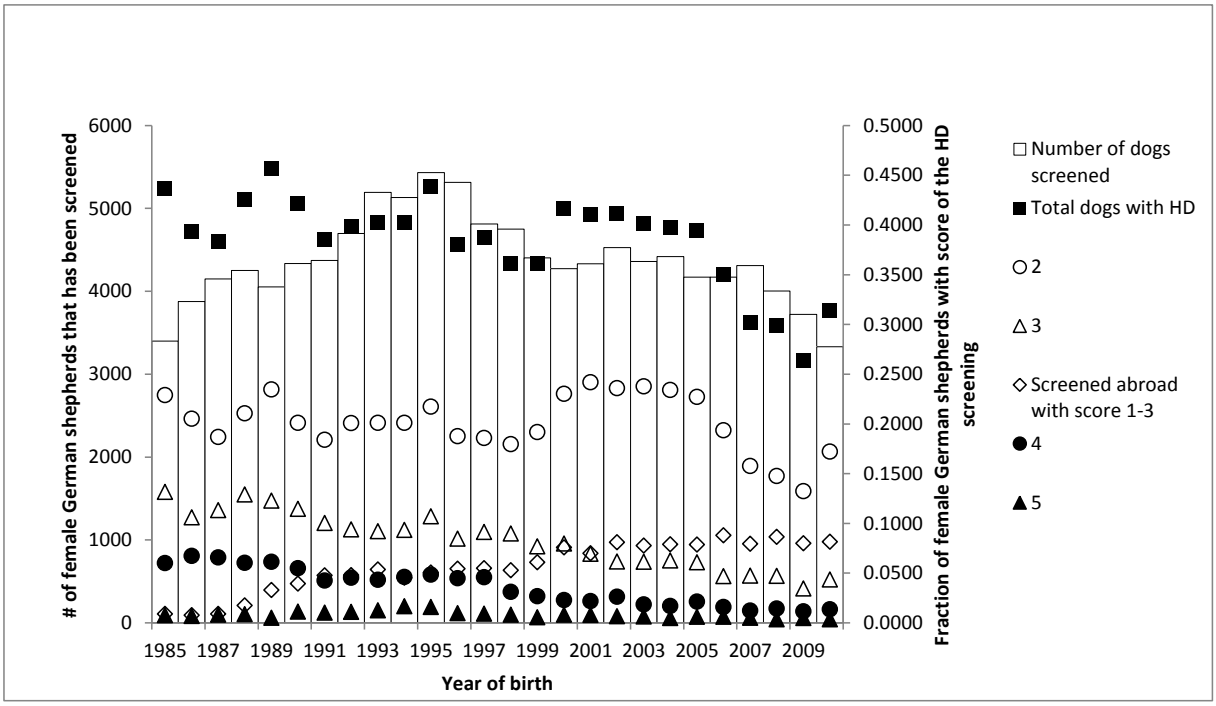

Figure 2. The distribution of the female pedigree German shepherds in the Netherlands and Germany that have been screened for HD. In this graph, 'Number of dogs screened' is the total number of female German shepherds that have been screened for HD arranged by year of birth. 'Total dogs with HD' is the fraction of dogs that has a score for HD of 2, 3, 4 or 5. 2 (almost normal) and 3 (still permitted) are mild forms of HD. 4 (medium) and 5 (severe) are worse forms of HD. Some dogs were tested in a foreign country and had a score of 1, 2 or 3.

A comparison of fractions was for both males and females for all six HD scores. Table 18 shows the number of dogs with 1985 or 2010 as a year of birth and the fraction of these dogs with a certain score for HD in 1985 and in 2010.

Table 17. The prevalence of in German shepherds (both male and female) with an FCI approved pedigree in 1985 and 2010 with a HD score of 1 to 3 or 4 to 5. Between brackets the residuals of the X^2 test are found to show which number of dogs deviate the most from the expected numbers.

	1985	2010	Total
HD score ≤ 3	6781 (-2.23)	5965 (2.45)	12746
HD score ≥ 4	533 (9.98)	102 (-10.96)	635
Total	7314	6067	13381

The X^2value is 230.57 (df=1, critical value=3.84). Scores for HD in German shepherds born in 1985 and in 2010 differ significantly, with dogs in 2010 having less severe HD than dogs born in 1985.

Table 18. The fractions of male and female German shepherds with an FCI approved pedigree that have been X-rayed for HD with year of birth 1985 and 2010.

	Female		Male	
	1985 (3399 dogs)	2010 (3330 dogs)	1985 (3915 dogs)	2010 (2727 dogs)
1	0.5631	0.6859	0.4174	0.7239
2	0.2289	0.1721	0.2930	0.1555
3	0.1315	0.0435	0.2074	0.0418
Abroad score 1-3	0.0088	0.0814	0.0049	0.0656
4	0.0600	0.0135	0.0710	0.0099
5	0.0076	0.0036	0.0064	0.0033

