Genetic and phenotypic analysis of elbow dysplasia in four large Swedish dog breeds – an evaluation of the screening programme and clinical symptoms

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Genetic and phenotypic analysis of elbow dysplasia in four large Swedish dog breeds – an evaluation of the screening programme and clinical symptoms

Genetisk och fenotypisk analys av armbågsdysplasi hos fyra storvuxna svenska hundrar – en evaluering av hälsoprogrammet och kliniska besvär

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Elbow dysplasia (ED) is a common hereditary disease in dogs. Elbow dysplasia develops during the critical growth period between 4-12 months of age in large breed dogs and causes pain and lameness in the front limbs. In worst case it can lead to euthanasia. Therefore, a control programme (implemented different years for different breeds) through the Swedish Kennel Club is applied for ED to improve the health of affected breeds. However, few studies have investigated the association between screening results and clinical symptoms. The aim of this thesis was therefore to investigate if the screening results are well associated with the clinical symptoms. Furthermore, this thesis will investigate how many individuals with severe clinical symptoms that do not undergo the official screening in the control programme at the age of 12 months or older.

Four breeds with high prevalence of ED were included in the study; Rottweilers, German Shepherd dogs, Labrador retrievers and Golden retrievers. Data from the official ED screening programme from the Swedish Kennel Club (SKK) database, as well as data from elbow related insurance claims from the insurance company Agria. Approximately 54 000 dogs had an official screening results, and 574 observations also had insurance claims for elbow related issues.

Results showed that most of the dogs with an insurance claim were younger than the official screening age of 12 months. It was also shown that dogs with insurance claims generally had higher scores for ED compared with the general screened population. However, there was a high proportion of dogs with a normal screening result (ED score = 0) that still had an insurance claim, which was unexpected. The heritability for ED was between 0.13-0.20. Males, compared to females, had higher regression coefficients for inbreeding coefficient, weight at screening and age at screening related to ED.

The conclusions are that the screening results seem to be a valuable indication of later ED-related clinical issues. However, a larger proportion of dogs than expected with an insurance claim had an official screening score of 0 (normal). The diagnosis fragmented coronoid process (FCP) had highest frequency in those dogs. Perhaps a second projection in the screening program could be beneficial in finding these cases. Also, the current routine control used today could perhaps be improved by including regressions nested within sex, litter effect and panellist.

The results from this thesis should be interpreted carefully since the number of observations were few. Also, there was no guarantee that animals not included in the merged data were healthy since they could have been insured in another insurance company. However, Agria has the largest market share among all the insurance companies for pets. Moreover, more research is needed with a more complete data to validate the results from this thesis.

Keywords: Elbow dysplasia, large breed dogs, FCP, osteochondritis dissecans, ununited anconeal process, elbow incongruity
Armbågsdysplasi (ED) är en vanlig ärftlig sjukdom hos hundar. Armbågsdysplasi utvecklas under den kritiska tillväxtperioden mellan 4–12 månaders ålder i storvuxna raser ochorsakar smärta och hälsa, men kan i värsta fall leda till avlivning. Ett hälso program för ED introducerades, olika årtal för olika raser, därför inom Svenska Kennelklubben för att förbättra hälsan inom drabbade raser. Det finns få studier som undersöker kopplingen mellan screening resultaten med kliniska symptom. Syftet med den här studien är därför att undersöka om screening resultaten är väl associerade med kliniska symptom samt även att undersöka hur många individer med grava symptom som inte genomgår officiell röntgen.

Fyra raser med hög prevalens av ED var inkluderade i studien; rottweilers, schäfer, labrador retrievers och golden retrievers. Data från den officiella armbågsscreeningen från Svenska Kennelklubbens (SKK) databas, samt data från armbågsrelaterade försäkringsärenden från försäkringsbolaget Agria användes. Ungefär 54 000 hundar hade officiellt röntgenresultat och 574 observationer hade även ett försäkringsärende kopplat till armbågsrelaterade besvär.

Resultaten påvisade att de flesta av hundarna med ett försäkringsärende kopplat till ED var yngre än den officiella screening åldern 12 månader. Resultaten visade även att hundar med ett försäkringsärende generellt hade högre frekvens av ED än den generella screenade populationen. Därtöver påvisades en oväntad hög andel av hundar med ett officiellt screening resultat på 0 (normal) som ändå hade ett försäkringsärende kopplat till ED. Arvbarheten låg mellan 0.13-0.20. Hanar, i jämförelse med tikar, hade högre regressionskoefficienter när det kom till inavelsgrad, vikt och ålder vid screening, kopplat till ED.

Slutsatserna är att screening resultaten verkar vara en värdefull indikation på framtida ED relaterade besvär. Däremot fanns en oväntad hög frekvens av hundar med ett försäkringsärende trots ett screening resultat på 0. Av dessa individer så var fragmenterad coronoid process (FCP) den vanligast förekommande diagnosen. Eventuellt skulle en extra projektion i hälso programmet underlätta att upptäcka dessa fall. Den nuvarande avelsvärderingen skulle eventuellt kunna förbättras genom att inkludera regressionerna, nästade inom kön, kulleffekt och även avläsare.

Resultaten borde tolkas med försiktighet eftersom det var få observationer. Dessutom finns ingen garanti att hundar som inte matchade i det hopslagna datasetet var friska individer eftersom de kan vara försäkrade i ett annat försäkringsbolag. Ytterligare studier skulle därmed behövas där mer komplett data finns tillgängligt för analys.

Nyckelord: Armbågsdysplasi, storvuxna hundraser, FCP, OCD, UAP, EI
Är hälsoprogram för armbågsdysplasi hos hund starkt kopplat till framtida kliniska besvär?

Hunden har länge ansetts vara människans bästa vän där den har en stor plats inom familjen. I många fall lever hunden ett friskt och långt liv, men i olyckliga fall kan man tvingas ta farväl av sin fyrbenta vän allt för tidigt. Armbågsdysplasi hos hund är en vanligt förekommande sjukdom som tyvärr oftast leder till mycket smärta och lidande för hunden och inte sällan slutar det i kostsamma operationer med livslång rehabilitering som följd, eller i värsta fall avlivning. För att komma till rätta med problemet har så kallade hälsoprogram införts för raser där armbågsdysplasi är vanlig förekommande. Men är resultaten från hälsoprogrammet starkt kopplat till eventuella framtida kliniska besvär?


Majoriteten av hundarna med ett försäkringsärende var dessutom yngre än 12 månader, vilket är den tidigaste åldern för hälsoprogrammet, vilket innebär att dessa hundar oftast går förlorade vilket kan påverka avelsvärden för individen samt närbesläktade hundar.