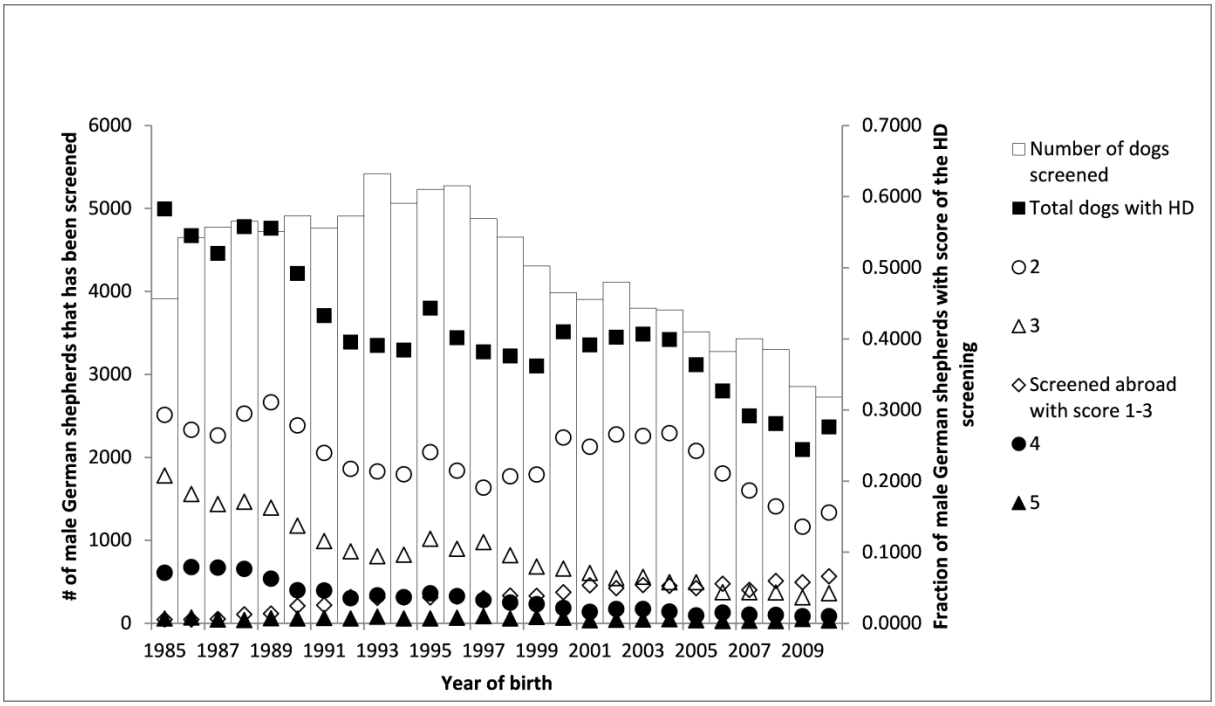

Figure 3. The distribution of the male pedigree German shepherds in the Netherlands and Germany that have been screened for HD. In this graph, 'Number of dogs screened' is the total number of male German shepherds that have been screened for HD arranged by year of birth. 'Total dogs with HD' is the fraction of dogs that has a score for HD of 2, 3, 4 or 5. 2 (almost normal) and 3 (still permitted) are mild forms of HD. 4 (medium) and 5 (severe) are worse forms of HD. Some dogs were tested in a foreign country and had a score of 1, 2 or 3.

The confidence intervals found with the comparison of fractions are shown in Table 19. These confidence intervals show that the number of dogs, both male and female, with a score 1 of (no HD) has significantly increased from 1985 to 2010, just as the number of dogs, both male and female with a score 6 (tested in a foreign country with a score of 1,2 or 3). The number of dogs, both male and female, with a score of 2, 3 and 4 has significantly decreased from 1985 to 2010, just as the number of females with a score of 5. Male dogs with a score of 5 do not significantly differ from 1985 to 2010.

Table 19. The confidence interval and possible significant difference for male and female German shepherds with an FCI approved pedigree X-rayed for HD with a certain score for HD. *CI=confidence interval. **increase/decrease/no

	Female		Male	
	95% CI*	**Significant difference ****	**95% CI**	**Significant difference ****
1	-0.1457, -0.0999	increase	-0.3293, -0.2837	increase
2	0.0377, 0.0759	decrease	0.1178, 0.1572	decrease
3	0.0747, 0.1013	decrease	0.1508, 0.1804	decrease
Abroad score 1-3	-0.0833, -0.0619	increase	-0.0702, -0.0512	increase
4	0.0376, 0.0554	decrease	0.0522, 0.0700	decrease
5	0.0004, 0.0076	decrease	-0.0002, 0.0064	no

3.3 Newly developed questionnaire

As a final source of information we developed a web-based questionnaire. After the draft version, on the 18th of November the questionnaire was made available online. In December the questionnaire was improved further over a period of two weeks The records of the questionnaire have been collected for analysis in March.

Dog owners reported, among other things, the type of dog they owned (pedigree, look-a-like, mixed breed) and if it suffered any (hereditary) disorder (see Table 20). A Chi-square test on the entries resulted in a X^2 value of 0.48 (df=2, with the critical value being 5.99). Thus, the observed numbers do not

significantly differ from the expected numbers. There was no evidence for some type of dogs being more at risk of disorders.

Table 20. The prevalence of all disorders looked at in the developed questionnaire in all dogs, divided in the groups pedigree (with an FCI approved pedigree), look-a-like (from 1 breed without an FCI approved pedigree) and mixed breed (multiple breeds in 1 dog) with the assumption that a dog can have only one hereditary disorder. Between brackets the residuals of the $X2$ test are found to show which number of dogs deviate the most from the expected numbers.

Owner reported	Pedigree	Look-a-like	Mixed breed	Total
Disorder	21 (-0.27)	3 (0.43)	5 (0.29)	29
No disorder	55 (0.17)	5 (-0.28)	10 (-0.19)	70
Total	76	8	15	99

Disorders can have different effects on the quality of life of the dog, and we also asked the owner whether the dog was affected by the two disorders that affected the dog the most, here concerning movability, pain and vitality. We also asked the overall movability and vitality of the dog, regardless whether the dog had a disorder. The quality of life overall and the veterinarian costs were examined as well. Outcomes were compared between pedigree dogs, look-a-likes and mixed breed dogs, both for owner reported disorders and veterinarian diagnosed disorder. The results are presented in Tables 21, 22 and 23, respectively and see Appendix D for details. In the tables, there is a significant effect on the traits looked at when the F-test value is larger than the critical value.

Table 21. The effect of Dog type (pedigree dog, look-a-like, mixed breed) on the factors listed in column one. For the disorders the dog were most affected by (maximum of 2) the quality of life and veterinary costs were reported.

	# dogs	Mean ± se	F-test Dog type	Critical value
Movability	195	8.7±0.12	1.87	3.09
Vitality	193	9.0±0.10	1.54	3.09
Disorder the dog is most affected by				
Movability	65	7.7±0.32	0.14	3.15
Pain	32	6.0±0.56	0.12	3.32
Vitality	60	7.8±0.31	0.53	3.18
Interaction with owner	29	5.8±0.56	0.08	3.35
Unaffected	61	8.5±0.23	0.97	3.18
Next disorder the dog is most affected by				
Movability	39	7.8±0.39	0.03	3.32
Pain	24	5.8±0.65	0.53	3.44
Vitality	37	7.9±0.40	0.02	3.32
Interaction with owner	18	5.5±0.72	1.36	3.63
Unaffected	34	8.3±0.37	0.49	3.32
Quality of life	109	9.0±0.13	0.02	3.09
Veterinarian costs	209	180.7±21.89	**3.22**	**3.04**

The ANOVA test shows that only the veterinarian costs are affected by a dog being a pedigree dog, a look-a-like or a mixed breed, with mixed breeds having higher veterinary costs than pedigree dogs and look-a-likes.
Table 22 shows that disorders (as reported by owners) affect especially the overall movability and vitality, with not having a disorder giving higher scores for the significant factors, but for the veterinarian costs (higher when the dog does have a disorder).

Table 22. The effect of disorders (here owner-reported) on the factors listed disorders of whether a dog is a pedigree dog, a look-a-like or a mixed breed dog.