Fler studier behövs för att validera dessa resultat eftersom studien utfördes på relativt få hundar.
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### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLUP</td>
<td>Best linear unbiased prediction</td>
</tr>
<tr>
<td>CT</td>
<td>Computerised tomography</td>
</tr>
<tr>
<td>EBV</td>
<td>Estimated breeding value</td>
</tr>
<tr>
<td>ED</td>
<td>Elbow dysplasia</td>
</tr>
<tr>
<td>EI</td>
<td>Elbow incongruity</td>
</tr>
<tr>
<td>FCP</td>
<td>Fragmented coronoid process</td>
</tr>
<tr>
<td>GR</td>
<td>Golden Retriever</td>
</tr>
<tr>
<td>GSD</td>
<td>German Shepherd dog</td>
</tr>
<tr>
<td>IEWG</td>
<td>International Elbow Working Group</td>
</tr>
<tr>
<td>LR</td>
<td>Labrador Retriever</td>
</tr>
<tr>
<td>MCD</td>
<td>Medial coronoid disease</td>
</tr>
<tr>
<td>MCPD</td>
<td>Medial coronoid process disease</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>OA</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>OCD</td>
<td>Osteochondritis dissecans</td>
</tr>
<tr>
<td>OCS</td>
<td>Optimum contribution selection</td>
</tr>
<tr>
<td>RW</td>
<td>Rottweiler</td>
</tr>
<tr>
<td>SKK</td>
<td>Swedish Kennel Club</td>
</tr>
<tr>
<td>UAP</td>
<td>Ununited anconeal process</td>
</tr>
</tbody>
</table>
Elbow dysplasia (ED) is one of the most common hereditary diseases in the domestic dog (*Canis familiaris*) (Cook & Cook, 2009; Janutta et al., 2006; Malm, 2010; Malm et al., 2007; Mäki, 2004). The prevalence of ED estimated in Rottweilers (RW), German Shepherd dogs (GSD), Labrador Retriever (LR) and Golden Retriever (GR) in different countries can be seen in table 1.

**Table 1. Breed prevalence (in % of screened population) of ED**

<table>
<thead>
<tr>
<th>Breed</th>
<th>Sweden¹</th>
<th>USA²</th>
<th>Belgium³</th>
<th>Finland⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rottweiler</td>
<td>24</td>
<td>39</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>German Shepherd dog</td>
<td>17</td>
<td>19</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>8</td>
<td>10</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>16</td>
<td>12</td>
<td>18</td>
<td>20</td>
</tr>
</tbody>
</table>


Elbow dysplasia is a collective term for multiple primary lesions (Beuing et al., 2000; Demko & McLaughlin, 2005; Hazelwinkel & Nap, 2009; How, 2018a; Moores et al., 2008). According to the definition by the International Elbow Working Group (IEWG), the primary lesions included are ununited anconeal process (UAP), fragmented coronoid process (FCP), osteochondritis dissecans (OCD) and elbow incongruity (EI) (Cook & Cook, 2009; Hazelwinkel & Nap, 2009; How, 2018a; Malm et al., 2007; Michelsen, 2013; Moores et al., 2008; Temwichitr et al., 2010).

Elbow dysplasia can lead to pain, lameness in the front limbs and loss of function in the locomotor system (Janutta et al., 2006; Malm, 2010; Moores et al., 2008; O’Neill et al., 2020). Even a mild grade of ED can cause limping and lameness due to the high amount of bodyweight put on the elbows (Beuing et al., 2000; Mäki, 2004). The symptoms may occur as early as 4-12 months of age (Bedford, 1994; Guthrie & Pidduk, 1990; Michelsen, 2013; Mäki, 2004) but can in some cases occur later in life (Michelsen, 2013). Moreover, the symptoms are likely to gradually
increase with age due to the development of secondary lesions such as osteoarthritis (OA) even if surgery has been done (Guthrie & Pidduk, 1990).

The scoring of ED follows a protocol from IEWG in most European countries, including Sweden (Beuing et al., 2010; Malm, 2010). The scale used for scoring goes from 0-3 where grade 0 is unaffected/normal and 3 is severe arthrosis (Audell, 1990; Hazelwinkel, 2018) (table 2).

Table 2. Definition of the different ED grading scores within IEWG (Audell, 1990; Hazelwinkel, 2018)

<table>
<thead>
<tr>
<th>ED grade</th>
<th>Description</th>
<th>Radiological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal elbow joint</td>
<td>No evidence of arthrosis or incongruity</td>
</tr>
<tr>
<td>1</td>
<td>Mild arthrosis</td>
<td>Presence of osteophytes &lt;2mm</td>
</tr>
<tr>
<td>2</td>
<td>Moderate arthrosis</td>
<td>Presence of osteophytes 2-5mm</td>
</tr>
<tr>
<td>3</td>
<td>Severe arthrosis</td>
<td>Presence of osteophytes &gt;5mm</td>
</tr>
</tbody>
</table>

Elbow dysplasia can cause a lot of distress for both dog and owner (Malm, 2010). Furthermore, some of the breeds with the highest prevalence are working dog breeds, making it more difficult to find healthy dogs for service within e.g. police and military (Mäki, 2004).

Even though radiographical assessment is the most common way to diagnose (Cook & Cook, 2009) by discovering the presence of secondary lesions such as Osteoarthritis (OA) (Beuing et al., 2000) and genetically evaluate ED throughout the world (Hedhammar, 2007; Hedhammar & Malm, 2008), there are few studies that have investigated the association between screening result and clinical symptoms (Malm, 2010). Genetic evaluation becomes more difficult by the fact that environmental factors also affect the development of ED (Mäki, 2004), e.g. weight, age, overfeeding and hormones (How, 2018a; Kealy et al., 2000).

Screening programmes have been implemented for several breeds, to aid breeders in selecting against ED. A screenings programme is a control programme for breeds with breed specific diseases (Svenska Kennelklubben, 2014a). Screening programmes are usually requested by the breed clubs if the breed is overrepresented in some genetic diseases, such as ED. A screening programme could be mandatory implying screening of all animals prior to breeding, or voluntary. In Sweden, all results from official elbow screening are recorded in the Swedish Kennel Club (SKK) database and made public through the SKK web services.

The screening for ED is based on radiographical assessment, where primary lesions are seldom seen (Moores et al., 2008). In Sweden, only one projection (flexed lateral position) is taken for the evaluation (Svenska Kennelklubben, 2020).
The earliest age when a dog can be screened officially is 12 months (Svenska Kennelklubben, 2014b), but many dogs with severe symptoms go through surgery for ED before that (Hedhammar & Malm, 2008). This could lead to loss of information about these individuals, which in turn could lead to biased evaluation of the breeding population.

The aim of this thesis was to investigate if the screening results for ED are well associated with clinical symptoms of ED. Furthermore, this thesis will investigate how many individuals with severe symptoms that do not undergo official screening.
2. Literature review

2.1. Breeding

Animal breeding is based on selective breeding, which means that only chosen animals that have passed certain criteria are used as parents (Oldenbroek & van der Waaij, 2014). In contrast, natural selection occurs in wild populations and is not controlled by humans. The use of selective breeding will genetically improve the population in a certain direction based on a predefined breeding goal. This means that the offspring will hopefully be better on average than its’ parents (Oldenbroek & van der Waaij, 2014). This is achievable due to the genetic variation within a species and the domestic dog has a large genetic variation (Ostrander & Ruvinsky, 2012) which is reflected in the large variation in size, behaviour and conformation (Oldenbroek & van der Waaij, 2014).

Because different dog breeds have been bred for different traits, there is a large genetic diversity between breeds (Ostrander & Ruvinsky, 2012), but at the same time reduced genetic variation within breeds (Leroy, 2011; Zajc et al., 1997). The reduced genetic variation within breeds can lead to increased risk for complications related to heritable diseases (Oldenbroek & van der Waaij, 2014) due to inbreeding. To date, there are more than 700 known heritable diseases in dogs. Some are controlled by single genes, but most are quantitative and thus controlled by many genes in combination with environmental factors (OMIA, 2020).

Contrary to livestock breeding, which is mainly based on economically important traits, the breeding goal for dogs are mainly based on morphology, behaviour and health (Malm, 2010). Dog breeding is mainly done as a hobby, whereas livestock breeding nowadays is controlled by a large industry (Oldenbroek & van der Waaij, 2014). Even so, dog breeders need to follow some regulations, both international and national. In Sweden, regulations that concern general rules and animal welfare are given by the Swedish Board of Agriculture (Jordbruksverket, 2019). Breeders that are members of SKK must also follow the regulations and breeding policy provided from SKK (Svenska Kennelklubben, 2019).
2.2. Hereditary aspects of elbow dysplasia

There is variation in incidence- and severity level for ED between and within breeds, and the proportion and severity of dysplastic offspring has been found to relate to the severity of ED in the parents (Swenson et al., 1997a; Swenson et al., 1997b). Several studies have shown that elbow dysplasia is a polygenic trait (Lau, 2018, Swenson et al., 1997a; Swenson et al., 1997b). The heritability for ED varies between 0.1-0.77 (Grøndalen & Lingaas, 1991; Guthrie & Pidduk, 1990, Malm et al., 2008; Mäki et al., 2000; Swenson et al., 1997a) which is considered low to moderate (Mäki, 2004).

The primary lesions within ED seems to have different genes that contribute to the disease (Grøndalen & Lingaas, 1991) and it is suggested that FCP in the Rottweiler is controlled by a major gene (Mäki, 2004; Mäki et al., 2004) but no candidate genes have been identified so far (Temwichitr et al., 2010).

Besides genetics, ED is also influenced by environmental effects (Svenska Kennelklubben, 2014b). Restricted feed intake as well as restricted exercise, e.g. chasing after balls, have been shown to affect the risk of developing ED (Kealy et al., 2000; Kealy et al., 1997; O’Neill et al., 2020; Sallander et al., 2006). A rapid growth rate and a high bodyweight are other risk factors (Case et al., 2010; O’Neill et al., 2020; Sallander et al., 2006). Also, males (neutered or intact) have higher risk of developing ED than females (O’Neill et al., 2020). It is thus not optimal to select breeding animals based only on their own phenotype, because the genotype is not fully explained by the phenotype (Malm, 2010). Genetic evaluation based on only the phenotype from the screening result is therefore imprecise and limits the genetic progress for ED.

2.3. Ethiology of elbow dysplasia

2.3.1. Overview of the elbow joint

The canine elbow consists of three bones, radius, ulna and humerus (ACVS, 2020) (figure 1). These bones connect in three different locations within the elbow joint that are called humeroradial, humeroulunar and radioulnar joints (How, 2018b).
Figure 1. A simplified overview of the canine elbow (Anna Medved, 2020).
Any growth abnormalities or abnormal weight distribution on the elbow joint can cause the three bones within the joint to fit badly (ACVS, 2020) and thus lead to the development of the following four primary lesions (How, 2018b).

### 2.3.2. Ununited anconeal process

The anconeal process plays an important role in stabilizing the joint and prevents mediolateral movement whenever humerus is involved (How, 2018b). In large breed dogs, the anconeal process has a separate ossification centre and the ossification occur between 10-16 weeks of age. The completed fusion between the anconeal process and ulna occurs between 16-20 weeks of age. However, if this fusion is incomplete or fails at 5 months of age, it will lead to ununited anconeal process (UAP). Ununited anconeal process can be bilateral and causes instability in the joint. It can also lead to a displacement of the anconeal process and will eventually lead to OA in the joint (How, 2018b) as a secondary lesion.

### 2.3.3. Osteochondritis dissecans

Osteochondritis dissecans (OCD) occurs in the humeral condyles, most often in the medial (How, 2018b). It is caused by a disturbance in the endochondral ossification process in the centre of the osteochondral junction (Demko & McLaughlin, 2005). This affects the cartilage within that area, where the cartilage fails to undergo the physiological calcification and ossification. The failure leads to a thickened layer of degenerative cartilage instead of bone. The degenerative cartilage and fibrous tissue are sensitive to mechanical tearing that occurs in the joint by normal weight distribution of the animal. This mechanical tearing can lead to a flap. The flap occurs when the degenerative cartilage releases from the underlying bone. When this happens, particles from the degenerative cartilage reaches the synovial fluid and thus contribute to joint pain, lameness and synovitis. It is most often the medial condyle of humerus that is affected by osteochondritis dissecans (Demko & McLaughlin, 2005; How, 2018b).

The causes for osteochondritis dissecans are not completely determined, but it is suggested to be multifactorial and complex due to factors such as genes, fast growth, over feeding, trauma, hormones and excess of calcium (How, 2018b).

### 2.3.4. Fragmented coronoid process / Medial coronoid process disease

The ethiology of fragmented coronoid process (FCP) is still uncertain, however, there are some theories that are currently discussed (Lau, 2018). Some common signs of FCP, or sometimes called medial coronoid process disease (MCPD) are incongruity and lack of the medial coronoid process (Gaschen, 2018). Fragmented
The coronoid process is the most frequent diagnosis that affects young large breed dogs (Lau, 2018; Moores et al., 2008).

There are several factors that can lead to FCP. Osteochondritis is one cause and is connected to the chondronecrosis which is the result from lack of blood flow to growing cartilage. Radioulnar incongruity may also lead to FCP since it puts an increased pressure on the coronoid process (How, 2018b; Lau, 2018; Nemanic et al., 2016; Temwichitr et al., 2010).

### 2.3.5. Elbow incongruity

Elbow incongruity (EI) is suggested to be secondary to length mismatch between ulna and radius (How, 2018b). A short radius increases the risk for developing FCP (Lau, 2018), due to an increase of abnormal pressure put on the medial coronoid process (How, 2018b). Moreover, the ulna might also be too short which might lead to displacement of the humeral head in relation to ulna. This will put an abnormal pressure on the anconeal process which could disturb the ossification of the anconeal process in breeds that have a separate ossification centre of this process and thus have a higher risk to develop ununited anconeal process.

The most common form of elbow incongruity is radioulnar incongruity. Radioulnar incongruity might occur from congenital factors and trauma (How, 2018b). Humeroulnar incongruity might also occur, which causes a displacement of the humeral head from the ulnar notch.

Elbow incongruity is most accurately diagnosed and discovered through arthroscopy or computerised tomography (CT) while radiographical assessment has a low sensitivity when it comes to diagnosing EI (How, 2018b).

### 2.4. Diagnosis of elbow dysplasia

There are different ways to diagnose ED. Dogs with clinical symptoms at a young age usually undergo a physical examination by a veterinarian (Bedford, 1994; O’Neill et al., 2020). The veterinarian takes the dog’s history and clinical symptoms into account when diagnosing. The diagnosis is then often confirmed through a radiographical assessment, CT, arthroscopy or magnetic resonance imaging (MRI) (O’Neill et al., 2020), where secondary OA can be detected (Bedford, 1994). However, in most cases, ED is diagnosed by the official screening programme at around 12 months of age (Malm, 2010; Mäki, 2004).