	# dogs	Mean	F-test disorder	Critical value
Movability	197	8.7±0.11	**34.30**	**3.94**
Vitality	195	9.0±0.10	**23.59**	**3.94**
Disorder the dog is most affected by				
Movability	65	7.7±0.32	1.04	4.00
Pain	32	6.0±0.55	0.05	4.17
Vitality	60	7.8±0.30	**4.89**	**4.03**
Interaction with owner	29	5.8±0.55	0.26	4.20
Not affected	61	8.5±0.22	**5.11**	**4.00**
Next disorder the dog is most affected by				
Movability	39	7.8±0.38	0.79	4.17
Pain	24	5.8±0.60	4.22	4.28
Vitality	37	7.9±0.39	0.98	4.17
Interaction with owner	18	5.5±0.76	0.01	4.45
Not affected	34	8.3±0.34	**6.28**	**4.17**
Quality of life	109	9.0±0.12	**26.35**	**3.94**
Veterinarian costs	210	180.3±21.08	**20.24**	**3.89**

The ANOVA tests summarized in Table 23 show again that the overall movability, vitality and veterinarian costs are affected by veterinarian diagnosed disorders. The movability and vitality of a dog are higher when the dog has no veterinarian diagnosed disorder than when the dog does have a disorder, while the veterinarian costs are higher when a dog does have a veterinarian diagnosed disorder.

Together the findings indicate that being a pedigree dog, look-a-like of mixed breed does not affect movability, vitality, pain and the quality of life, while disorders, either reported by the owner, or diagnosed by the veterinarian do affect some of these traits.

Table 23. The effect of veterinarian diagnosed disorders on the movability, pain and vitality on the dog overall and for the maximum of two hereditary disorders the dog is most affected by, the quality of life and the veterinarian costs.

	# dogs	Mean	F-test disorder	Critical value
Movability	197	8.7±0.11	**23.62**	**3.94**
Vitality	195	9.0±0.10	**18.08**	**3.94**
Disorder the dog is most affected by				
Movability	65	7.7±0.31	1.61	4.00
Pain	32	6.0±0.53	2.85	4.17
Vitality	60	7.8±0.30	2.60	4.03
Interaction with owner	29	5.8±0.54	0.62	4.20
Not affected	61	8.5±0.23	0.54	4.00
Next disorder the dog is most affected by				
Movability	39	7.8±0.38	1.22	4.17
Pain	24	5.8±0.60	3.63	4.28
Vitality	37	7.9±0.38	1.40	4.17
Interaction with owner	18	5.5±0.76	0.01	4.45
Not affected	34	8.3±0.36	2.84	4.17
Quality of life	109	9.0±0.13	3.46	3.94
Veterinarian costs	210	180.3±21.53	**10.60**	**3.89**

3.4 Comparison of scientific literature and other databases

Next, the information from different sources was compared as to establish the prevalence of hereditary disorders in pedigree dogs and look-a-likes. All comparisons made are shown in Tables 24, 25 and 26 for HD, ED and CA respectively.

Table 24. Prevalences of HD in German shepherds and Rottweilers. The source (e.g. country, database, questionnaire) is shown, just as the number of dogs used in the study and the prevalence, divided in pedigree dog (a dog with an FCI approved pedigree), look-a-like (a dog without an FCI approved pedigree), both (both dogs with and without an FCI approved pedigree), or not determined (not specified whether the study was with pedigree dogs, look-a-likes or both). Values that share a letter are not significantly different (a is the lowest prevalence and h is the highest). To see if there are differences between breeds, the German shepherd and the Rottweiler were compared with each other. *ND=not determined. **This article did not mention the number of dogs.

		Prevalence (%)			
Source	**# dogs**	**Pedigree dog**	**Look-a-like**	**Both**	**ND***
German shepherds					
Belgium	1245	23[d]			
United Kingdom	ND	<50**			
Finland	25308	37[g]			
Missouri	149			32.9[fg]	
Canada	402			46.8[h]	
Questionnaire Dier&Recht	63	20 (#51)[bcdeg]	17 (#12)[bcdef]	19 (#63)[bcd]	
Database German shepherd	6057	29.7[e]			
Rottweilers					
Belgium	346	10[b]			
United Kingdom	ND	20-25**			
Finland	11746	32[f]			
Sweden	14693				16.6[c]
Missouri	99			35.4[efg]	
Canada	26			30.8[defgh]	
Questionnaire Dier&Recht	23	0 (#12)[a]	9 (#11)[abcd]	4 (#23)[ab]	

Table 24 reflects how look-a-likes and pedigree dogs do not differ in the prevalence of HD. German shepherds tend to have a higher prevalence of HD than Rottweilers and countries outside Europe have a higher prevalence of HD in both German shepherds and Rottweilers than countries within Europe.

From Table 25 it becomes apparent that look-a-likes and pedigree dogs have no significant difference in the prevalence of ED also. Rottweilers tend to have a higher prevalence for ED than German shepherd. There is no major difference in the prevalence of ED within and outside Europe. The German shepherds have a similar prevalence of ED in all countries evaluated, while for Rottweilers there is more fluctuation among countries, concerning the prevalence of ED.

Table 25. Prevalences of ED in German shepherds and Rottweilers. The source (e.g. country, database, questionnaire) is shown, just as the number of dogs used in the study and the prevalence, divided in pedigree dog (a dog with an FCI approved pedigree), look-a-like (a dog without an FCI approved pedigree), both (both dogs with and without an FCI approved pedigree), or not determined (not specified whether the study was with pedigree dogs, look-a-likes or both). Values that share a letter are not significantly different (a is the lowest prevalence and h is the highest). To see if there are differences between breeds, the German shepherd and the Rottweiler were compared with each other. *ND=not determined.

		Prevalence			
Source	**# dogs**	**Pedigree dog**	**Look-a-like**	**Both**	**ND***
German shepherds					
Belgium	130	12[a]			
Finland	5687	19[a]			
South Africa	24				20.8[ab]
United states of America	23088				19.5[a]
Questionnaire Dier&Recht	63	12 (#51)[a]	8 (#12)[a]	10 (#63)[a]	
Rottweilers					
Germany	2114	54.21[d]			
Belgium	135	33[b]			
Finland	8636	44[c]			
Sweden	11891				38.67[b]
South Africa	148				54.7[d]
United states of America	9407				40.9[b]
Questionnaire Dier&Recht	23	25 (#12)[abc]	18 (#11)[ab]	22 (#23)[ab]	

Table 26 illustrates how there is little information on cataract in German shepherds and Rottweilers. The information that is available suggests CA does not occur much in these breeds. For this reason, no conclusions can be made about the prevalence of CA in pedigree dogs and look-a-likes.

Table 26. Prevalences of CA in German shepherds and Rottweilers. The source (e.g. country, database, questionnaire) is shown, just as the number of dogs used in the study and the prevalence, divided in pedigree dog (a dog with an FCI approved pedigree), look-a-like (a dog without an FCI approved pedigree), or both (both dogs with and without an FCI approved pedigree). Values that share a letter are not significantly different (a is the lowest prevalence and h is the highest). To see if there are differences between breeds, the German shepherd and the Rottweiler were compared with each other.