In Sweden, the elbows are x-rayed in a lateral position where the elbow is fully flexed (SKK, 2020) and the results can then be used as a prediction for future clinical issues connected to ED. Flexed, lateral position is preferred since UAP and OCD are easy to detect in that position (Cook & Cook, 2009; Gaschen, 2018). On
the other hand, FCP is difficult to detect radiographically and is usually diagnosed when no other primary lesion is detected while secondary lesions are present (How, 2016). However, FCP cannot be ruled out just because there are not any joint changes detected in the x-ray (Cook & Cook, 2009). In these cases, a CT or arthroscopy will give a more accurate diagnosis than an x-ray. The reason for this is that x-rays primarily detect secondary lesions such as OA and rarely primary lesions (Gaschen, 2018).

Different positions of the elbow during radiographical assessment have higher probability of detecting different primary lesions. As mentioned before, UAP and OCD are best detected in a lateral flexed position (Cook & Cook, 2009; Gaschen, 2018), while FCP and incongruity has best chance of detection in a mediolateral extended position (Gaschen, 2018). The IEWG recommend four different radiographical projections (How, 2016) for the most accurate diagnosis, but the official screening programme in Sweden uses one projection.

2.4.1. Screening programmes

The SKK has implemented different screening programmes to improve the health of Swedish dogs (Svenska Kennelklubben, 2014a). The screening programmes have three different levels with different requirements. Elbow dysplasia is one of the diseases with a screening programme (table 3).

Table 3. Description of the three screening levels administered by the Swedish Kennel Club (SKK) and number of breeds connected to each screening level (n) for elbow dysplasia (ED). (Svenska Kennelklubben, 2014a)

<table>
<thead>
<tr>
<th>Level</th>
<th>n</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All</td>
<td>Screening is voluntary. Evaluation and health recording.</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>Mandatory screening for all breeding animals</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Only dogs with ED grade 0 are accepted for breeding</td>
</tr>
</tbody>
</table>

Three breeds have a screening level 3 (table 3): German Shepherd dog, Mastino napoletano and Bouvier des flandres. Rottweilers belong to screening level 2 but Golden Retrievers and Labrador Retrievers on the other hand, do not require a mandatory screening result for the breeding animals (SKK, 2014a) but do have a high prevalence of ED (O’Neill et al., 2020).

The implementation of the screening programme for ED varies for each breed, level 3 for German Shepherd dogs was implemented 2008 and level 2 for Rottweiler was implemented 1990.

There are two kinds of screening result within the screening programme. One is preliminary screening results (under 12 months of age) and an official result (12
months of age or older). It is the official screening result that is included in the routine genetic evaluation.

2.5. Dog breeds predisposed for elbow dysplasia

Young large- and giant dog breeds are predisposed to develop ED (Hazelwinkel & Nap, 2009). Within this group of breeds, there are some breeds that have a higher occurrence of ED than other large breed dogs: Rottweilers, German Shepherd dog, Labrador Retriever and Golden Retriever being among those breeds (Beuing et al., 2000; O’Neill et al., 2020). According to Beuing et al., (2000), the frequency of ED in the German rottweiler is 54.2% with many cases of moderate to severely affected dogs.

Rottweilers tend to develop FCP (Grøndalen, 1982) and OCD (Guthrie & Pidduk, 1990), while German Shepherd dogs suffers more often from UAP (Meyer-Lindenberg et al., 2006). A high frequency of OCD is also seen in Labrador Retrievers (Guthrie & Pidduk, 1990).

The heritability was found to be 28% in Rottweilers, which indicates enough genetic background to improve the elbow health by breeding, but not sufficient enough to select breeding animals without the knowledge of ancestry (Beuing et al., 2000).

2.6. Breeding for better elbow health

Because dog breeding is done mostly as a hobby by ordinary pet owners, it is very common to select the breeding animals based on the individual’s own phenotype (Oldenbroek & van der Waaij, 2014), which might not be the optimal selection. Elbow dysplasia is a categorical trait, but two individuals with the same screening result may still have different genetic background.

It is important to include the phenotype of relatives as well as the individual’s phenotype when assessing genetic evaluation. Instead of only using the individual’s phenotype, breeding values based on best linear unbiased prediction (BLUP) is to prefer. By using BLUP, the genetic gain per generation improves more than only by phenotypic selection, but it also tends to increase the inbreeding rate per generation. However, this could be prevented by using optimum contribution selection (OCS). Optimal contribution selection maximises the genetic gain per generation while keeping the inbreeding rate below a set value (Clark et al., 2013; Granleese et al., 2015).

In Sweden, BLUP breeding values are routinely estimated for some affected breeds when it comes to ED. These breeding values are based on the radiographical
screening programmes for hip- and elbow dysplasia. Unfortunately, even though the screening programme is applied, the genetic improvement for ED is still lower than expected (Malm, 2010). The lack of success can be due to several factors, e.g. that ED has lower priority compared to other traits in the breeding goal (Mäki et al., 2005) or that ED has unfavourable genetic correlations with other traits in the breeding goal, e.g. mentality traits.
3. Material and Methods

3.1. Data

3.1.1. Swedish Kennel Club data

Data including identification number, chip number, birth date, identity of sire and dam, sex, ED score, date of screening, ED index, screening clinic and panellist was provided by the SKK for the breeds Rottweiler (RW), German Shepherd dog (GSD), Labrador Retriever (LR) and Golden Retriever (GR).

The datafile included dogs born between the years 2005-2015 with a total of 90 526 individuals. After some general editing, i.e. removing unrealistic/invalid ED grading scores, ED indexes below 0, removal of duplicates, weights above 70 kgs, ages below 0 months etc, there were in total 89 765 individuals. Out of these, 54 549 dogs had an ED result and 53 946 had an official ED score (table 4). The sex distribution was 50.5% males and 49.5% females. The prevalence of ED in the four breeds is shown in table 4. Figure 2 shows the distribution of screening age for each breed. Of all official screenings, 92% were done between 12 and 24 months of age.

Table 4. Total number of ED scores, number of official ED scores, and prevalence of elbow dysplasia (ED score) in percent at official ED screening and the frequency of preliminary screening scores (dogs less than 12 months at screening) where the numbers within the brackets are the number of observations. Rottweilers (RW), German Shepherd dogs (GSD), Labrador Retrievers (LR) and Golden Retrievers (GR).

<table>
<thead>
<tr>
<th>Breed</th>
<th>RW</th>
<th>GSD</th>
<th>LR</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of ED-scores</td>
<td>7,688</td>
<td>16,556</td>
<td>16,523</td>
<td>13,782</td>
</tr>
<tr>
<td>No. of official scores</td>
<td>7,639</td>
<td>16,302</td>
<td>16,338</td>
<td>13,667</td>
</tr>
<tr>
<td>ED score 0</td>
<td>73.88</td>
<td>83.00</td>
<td>90.92</td>
<td>83.68</td>
</tr>
<tr>
<td>ED score 1</td>
<td>20.24</td>
<td>11.01</td>
<td>5.35</td>
<td>10.98</td>
</tr>
<tr>
<td>ED score 2</td>
<td>4.90</td>
<td>3.27</td>
<td>2.04</td>
<td>4.10</td>
</tr>
<tr>
<td>ED score 3</td>
<td>0.98</td>
<td>2.72</td>
<td>1.69</td>
<td>1.24</td>
</tr>
<tr>
<td>Prel. ED score</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>---------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>0</td>
<td>40.82 (20)</td>
<td>48.43 (123)</td>
<td>15.68 (29)</td>
<td>26.96 (31)</td>
</tr>
<tr>
<td>1</td>
<td>20.41 (10)</td>
<td>12.60 (32)</td>
<td>27.57 (51)</td>
<td>16.52 (19)</td>
</tr>
<tr>
<td>2</td>
<td>18.37 (9)</td>
<td>10.63 (27)</td>
<td>23.78 (44)</td>
<td>22.61 (26)</td>
</tr>
<tr>
<td>3</td>
<td>20.41 (10)</td>
<td>28.35 (72)</td>
<td>32.97 (61)</td>
<td>33.91 (39)</td>
</tr>
</tbody>
</table>

**Figure 2.** Distribution of age at official screening by breed (Rottweilers (RW), German Shepherd dogs (GSD), Labrador Retriever (LR) and Golden Retriever (GR)) with official screening scores. Dogs with an age over 30 months, as well as dogs younger than 12 months were excluded from the diagram.

### 3.1.2. Insurance data from Agria

Data of insurance claims related to elbow dysplasia/arthritis in the elbow joint between 2010 and 2018 for the four breeds included in the study was provided by the insurance company Agria. The datafile included information on breed, birthdate, name of the dog, registration number, chip number, sex, date of insurance claim, type of claim (life- or veterinary claim) and diagnosis. In total, 2 357 observations were included in this dataset. After removing duplicates (i.e. dogs with several claims) and keeping only the first claim date for each individual, there were 779 individual dogs left (64% males and 36% females). The number of observations and diagnosis distribution within the four breeds can be seen in table 5.
Table 5. Breed distribution in the Agria insurance data for elbow related claims for the four breeds analysed and the relative diagnosis frequency in percent for each breed. In total 779 observations, including data on the first claim for each dog.

<table>
<thead>
<tr>
<th>Breed</th>
<th>n</th>
<th>FCP</th>
<th>OCD</th>
<th>UAP</th>
<th>EI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rottweiler</td>
<td>123</td>
<td>78.1</td>
<td>8.9</td>
<td>9.8</td>
<td>3.3</td>
</tr>
<tr>
<td>German Shepherd dog</td>
<td>210</td>
<td>45.7</td>
<td>8.6</td>
<td>42.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>339</td>
<td>77.3</td>
<td>12.1</td>
<td>9.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>107</td>
<td>71.0</td>
<td>13.1</td>
<td>12.2</td>
<td>3.7</td>
</tr>
</tbody>
</table>

Where FCP=Fragmented coronoid process, OCD=Osteochondritis dissecans, UAP=Ununited anconeal process and EI=Elbow incongruity

Out of the 779 observations, 79% had a veterinary claim, 5% had a life claim and 16% had both a veterinary claim and a life claim. A life claim is when the dog is euthanized by a veterinarian. For dogs with both a veterinary claim and life claim, the first date for veterinary care claim was kept as well as the date for the life claim.

3.1.3. Combination of Agria data and SKK data

The datafiles from SKK and Agria were merged together in order to evaluate the association between the screening result and reported incidence of elbow-related veterinary care and/or death/euthanasia. The datafiles were merged based on the dog’s registration number and/or chip number. There were in total 574 observations that matched in both the SKK dataset and the Agria dataset. 205 observations from the Agria data did not match with any dog in the SKK data. 147 of these were observations outside of the birth range that were in the SKK dataset (born before 2005 or after 2015). The remaining 58 dogs could be dogs not registered in the SKK, or with errors in identification information. The number of observations and diagnosis distribution within each breed in the merged dataset be seen in table 6.

Table 6. Number of records (n) and diagnosis frequencies in percent for each breed in the merged dataset. A total of 574 observations

<table>
<thead>
<tr>
<th>Breed</th>
<th>n</th>
<th>FCP</th>
<th>OCD</th>
<th>UAP</th>
<th>EI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rottweiler</td>
<td>88</td>
<td>76.1</td>
<td>9.1</td>
<td>10.2</td>
<td>4.6</td>
</tr>
<tr>
<td>German Shepherd dog</td>
<td>153</td>
<td>48.4</td>
<td>8.5</td>
<td>39.9</td>
<td>3.8</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>253</td>
<td>75.1</td>
<td>13.8</td>
<td>10.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>80</td>
<td>72.5</td>
<td>8.8</td>
<td>13.8</td>
<td>5</td>
</tr>
</tbody>
</table>
Out of the 574 observations, 337 observations had ED scores (288 observations with official screening scores and 49 observations with preliminary screening scores). Out of the 337 observations with both an ED score and insurance claim, 314 observations had a veterinary care claim and 23 observations had a life claim. 44 observations out of the 314 with veterinary care claim, also had a life claim. The definition of both veterinary care and life claim were observations with one recorded date for veterinary care, and one recorded date for a life claim.

### 3.1.4. Summary of all datasets

An overview of data used in this thesis can be seen in table 7. Only one record for each individual was included. The official record for dogs with multiple screening records (preliminary or official) was kept. Dogs with both a veterinary care claim and life claim, only the first veterinary care claim was kept together with the date of life claim.

<table>
<thead>
<tr>
<th>Dataset</th>
<th>SKK</th>
<th>Agria</th>
<th>Agria * SKK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Official screening result</td>
<td>53 946</td>
<td></td>
<td>288</td>
</tr>
<tr>
<td>Preliminary screening result</td>
<td>603</td>
<td></td>
<td>49</td>
</tr>
<tr>
<td>No. without screening result</td>
<td>35 216</td>
<td></td>
<td>237</td>
</tr>
<tr>
<td>Life claim</td>
<td></td>
<td>36</td>
<td>29</td>
</tr>
<tr>
<td>Veterinary claim</td>
<td></td>
<td>619</td>
<td>446</td>
</tr>
<tr>
<td>Veterinary + life</td>
<td></td>
<td>124</td>
<td>99</td>
</tr>
<tr>
<td>Total number of obs</td>
<td>89 765</td>
<td>779</td>
<td>574</td>
</tr>
</tbody>
</table>

### 3.2. Statistical analyses

For statistical analyses, the SAS software (ver. 9.4; SAS Inst. Inc., Cary, NC) and DMU (Madsen & Jensen, 2013) were used. SAS was used to edit the data and to calculate frequencies, apply analysis of variance (PROC MIXED) to estimate least square means (lsmeans) for factors included in the statistical model. Also, the SAS software was used to analyse differences between ED score means within the general breed population versus the breed population in the insurance data etc.
DMU was used to estimate the additive genetic variance for ED. With the variance components, the heritability for ED within the four breeds was estimated.