		Prevalence		
Source	**# dogs**	**Pedigree dog**	**Look-a-like**	**Both**
German shepherds				
Questionnaire Dier&Recht	45	0 (#34)[a]	0 (#11)[a]	0 (#45)[a]
Rottweilers				
Questionnaire Dier&Recht	18	0 (#9)[a]	0 (#9)[a]	0 (#18)[a]

Together, the findings show that the prevalences of HD and ED differ between breeds and across countries. While the prevalence of HD is higher in German shepherds than in Rottweilers, the prevalence of ED is higher in Rottweilers than in German shepherds. This means that the prevalence of HD and ED cannot be generalised over all breeds and that somewhat similar hereditary disorders (e.g. HD and ED, both joint disorders), do not have similar prevalences.

4 Discussion

Relatively low genetic variation resulting from a restricted breeding population causes pedigree dogs to be more at risk of hereditary disorders (Rooney, 2009), but many aspects to this are yet unclear; like the size of such risks, if look-a-like dogs without a pedigree certificate are similarly at risk and if on-going breeding strategies to prevent hereditary disorders are effective. Here, we aimed to provide further insight in these matters. The primary objective of this study was to determine whether there is a difference in prevalence of hereditary disorders in pedigree dogs and look-a-likes, for which we performed a literature study, analysed existing databases and developed a questionnaire. Secondary aims were about assessing the current situation of (hereditary) disorders in pedigree dogs by comparing their (veterinary diagnosed, owner-reported) health status to that of look-a-likes and mixed breeds or observe changes over time.

In most studies, prevalences of hereditary disorders are estimated in an indirect way. Instead of assessing diagnosed cases of illness, screening outcomes are used to determine the proportion of individuals with unfavourable physical characteristics assumed to be early stage signs of a developing disorder. This means that prevalences reported here are useful for detecting effects (e.g. of dog subpopulations) and trends (e.g. across time following the introduction of breeding policies), but overestimate the absolute numbers of dogs that suffer from the physical consequences of a disorder. A disorder with an established strong genetic component in its aetiology is labelled here as a hereditary disorder, meaning the latter is not grounded on DNA sequence based confirmation of individual cases. Thus, proxies are used to estimate prevalences of hereditary disorders, overestimating the number of cases actually submitted to veterinarians, but this is the case in all groups (i.e. the pedigree dogs, look-a-likes and mixed breeds), which means that the relative prevalences are of use for answering research questions.

Genetically, certified pedigree dogs may be very similar to look-a-likes, but the latter may miss out on the preventive strategies against hereditary disorders that are in place for pedigree dogs. This raises the question if look-a-likes are differently at risk of hereditary disorders than pedigree dogs. Mixed breeds differ from purebred dogs genetically. There are no breed restrictions in the effective breeding population, making mixed breeds less prone to inbreeding and mixed breeds may benefit from hybrid vigor, resulting in healthier dogs (Bellumori, 2013). Here, questionnaires were used to estimate the prevalence of hereditary disorders in pedigree dogs and look-a-likes. Owners were asked to skip questions on their dog's health if it did not have a hereditary disorder, but obviously owners may not always be knowledgeable about the genetic background of a disorder. A point of attention regarding the questionnaires is that it for some data sets it was assumed that a dog could have a maximum of 1 disorder, with the risk of overestimating the prevalence of disorders as dog-disorder combinations were the units of records. Regarding the use of owner-reports, for owners it may be hard to determine the amount of pain a dog has due to a disorder, or whether the dog is impaired in any way by the disorder. However, such imperfections apply to both pedigree dogs and look-a-likes, so the comparison remains valid. During the study we learned that a given questionnaire may be filled in by owners that have strong opinions about pedigree dogs, the health and breed of their own dog and the value of the study. Such biases may in part be overcome by a high number of entries, but readily compromise small data set. With questionnaires it is hard to find a test population that represents the whole population, since mainly people that relate strongly to the subject fill in the questionnaire.

It has been suggested that 40% of all purebred dogs have a hereditary disorder (Gubbels and Scholten 2005), but the present study illustrates such exact statements are oversimplifying things. Prevalence estimates for hereditary disorders differ substantially between studies, for example depending on disorder types, dog breeds and dog populations (e.g. countries). Because of the variation between countries and between disorders, it is hard to make a general statement and defend it with credible arguments. Our findings on HD and ED in German Shepherd dogs and Rottweilers illustrate this. The present literature study in combination with that of Jutta Wirth (Prevalence of genetic disorders in dog breeds: a literature review), shows that in the Netherlands and Belgium the prevalence of HD in Germans Shepherd dogs is about 20% (Coopman et al. 2008, Lavrijsen et al. 2014). This estimate is based on the FCI diagnostic system, and compares with results from the US as based on the Orthopedic Foundation for Animals (OFA) method (estimated prevalence of 19%) and Pennsylvania Hip Improvement Program (PennHIP) method (25%), but deviates from findings in

Finland (33 to 46%) and Germany (9 to 13%). Thus, the prevalence of HD in Dutch Germans Shepherd dogs is about twice that or half that of other Germans Shepherd populations in Europe, which illustrates the pronounced variation. For HD in Dutch purebred Rottweilers, Lavrijsen et al. (2014) estimated a prevalence of about 10%, similar to estimates for Belgium Rottweilers (Coopman et al. 2008) but below those for Finish Rottweilers (i.e. ~30%, Mäki et al. 2001) and US populations (20 to 35%). For ED, prevalences are estimated at 7% and 14 % for Dutch German Shepherd dogs and Rottweilers, respectively (Lavrijsen et al. 2014). These estimates are substantially lower than those reported for other European countries or the US, being 19% (German Shepherds) and 33 to 65% (Rottweilers). The exception is the ~12% prevalence of ED in German Shepherd dogs in Belgium (Coopman et al. 2008).

Differences between breeds can be illustrated by the prevalence of HD in European German shepherds and Rottweilers, with prevalence estimates ranging between about 10% and near 50% in the former and between 10% and 35% in the latter. Mind that a possible breed difference of about 15% would be within the range of strongly varying estimates from different studies and countries. Similar findings emerged for ED, of which the prevalence in Europe varied from below 10 to about 20% in German shepherds and from about 15% to over 50% in Rottweilers. The variation in prevalence is not only the case for German shepherds and Rottweilers, but also for other breeds concerning HD, ED and humeral head osteochondrosis (Coopman *et al.*, 2008). HD and ED are mainly a problem in larger breeds, so it will be hard to find information on these disorders in, for instance, a Chihuahua. CA seems to be a minor problem in German shepherds and Rottweilers, while it occurs more in other breeds.