A mixed linear model (SAS; PROC MIXED) was applied to the SKK data, to analyse the impact of fixed and random factors on ED score.

To find which effects were significant, a general model (1) was used where all four breeds were included. The model was a mixed linear model:

\[
ED \text{ grade} = \mu + \text{breed} + \text{sex} + ED \text{ year} + \text{season} + \text{panellist} + ED \text{ age(sex)} + \text{weight(sex)} + \text{inbreeding(sex)} + \text{clinic} + \text{error} \tag{1}
\]

\[
ED \text{ age(sex)}, \text{ weight(sex)} \text{ and inbreeding(sex)} \text{ were not used as regressions for the phenotypic analysis, which was based on this model, for dogs with a screening record in the SKK database. Instead, the effects were grouped into classes. ED age, weight and inbreeding nested within breed and sex were tested, however, it was not significant and therefore not used.}
\]

The significance level is described with stars, where \( p<0.05 = * \), \( p<0.01 = ** \), \( p<0.001 = *** \). The smaller the \( p \)-value, the stronger the evidence that the null hypothesis should be rejected. The null hypothesis is that the variables studied have no influence on the variable analysed. Note that the level of significance does not say anything about the magnitude of the effect of each variable analysed.

### 3.2.1. Genetic analysis from SKK data

To calculate the heritability of ED, the software DMU (Madsen & Jensen, 2013) was used to estimate variance components. The genetic analysis was based on official screening results from the official screening results from SKK. The minimum screening age of the individual was 12 months up to 30 months of age. In total, 49 459 observations were used (RW=7 127, GSD=14 452, LR=14 989 and GR=12 891) and the sex distribution was 47.5% males and 52.5% females.

The model used for the genetic analysis was a mixed linear animal model for each breed separately (2):

\[
ED \text{ grade} = \mu + \text{sex} + ED \text{ year} + \text{season} + \text{panellist} + ED \text{ age(sex)} + \text{weight(sex)} + \text{inbreeding(sex)} + \text{animal ID} + \text{clinic} + \text{litter ID} + \text{error} \tag{2}
\]

where \( ED \text{ grade} \) is a score from the screening programme, \( sex \) is the effect of males vs females, the effect \( ED \text{ year} \) implies the year of ED screening, and \( season \) was defined as four seasons at birth, where December, January and February = winter, March, April and May = spring, June, July and August = summer and September, October and November = autumn. \( ED \text{ age(sex)} \) is a regression of age (in days) at screening, nested within sex, \( \text{weight(sex)} \) is the effect of weight at screening as a
regression nested within sex and \( inbreeding(sex) \) is the effect of inbreeding percentage, calculated over five generations, as a regression nested within sex. \( Animal \ ID \) is the identity of the animal, \( clinic \) is the clinic performing the radiography, \( litter \ ID \) is the effect of birth litter and \( error \) is the residual. \( Animal \ ID, clinic, litter \ ID \) and \( error \) are included as random effects. \( Animal \ ID \) is the additive genetic effect of the dog, \( \sim \text{ND} \left( 0, \ A \sigma^2_a \right) \), where \( A \) is the additive relationship matrix using pedigree information, traces back five generations. \( Litter \ ID \) and \( clinic \) are environmental effect of the dog, \( \sim \text{ND} \left( 0, \ I \sigma^2_{litter} \right) \) and \( \sim \text{ND} \left( 0, \ A \sigma^2_{clinic} \right) \), and \( error \) is the random residual, \( \sim \text{ND} \left( 0, \ I \sigma^2_e \right) \).

The model was also run in SAS to investigate the significance of the fixed effects for each breed, however, \( animal \ ID \) was not included as a random effect in that analysis.

### 3.2.2. Phenotypic analysis of SKK data

The phenotypic analysis of ED was based on the mixed linear model (1). The model was run with all breeds included, but also for each breed separately. ED age was classified into months (12 = 11.5-12.5 etc) instead of days, weight was classified with 4 kg interval: 20-23; 24-27 etc. Inbreeding was classified as inbreeding 0=0, 0.1-1=1, 1.1-2=2 etc up to 6.1% and higher=7. By this, the lsmeans for ED score could be calculated for these effects, and in the diagrams presented, trend lines could be plotted in the software Excel. The phenotypic analysis was based on 49,459 observations (officially screened animals between 12-30 months of age), and the sex distribution was 47.5% males and 52.5% females.

### 3.2.3. Phenotypic analysis of insurance data

The software SAS 9.4 was used to produce descriptive analysis of the merged dataset and Agria data. In this analysis, also dogs without ED score or a preliminary screening result in the SKK data were included, as they could give important information about cases that have insurance claim related to ED.

Furthermore, a non-parametric statistical test (npar1way) was performed to compare the mean ED score for all dogs in the screening data with the mean ED score for dogs with an insurance claim for elbow related issues in the Agria database, to investigate if there was an effect of ED score on the risk for an elbow related injury.
4. Results

4.1. Genetic analysis on SKK data

Table 8 shows the estimated variance components for the random effects and the heritability for Rottweilers, German Shepherd dogs, Labrador Retrievers and Golden Retrievers. The heritability was calculated as: \( h^2 = \frac{\sigma^2_a}{\sigma^2_a + \sigma^2_e} \), where \( \sigma^2_a \) is the additive genetic variance and \( \sigma^2_e \) is the residual variance.

Table 8. Estimated clinic variance (\( \sigma^2_{\text{clinic}} \)), litter variance (\( \sigma^2_{\text{litter}} \)), additive genetic variance (\( \sigma^2_a \)), residual variance (\( \sigma^2_e \)) and heritability (\( h^2 \)) for Rottweilers, German Shepherd dogs, Labrador Retrievers and Golden Retrievers. The heritability is calculated as: \( h^2 = \frac{\sigma^2_a}{\sigma^2_a + \sigma^2_e} \).

<table>
<thead>
<tr>
<th>Breed</th>
<th>( \sigma^2_{\text{clinic}} )</th>
<th>( \sigma^2_{\text{litter}} )</th>
<th>( \sigma^2_a )</th>
<th>( \sigma^2_e )</th>
<th>( h^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rottweiler</td>
<td>0.002</td>
<td>0.013</td>
<td>0.068</td>
<td>0.275</td>
<td>0.20</td>
</tr>
<tr>
<td>German Shepherd dog</td>
<td>0.000</td>
<td>0.027</td>
<td>0.054</td>
<td>0.330</td>
<td>0.14</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>0.001</td>
<td>0.013</td>
<td>0.031</td>
<td>0.217</td>
<td>0.13</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>0.001</td>
<td>0.015</td>
<td>0.040</td>
<td>0.267</td>
<td>0.13</td>
</tr>
</tbody>
</table>

4.2. Phenotypic analysis of SKK data

ED year showed no significance for ED in the model with all four breeds included (1), and sex had a one-star significance. The other effects had a three-star significance level. The corrected average (lsmean) ED score for the different breeds varied from 0.18 to 0.25, with the lowest score for Labrador and the highest for German shepherd. The lsmean for ED score for males were 0.23 and for females 0.21 (**). However, the difference of lsmeans for ED score between males and females for each breed respectively was only significant for Rottweilers.
(males=0.36, females=0.29; ***). The effect significance from the model applied within each breed can be seen in table 9.
Table 9. The significance of the fixed effect from Model 2 (applied within breed: Rottweilers, German Shepherd dog, Labrador Retriever and Golden Retriever). Data from the Swedish Kennel Club (SKK) dataset. *=p<0.05, **=p<0.01, ***=p<0.001