Clearly, differences in prevalence estimates across earlier studies are the result of many factors. Methodologically, the study populations sizes varied from many thousand to only hundred(s) and the latter studies seem of relatively limited value. Differences between studies regarding diagnostic systems and criteria, or age of test subjects, explain different outcomes, and it seems tricky to use reports from other countries to evaluate absolute prevalences, in the meaning of clinical cases, in the Netherlands. The difference in prevalence of disorders between countries may be a reflection of population specific genetics and/or implementation of country specific health monitoring-breeding strategies. In the near future, the prevalence of hereditary disorders may become more similar across countries due to the exchange of studs across countries. From the perspective of genetic diversity of a breeding population, it may be beneficial to import dogs from other countries to introduce new genes in the population. According to the Dutch Kennel Club (Raad van Beheer), 1926 dogs of different breeds were imported in 2013 (Raad van Beheer, 20102). Ideally, it is monitored if this introduction of new genes in the population affects the prevalence of hereditary disorders, as to determine follow-up actions. One way of monitoring health is via the database of veterinarians. A good health-disease database with information on both purebreds and look-a-likes would have been ideal for answering our questions, though collecting such data may be time consuming and costly. In the case of HD and ED, the costs to make an X-ray are different per veterinarian, but usually they are around 100 euro and the costs to grade the X-ray of the hips and elbows of a dog are 46 and 56 euro, respectively and only dogs with an FCI approved pedigree will be graded by Raad van Beheer (Raad van Beheer, 2010[4,5]). For many owners with a look-a-like dog this is not an amount of money they will pay for an X-ray if there is no direct reason to do so, especially if Raad van Beheer does not grade the X-rays.

Even though hereditary disorders are in part controlled by genes, there are other influences on the expression of genetic disorders. For example, Worth *et al.* (2012) found that New Zealand German shepherds and Rottweilers have a lower total hip score when born in the autumn months March and April. The scores were based on X-rays and evaluated by the New Zealand Veterinary Association. The lower hip score in the autumn was associated with the weather and possibly another seasonal factor that may have an environmental effect on the phenotype of the coxofemoral joint. In the United Kingdom, Lewis *et al.* (2013) examined fifteen dog breeds for the heritability of HD and ED. All dogs were screened for HD and for 5 breeds the dogs were also screened for ED and the radiographs were scored for the degree of HD and ED found. The pedigrees of all dogs were known and provided by the Kennel Clubs. With this information the heritability of HD and ED can be calculated (see Table, Lewis *et al.*, 2013).

Table 27. The heritability of HD and ED in German shepherds and Rottweilers in the United Kingdom.

Breed	Heritability for HD	Heritability for ED
German shepherd	0.35	0.18
Rottweiler	0.39	0.14

For breeders, it is important to know that with a low heritability it is harder to eliminate hereditary disorders by a good breeding scheme. Both breeds in the Table have a heritability of about 0.35 for HD and 0.15 for ED, which means that the expression of the trait can be readily changed across generations. Environmental factors determine the manifestation of a disorder, but selecting against an hereditary disorder omits the genetic cause of the disorder and decreases the prevalence and, in polygenic disorders, possibly the severity of the disorder.

The main objective of this study was to find a possible difference in the prevalence of hereditary disorders between pedigree dogs and look-a-likes. The scientific literature study was inconclusive regarding this. Available studies typically reported on pedigree dogs only or a combined group of pedigree dogs and look-a-likes, sometimes as compared to mixed breeds. The present data analyses show no significant difference in the prevalence of HD, ED and CA in German shepherd and Rottweiler pedigree dogs and look-a-likes, though this can be attribute to the small sample sizes. The prevalence of HD in German shepherds has significantly decreased from 1985 to 2010, showing that a good breeding plan can have a positive effect on the prevalence of hereditary disorders. For future studies on the difference in prevalence for hereditary disorders in pedigree dogs and look-a-likes it is important to have a usable health database that clearly identifies look-a-like dogs. Scientific studies have demonstrated how purebred dogs are more at risk of hereditary disorders than mixed breeds, though the risk varies significantly with the type of disorder. Findings on HD and ED in Rottweilers and German Shepherds illustrate the importance of dog breed in this. The data set of Dier&Recht (1,074 records) indicates pedigree dogs are significantly more at risk of (any) hereditary disorders than look-a-likes, with (maximum) estimates of respectively 40% and 30%. In other owner-reported data sets (i.e. those of the WUR) there were no indications that purebred dogs were less healthy than mixed breeds and / or look-a-likes. Owners of purebred dogs were even relatively satisfied with their dog. Biases in owner perceptions, like being enthusiastic about a certain breed, and survey participant group compositions seem to partly determine the outcomes of owner-reported surveys on dog health. Studies based on veterinarian conducted health measurements seem to generate different results regarding dog (hereditary) disorder prevalence than those based on owner reports, and where the former typically find increased health risk for purebreds compared to mixed breeds that latter may fail to register this. The validity of owner reports in recording dog health may be limited, and a veterinarian conducted dog health monitoring approach is needed for establishing to what degree purebreds and look-a-likes are differently at risk of hereditary disorders.

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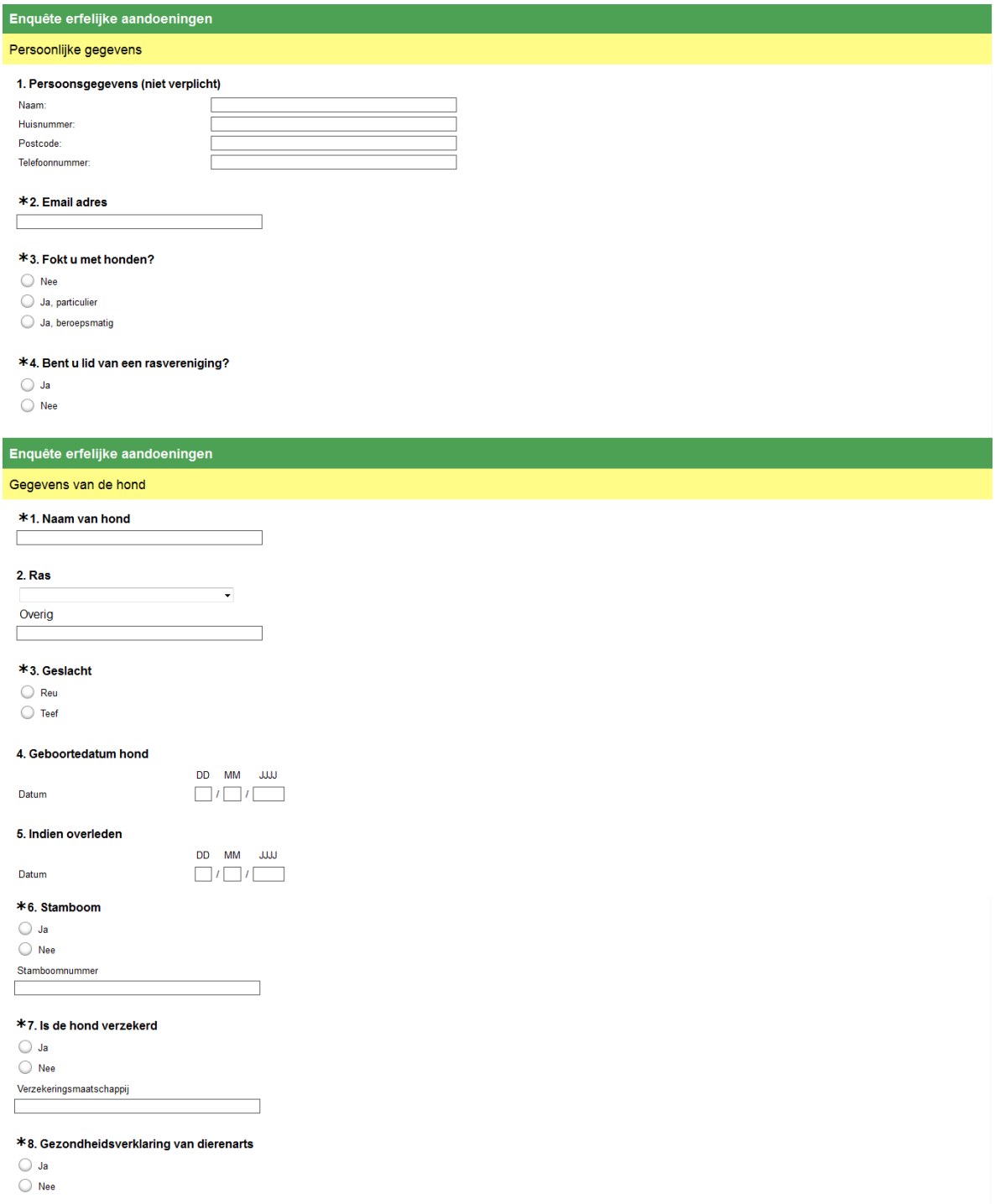
Appendices

Appendix A. Questionnaire of Dier&Recht

The questionnaire found on the site http://www.rashondenwijzer.nl. Because the site is Dutch and the questionnaire is meant for the Netherlands, the questions are in Dutch. The pictures of the questions have been made on 29-08-2013.



Enquête erfelijke aandoeningen

Persoonlijke gegevens

1. Persoonsgegevens (niet verplicht)

Naam:
Huisnummer:
Postcode:
Telefoonnummer:

***2. Email adres**

***3. Fokt u met honden?**

- Nee
- Ja, particulier
- Ja, beroepsmatig

***4. Bent u lid van een rasvereniging?**

- Ja
- Nee

Enquête erfelijke aandoeningen

Gegevens van de hond

***1. Naam van hond**

2. Ras

Overig

***3. Geslacht**

- Reu
- Teef

4. Geboortedatum hond

Datum DD / MM / JJJJ

5. Indien overleden

Datum DD / MM / JJJJ

***6. Stamboom**

- Ja
- Nee

Stamboomnummer

***7. Is de hond verzekerd**

- Ja
- Nee

Verzekeringsmaatschappij

***8. Gezondheidsverklaring van dierenarts**

- Ja
- Nee

Enquête erfelijke aandoeningen

Aankoop hond

***1. Hond is aangeschaft bij een**

- ○ Particuliere hondenfokker
- ○ Beroepsmatige hondenfokker

2. Fokker

	Provincie	Naam
Informatie		

Andere fokker

***3. Koopovereenkomst**

- ○ Ja
- ○ Nee

***4. Aankoopbedrag**

***5. Is de hond gefokt volgens het fokreglement van de rasvereniging?**

- ○ Ja
- ○ Nee
- ○ Geen idee

***6. Met welk doel heeft u de hond aangeschaft**

- ○ Huishond
- ○ Showhond
- ○ Waakhond
- ○ Jachthond

Anders

***7. Over welke punten bent u ingelicht door de verkoper**

- ☐ opvoeding
- ☐ verzorging
- ☐ karakter
- ☐ rastypische kenmerken
- ☐ erfelijke aandoeningen

Anders

Enquête erfelijke aandoeningen

Gezondheid van de hond

***1. Heeft uw hond gezondheidsproblemen**

- ○ Ja
- ○ Nee

2. Aandoeningen bij uw hond

	Soort	Naam	Ernst	Doodsoorzaak
Aandoening 1				
Aandoening 2				
Aandoening 3				
Aandoening 4				
Aandoening 5				
Aandoening 6				

Andere aandoening

***3. Dierenartskosten**

- ○ Tussen de 0 - 500 euro
- ○ Tussen de 500 - 1000 euro
- ○ Tussen de 1000 - 2000 euro
- ○ Meer dan 2000 euro

Enquête erfelijke aandoeningen

Gedragsgegevens van de hond

***1. Hoe omschrijft u het karakter van uw hond**

- [ ] Rustig
- [ ] Aanhankelijk
- [ ] Nerveus
- [ ] Fel
- [ ] Actief
- [ ] Grommerig
- [ ] Blafferig
- [ ] Bang
- [ ] Vrolijk
- [ ] Vriendelijk
- [ ] Beweeglijk

Anders

***2. Gehoorzaamheid**

- [ ] Zeer goed
- [ ] Goed
- [ ] Matig
- [ ] Slecht
- [ ] Zeer slecht

Enquête erfelijke aandoeningen

Afsluiting

***1. Bent u donateur van Dier&Recht?**

- ( ) Ja
- ( ) Nee

***2. Mogen we u benaderen met informatie over Dier&Recht?**

- ( ) Ja
- ( ) Nee

Appendix B. List of disorders Dier&Recht used in their questionnaire

In the questionnaire developed by Dier&Recht one question gives the option to select a disorder the dog is suffering from. The list of 180 options is given below.