<table>
<thead>
<tr>
<th>Model (fixed effects)</th>
<th>Sex</th>
<th>Season</th>
<th>ED year</th>
<th>Panellist</th>
<th>Weight (sex)</th>
<th>ED age (sex)</th>
<th>Inbreeding (sex)</th>
<th>Lsmean for ED score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rottweiler</td>
<td>NS</td>
<td>***</td>
<td>NS</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>0.21</td>
</tr>
<tr>
<td>German Shepherd dog</td>
<td>NS</td>
<td>NS</td>
<td>**</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>NS</td>
<td>0.25</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>***</td>
<td>***</td>
<td>*</td>
<td>0.18</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>NS</td>
<td>0.24</td>
</tr>
</tbody>
</table>
The lsmean ED score by screening age for each breed, nested within sex, followed the same direction as the general trend seen in figure 3, except for Golden Retrievers, where females had higher regression coefficient than males.

![Figure 3](image)

*Figure 3. The lsmean for ED score for classified screening age, nested within sex (Model 1). Dogs with a screening age above 30 months were excluded. The trend line is estimated in Excel.*

The lsmean for ED score for the inbreeding coefficient within each respective breed, nested within sex, followed for German Shepherd dogs and Labrador Retrievers, but not for Rottweilers and Golden Retrievers, the same direction as for all breeds (figure 4). For Rottweilers, females had slightly higher regression coefficient than males (0.017 vs 0.012). For Golden Retrievers, Females also had a higher regression coefficient than males (0.01 vs 0.004). The inbreeding percentage is calculated over five generations.
The lsmean of ED score for weight at screening for each breed (Model 2), nested within sex, followed the same direction as seen in figure 5.

Figure 5. The lsmean for ED score by weight at screening, nested within sex (Model 1). Uncertain lsmean values, based on 50 observations or less, are not shown (12 obs for females at 52 kg and 7 females at 56 kg). The trend line is estimated in Excel.
4.3. Phenotypic analysis of insurance data

The mean ED score for dogs with a life claim is 2.40 (n=23) whereas the mean ED score for dogs with a veterinary care claim is 1.68 (n=314).

The mean ED score for each sex within the Agria*SKK dataset was based on 211 males and 126 females. The males had a mean ED score of 1.75 and the females had a mean ED score of 1.67. The preliminary screening scores are included. The mean ED score for each breed can be seen in table 10.

Table 10. The mean ED score for each breed in the Agria*SKK dataset with a total of 337 obs (also the preliminary screening scores were included). n=number of observations

<table>
<thead>
<tr>
<th>Breed</th>
<th>n</th>
<th>Ed score mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rottweiler</td>
<td>57</td>
<td>1.14</td>
</tr>
<tr>
<td>German Shepherd dog</td>
<td>99</td>
<td>2.23</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>138</td>
<td>1.49</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>43</td>
<td>2.07</td>
</tr>
</tbody>
</table>

Figure 6 describes the age distribution for elbow related insurance claims for all dogs in the Agria dataset. Both veterinary claims and life claims are included. The age of the dog at the time the insurance was claimed varied from 2 months to 155 months. There was no change in frequency after approximately 55 months of age (figure 6 shows only until 80 months). Most insurance claims occur before the official screening age of 12 months (indicated by red line in figure 6).

Figure 6. The age distribution for elbow related insurance claims, based on the Agria dataset with 779 obs. The red line represents 12 months of age, i.e. the earliest age at which the dog can get an official screening record for ED. 12 months of age = 11.5-12.5 months etc.
Figure 7 shows the distribution of age of the dog when insurance was first claimed for dogs with no screening results, preliminary- and official screening result respectively. The majority of dogs (77%) where insurance was claimed for ED-related issues before 12 months of age were not screened for ED.

![Age distribution for elbow related insurance claims with/without screening results](image)

Figure 7. Age distribution for ED-related veterinary insurance claim for dogs with no ED score (n=237), official ED score (grade 0-3, n=288) and preliminary ED score (n=49). The red line represents 12 months of age, i.e. the earliest age at which the dog can get an official screening record for ED. The x-axis was cut at 40 months of age because the lines flattened after 32 months of age and looked the same up to 128 months of age. Based on the Agria*SKK dataset. 12 months of age = 11.5-12.5 months.

Figure 8 shows that the most common screening result dogs with an insurance claim related to ED was grade 3. Of the screened dogs with an insurance claim, 76% had some level of ED at screening (official or preliminary grade 1-3). However, 24% of the screened dogs with an insurance claim for elbow related issues were scored as normal at screening. Moreover, the distribution of ED scores is compared for all dogs screened in SKK (official and preliminary results) with dogs with an insurance claim. The frequency of ED is higher for dogs with an insurance claim related to elbow related issues.
As seen in figure 8, there are 24\% dogs (n=76) that are screened as normal but still has an insurance claim for elbow related issues. The distribution of ED diagnoses for dogs with normal screening results and an insurance claim for elbow related issues can be seen in figure 9. The majority of dogs with ED grade 0 at screening (official and preliminary), and a later insurance claim related to ED, had the diagnosis FCP. The frequency of FCP for all dogs with an insurance claim for ED was 68\%.

Out of the dogs with FCP in figure 10, 73\% were between 12-15 months of age when screened and 27\% were between 16-25 months of age when screened. The date of insurance claim was between 10-88 months of age. The distribution of FCP for all dogs with an official ED score in the merged Agria*SKK data where the following: ED score 0 (32.7\%), ED score 1 (21.3\%), ED score 2 (14.4\%) and ED score 3 (31.9\%). In figure 10, the distribution of diagnoses for each breed is shown, based on the total Agria dataset (n=779). Fragmented coronoid process was the most common diagnosis in all breeds. However, in the German Shepherd dog, also UAP is a common cause of life- or veterinary claim.

Figure 8. ED score distribution for screened dogs in SKK (official and preliminary; n=54,549), and dogs with elbow related insurance claim and recorded ED score (Agria off =288 obs; Agria prel =49 obs).
The distribution of diagnoses in dogs with ED score 0

Figure 9. Distribution of diagnoses in the merged Agria*SKK data for dogs with an insurance claim and with an official screening result of ED score=0 in the SKK data (i.e. normal elbow status, n=76). FCP = Fragmented coronoid process, OCD = Osteochondritis dissecans and UAP = Ununited anconeal process.

The distribution of diagnoses within breeds

Figure 9. The distribution of diagnoses for Rottweilers (RW, n=123), German Shepherd dogs (GSD, n=210), Labrador Retrievers (LR, n=339) and Golden Retrievers (GR, n=107). The distribution is based on the Agria data with 779 obs in total. FCP=Fragmented coronoid process, OCD=Osteochondritis dissecans, UAP=Ununited anconeal process and EI=Elbow incongruity. Both veterinary care and life claims are included in the dataset.
There was a significant difference in mean ED score at screening for all dogs in the SKK dataset compared to those with an insurance claim related to ED. The difference was significant in all four breeds (table 11).