Abnormal dwarf growth	Alopecia areata	Amyloidosis
Aorta stenosis	Arteria coronaria vasculitis	Artritis
Aseptic meningitis	Atopy	Atrium septum defect
Auto immune thyroiditis	Bacterial folliculitis	Basal cell carcinoma
Basset hound thrombopathy	Beagle pain syndrome	Blue merle syndrome
Brachycephal obstruction syndrome	Brain tumour	Calve-Legg-Perthes disease
Cataract	Cerebellar ataxia	Cerebellar hypoplasia
Ceroid lipofuscinosis	Cherry eye	Chondro dysplasia
Chronic hepatitis	Chronic sesamoiditis	Chronic superficial keratitis
Collie eye anomaly	Complement insufficiency	Congestive/dilative cardiomyopathy
Colour mutant alopecia	Contact allergy	Cornea dermoid
Craniomandibular osteopathy	Cryptorchidia	Cutaneous mucinosis
Cystinury	Dalmatian bronzing syndrome	Degenerative myelopathy
Demodicosis	Dermatomyositis	Dermoid sinus
Diabetes mellitus	Distichiasis	Dystocia
Ectodermal defect	Ectopic cilia	Ectopic urethra
Ectropion	Ehlers Danlos syndrome	Elbow dysplasia
Endothelial cornea dystrophy	Enostosis	Entropion
Epidermal dysplasia	Epilepsy	Epithelial cornea dystrophy
Exocrine pancreas insufficiency	Exophthalmos	Exposure keratopathy syndrome
Familial kidney disorder	Familial Shar Pei fever	Familial vasculopathy
Fibrosarcoma	Follicular dysplasia	Food hypersensitivity
Fucosidosis	German shepherd pyodermy	Glaucoma
Glandula sebacea tumour	Globoid cell leukodystrophy	Glycogen storage disease
Growth hormone responsive dermatitis	Heart base tumour	Haemangioma sarcoma
Hemi vertebrae hemophilia	Hereditary deafness	Hereditary Leonberger polyneuropathy
Hereditary necrotising myelopathy	Hereditary neutropeny	Hernia nuclei pulposi
Hernia umbilicalis	Hip dysplasia	Histiocytar sarcoma
Histiocytar ulcerative colitis	Histiocytoma	Hydrocephalus
Hyperadrenocorticism	Hyperlipoproteinaemia	Hypertrophic osteodystrophy
Hypo/demyelinisation	Hypoadrenocorticism	Hypotrichosis
Ichthyosis	Immune mediated haemolytic anemia	Immune mediated trombocytopeny
Insulinoma	Intertrigo	Keratoconjunctivitis sicca
L2-hydroxyglutaric aciduria	Labrador retriever myopathy	Larynx paralysis
Lens luxation	Lissencephaly	Loose processus coronoideus
Lupus erythematosis	Lymphedema	Lymphoma
Mast cell tumour	Masticatory nyositis	Mega oesophagus
Melanoma	Microphthalmos	Mitralis valve dysplasia
Multidrug resistance gen 1	Myasthenia gravis	Myxomatous mitralis valve
Narcolepsy	Necrotising meningoencephalitis	Neuroaxonal dystrophy
Nodular dermatofibrosis	Open fontanel	Optic nerve hypoplasia
Osteochondritis dissecans	Osteosarcoma	Palatoschisis

Palmoplantar hyperkeratosis	Pancreatitis	Patella luxation
Pemphigus erythematosis	Pemphigus foliaceus	Peripheral neuropathy
Persisting Müllers tube	Persisting ductus arteriosis	Persisting hyperplastic tunica vasculosa lentis
Persisting pupillary membranes	Persisting right arotabow	Phosphofructokinase deficiency
Portosystemic shunt	Primary acanthosis nigricans	Primary hypothyreoidy
Primary idiopathic sereborroe	Primary secretory otitis media	Progressive ataxia
Progressive retina atrophy	Protein losing enteropathy	Psoriasiformlichenoid dermatosis
Pulmonalis stenosis	Puppy paralysis	Pyruvate kinase deficiency
Retina dysplasia	Sebaceous adenitis	Selective IgA deficiency
Shaker dog syndrome	Sick sinus syndrome	Skinfold dermatitis
Spina bifida	Spondylosis	Squamous cell carcinoma
Stomach dilative volvulus	Stomatocytosis	Subarotastenosis
Syndrome of Fanconi	Syringomyely	Tetralogy of Fallot
Trachea collaps	Tracheahypoplasia	Tricuspidalis dysplasia
Urolithiasis	Uveodermatologic syndrome	Ventricle septum defect
Vertebral stenosis	Vitamin A responsive dermatosis	Vitiligo
Von Willebrands disease	Wobbler syndrome	Wolff-Parkinson-White syndrome
X-chromosome bound muscle dystrophy	Zinc responsive dermatosis	

Appendix C. Developed questionnaire

This questionnaire has been developed to assess the prevalence of hereditary disorders in different breeds. It also looks at the perception of dog breeders on hereditary disorders and the rules and laws they need to abide concerning these disorders. Below the introduction and the questions for the dog owners are found. The questions for the breeders are not relevant for this study, so they are not shown. The pictures of the questions have been made on 28-12-2013.

Gerichte vragen voor fokkers van Duitse Herdershonden of Rottweilers komen pas later beschikbaar.

Welkom bij de enquête over erfelijke aandoeningen bij honden. De enquête inventariseert mogelijke verschillen in erfelijke aandoeningen (aantallen) bij rashonden en look-a-likes. Voor specifieke erfelijke aandoeningen wordt gekeken hoe deze verhoudingsgewijs worden gerapporteerd door eigenaren van rashonden en look-a-likes. Ook wordt de mening (perceptie) van fokkers over erfelijke aandoeningen gevraagd. Informatie over de percepties van hondenfokkers, hun fokkerij-strategieën en aantallen erfelijke gebreken, draagt bij aan initiatieven om erfelijke aandoeningen te verminderen.

De antwoorden worden anoniem verwerkt en zijn niet beschikbaar voor andere doeleinden dan het huidige onderzoek.

Wij danken u vriendelijk voor uw interesse en vragen u de enquête zo volledig mogelijk in te vullen.

1. U vult deze enquête in als ..
*

- ○ Hondeneigenaar

U bent nu aangekomen bij de vragen specifiek voor eigenaren. De vragen hebben betrekking op één hond en u kunt de vragenlijst nogmaals starten en invullen als u meerere honden bezit.

2. Wat is uw achternaam?

3. Wat is uw geslacht?

- ○ Man
- ○ Vrouw

4.

Wat is de naam van uw hond?

5. Welk ras of wat voor kruising is uw hond (bij ras/kruising onbekend: Onbekend)?

6. In welke rasgroep past uw hond? Zie eventueel onderstaande afbeeldingen en voor deze en extra informatie ga naar de site van de Raad van Beheer (klik hier).

FCI Groep 1 - Herdershonden en Veedrijvers

FCI Groep 2 - Pinschers, Schnauzers, Molossers en Sennenhonden

FCI Groep 3 - Terriers

FCI Groep 4 - Dashonden

FCI Groep 5 - Spitsen en oertypen

FCI Groep 6 - Lopende honden en zweethonden

FCI Groep 7 - Voorstaande honden

FCI Groep 8 - Retrievers, Spaniels en Waterhonden

FCI Groep 9 - Gezelschapshonden

FCI Groep 10 - Windhonden

- ◯ Herdershonden en Veedrijvers
- ◯ Pinschers, Schnauzers, Molossers en Sennenhonden
- ◯ Terriers
- ◯ Dashonden
- ◯ Spitsen en oertypen
- ◯ Lopende honden en zweethonden
- ◯ Voorstaande honden
- ◯ Retrievers, Spaniels en Waterhonden
- ◯ Gezelschapshonden
- ◯ Windhonden

7. Heeft uw hond een registratie in het Nederlands Honden Stamboek (NHSB), en daarmee een FCI erkende stamboom?

- ○ Ja, NHSB stamboomnummer (geef zo mogelijk het nummer)
- ○ Nee

8. Geeft u eventueel het chipnummer van de hond (niet noodzakelijk).

9. Wat is het geboortejaar van uw hond?

10. Wat is het geslacht van uw hond?

	Intact	Gecastreerd/gesteriliseerd
Teef	○	○
Reu	○	○

11. Wat is de herkomst van de hond?

- ○ Fokker met honden met stamboom
- ○ Fokker met honden zonder stamboom
- ○ Eigen fok
- ○ Asiel
- ○ Via herplaatsingsbemiddeling
- ○ Via familie of vrienden of bekenden
- ○ Anders, namelijk:

12. Hoe oud was de hond toen deze bij u in huis kwam?

○ Jonger dan 1 jaar	○ 4 jaar	○ 8 jaar
○ 1 jaar	○ 5 jaar	○ 9 jaar
○ 2 jaar	○ 6 jaar	○ 10 jaar
○ 3 jaar	○ 7 jaar	○ Ouder dan 10 jaar

13. Hoe typeert u de hond?
Look-a-likes zijn honden met alle raskenmerken, maar zonder stamboom. Kruising is hier een combinatie van maximaal twee rassen.

- rashond
- look-a-like (hond met alle raskenmerken, maar zonder stamboom)
- kruising van twee rassen
- kruising van meer dan twee rassen

14. Bezoekt u met uw hond de dierenarts?

- Nee
- Ja, alleen voor vaccinaties
- Ja, om de volgende reden(en): (graag ook aangeven hoe vaak u naar de dierenarts gaat met uw hond)

15. Wat zijn de jaarlijkse dierenartskosten (ongeveer) voor uw hond?

16. Heeft uw hond gezondheidsproblemen in een van onderstaande categorieën? Zo ja, kan u de ziekte benoemen? Is deze gediagnosticeerd door de dierenarts/specialist? Wanneer uw hond geen erfelijke aandoeningen heeft, kunnen deze en vragen 18 t/m 23 worden overgeslagen.

	Ja	Nee	Naam	Gediagnosticeerd door dierenarts/specialist	Niet gediagnosticeerd
Ademhalingsstelsel					
Afweersysteem					
Bloed					
Geslachtsorganen					
Hart- en bloedvaten					
Hormoonsysteem					
Huid en haar					
Kanker					
Lever en nieren					
Ogen en oren					
Skelet					
Spier- en zenuwstelsel					
Spijsvertering					
Stofwisseling					
Voortplanting					

17. Wat voor cijfer (van 1 tot 10) geeft u voor:

De bewegelijkheid van uw hond? (hoe hoger het cijfer, hoe bewegelijker uw hond)

1

De vitaliteit (levenskracht) van uw hond? (hoe hoger het cijfer, hoe vitaler uw hond)

1

18. In hoeverre (op een schaal van 1 tot 10) denkt u dat het onderstaande bij uw hond wordt beïnvloed door de eerdergenoemde erfelijke aandoening, of twee meest ernstige aandoeningen?

De bewegelijkheid mbt aandoening 1? (hoe hoger het cijfer, hoe bewegelijker uw hond)

1

De bewegelijkheid mbt aandoening 2?

1

De pijn mbt aandoening 1? (hoe hoger het cijfer, hoe meer pijn)

1

De pijn mbt aandoening 2?

1

De vitaliteit mbt aandoening 1? (hoe hoger het cijfer, hoe vitaler uw hond)

1

De vitaliteit mbt aandoening 2?

1

19. In hoeverre wordt uw omgang en interactie met de hond negatief beïnvloed door bovengenoemde aandoening(en)?
Hoe hoger het cijfer (op een schaal van 1 tot 10) des te sterker de negatieve effecten.

Mbt aandoening 1

1

Mbt aandoening 2

1

20. In hoeverre kan uw hond, met betrekking tot de aandoening(en), ongehinderd doen wat hij wil doen?
Hoe hoger het cijfer, hoe vrijer de hond (10 = ongehinderd alles kunnen doen).

Mbt aandoening 1

1

Mbt aandoening 2

1

21. Welk cijfer (van 1 tot 10) geeft u de kwaliteit van leven van uw hond?
Hoe hoger het cijfer, hoe beter de kwaliteit van leven.

1

22. Wat voor invloed heeft (hebben) de aandoening(en) van uw hond op

	Zeer negatief	Negatief	Neutraal/geen invloed	Positief	Zeer positief
Uw gezin	○	○	○	○	○
De band met uw hond	○	○	○	○	○

23. Heeft u verder nog vragen of opmerkingen?

De vragenlijst voor hondeneigenaren is nu klaar. **Belangrijk**: alleen door naar de volgende pagina te gaan slaat u de antwoorden op! Eigenaren met een tweede hond kunnen op de volgende pagina in de webbrowser, via vorige pagina, de enquête aanpassen en nogmaals opslaan.

Hartelijk dank voor uw medewerking!

Appendix D. The mean numbers of the factors affecting the dogs welfare

In this appendix the mean numbers of movability, vitality, being affected by the disorder, quality of life and veterinarian costs for pedigree dogs, look-a-likes, mixed breeds, dogs having and not having an owner reported disorder and dogs having and not having a veterinarian diagnosed disorder.

Table 28. The mean veterinarian costs for pedigree dogs, look-a-likes and mixed breeds.

Mean	Pedigree dog	Look-a-like	Mixed breed
Veterinarian costs	160.5	154.0	328.3

Table 29. The mean score for factors affected by either having an owner reported disorder or not.

Mean	Owner reported disorder	No owner reported disorder
Movability	7.207	8.994
Vitality	7.852	9.225
Disorder dog is most affected by		
Vitality	6.909	8.282
Not affected	7.826	8.872
Next disorder dog is most affected by		
Not affected	7.231	9.000
Quality of life	7.870	9.345
Veterinarian costs	427.8	144.0

Table 30. The mean score for factors affected by either having a veterinarian diagnosed disorder or not.

Mean	Veterinarian diagnosed disorder	No veterinarian diagnosed disorder
Movability	6.786	8.880
Vitality	7.462	9.148
Veterinarian costs	453.8	162.3