### Table 11. A npar1way test, performed within breed (Rottweilers (RW), German Shepherd dogs (GSD), Labrador Retrievers (LR) and Golden Retrievers (GR)), between the mean ED score for all dogs in the SKK dataset and in the Agria*SKK data, including dogs with both an ED-score and an insurance claim related to ED. The numbers within brackets are number of observations. Also, the preliminary screening results are included. The differences were highly significant (p<0.001) for all breeds. ***=p<0.001

<table>
<thead>
<tr>
<th>Dataset</th>
<th>RW</th>
<th>GSD</th>
<th>LR</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKK ED mean</td>
<td>0.33 (7 631)</td>
<td>0.26 (16 457)</td>
<td>0.15 (16 385)</td>
<td>0.23 (13 739)</td>
</tr>
<tr>
<td>Agria*SKK ED mean</td>
<td>1.14 (57)</td>
<td>2.23 (99)</td>
<td>1.49 (138)</td>
<td>2.07 (43)</td>
</tr>
<tr>
<td>Significance difference</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
</tr>
</tbody>
</table>
5. Discussion

Elbow dysplasia (ED) usually develops during the fastest growth period in large breed dogs. This is normally between 4-12 months of age (Bedford, 1994; Guthrie & Pidduk, 1990; Michelsen, 2013). Many dogs diagnosed with ED receive veterinary treatment, e.g. surgery, before the official screening age, which leads to a loss of information about these individuals (Hedhammar & Malm, 2008). Hence, the individual, its parents and siblings might get a better breeding value for ED based on the official screening records than they should.

Elbow dysplasia can be painful for the dog and stressful for the owner. In many cases the dog must be subjected to costly surgery and lifelong rehabilitation, or in worst case euthanasia. A dog with hip dysplasia can in some cases have a good quality life if the pelvis muscles are well built. However, when it comes to ED, muscles cannot offload pressure on the joint in the same way, and even a mild grade of ED can be painful for the dog (Beuing et al., 2000). Another limitation with the official screening programme is that ED is measured based on available osteophytes, in other words, the secondary changes in the joint, visible when the damage is already done in contrary to hip dysplasia. Perhaps more research could find better ways to discover ED at earlier stages.

Environmental factors play an important role for risk of developing ED. Kealy et al., (2000) found that 25% less feed intake reduces the risk of developing ED. Less feed could lead to a slower growth rate in large breed dogs, which is to prefer. Slower growth rate could affect the growth plates in a way that the ossification occurs instead of building up soft, degenerative cartilage. Reduced feed intake will also lead to a lower body weight. High body weight has been related to the development of ED (Case et al., 2010; O’Neill et al., 2020; Sallander et al., 2006), and the same could be seen in this thesis for all studied breeds.

Harsh play and exercise during the most critical growth period could probably also increase the development of ED (Sallander et al., 2006). Elbow dysplasia is thus a very complex trait that depends on multiple factors and not only genetics.
5.1. Analysis of screening data from SKK

A mixed linear animal model was used for the genetic analysis of SKK screening data. The mixed linear model assumes that traits (or at least the residuals) are continuous and normally distributed. ED is a categorical trait that is not normally distributed and a generalized linear mixed model (e.g. PROC GLIMMIX) would be a better choice. However, GLIMMIX did not work for our data. The analyses did not converge and that could be due to sub-optimal data structure.

When determining which fixed effects to include in the model for the genetic analysis, the general approach was to keep those that were significant in the GLM-analyses in SAS in the model for genetic analysis in DMU. Screening year was not significant but was kept anyway. The reason for this was that the protocols and procedures around the screening might have changed slightly over the years and this may have influenced scoring and thus the prevalence of ED. In the model for routine genetic evaluation of ED at the SKK, a combined effect of clinic and screening year is included. However, in this thesis there were no obvious clinic/screening year that stood out more than others. Therefore, screening year was included as a fixed effect on its own, not in combination with clinic.

5.1.1. Phenotypic analysis

The effect of panellist was significant, which was also seen in the study by Mäki (2000). This could be interesting to investigate further since panellist is not included in the model for routine breeding evaluation today. This is due to challenges in the data structure, e.g. bias in the selection of X-rays in the way that new panellists learn from a more experienced panellist and does not score difficult X-rays in the beginning. Also, dogs scored by the appeal panel (the Nordic panel) as well as foreign dogs comprise selected groups with respect to ED scores which would bias the genetic evaluation. These factors make it difficult to correct for the effect of panellist in an accurate way.

The effect of sex had a significant effect on ED score when all breeds were analysed together. However, for each breed separately, sex was not significant for any of the breeds. The reason for this could be that more observations were needed since the p-value for effect of sex only reached one-star level when all breeds were analysed together. When the breeds were separated in Model 2, there might have been too few observations to reach a significance level. Other studies have also found an effect of sex on ED score (Beuing et al., 2000; Grøndalen & Lingaa, 1991; Guthrie & Pidduk, 1990; O’Neill et al., 2020; Studdert et al., 1991). The influence of sex could be due to hormones, as mentioned by How (2018a) or that males might also grow faster compared to females. This theory is backed up
by the results in figure 5 where the regression coefficient is steeper for males than females when it comes to weight.

As shown in figure 3, there was an increase in lsmean for ED score with age, which is to be expected since the occurrence of osteophytes, or osteoarthritis, increases with age. The reason why the curve jumps between 25-30 months of age could be that there were fewer observations with screening results at that age.

5.1.2. Genetic analysis
The estimated heritability for each breed were in line with the study from Grøndalen & Lingaas (1991). Heritabilities are given as a number between 0 and 1. Low heritabilities are close to zero, which means that most of the variability of the trait is due to environmental effects (NIH, 2020). The heritabilities from this thesis were 0.13-0.20 which can be seen as low. Low heritabilities make it more difficult to change a trait through selection. If the trait also has unfavourable correlations with other traits it will become even more difficult to select against ED. Common litter explained 4-7% of the total variance in ED screening score. Littermates can be an environmental effect just like the effect of clinic and might affect the development of ED through trauma from rough play or rivalry for feed.

In this thesis, dogs above 30 months of age were excluded when calculating the heritability. Dogs older than 30 months of age could have some arthrosis due to trauma or from normal wear and tear and not due to genetics. It is recommended to screen dogs between 12-24 months of age. As for the effects included in the model, inbreeding, weight and age were used as regressions nested within sex. Other studies have not included these as regressions nested within sex. The results from this thesis show that males tended to have a higher regression coefficient than females from the model with all breeds included (figure 3, 4 and 5) and indicates that it could be relevant to include regressions nested within sex into the official routine model. In the official routine model that the SKK uses, regressions nested within sex are not used.

5.2. Analyses from the insurance data from Agria
Even though the screening programme has been applied for several years, the prevalence of ED is still high (table 1). Today, only one radiographical projection is taken in Sweden, a flexed lateral position. However, this projection is not the most efficient at discovering the most common diagnosis for ED, which is FCP (Lau, 2018; Moores et al., 2008). The results from this thesis shows that around 23% of the dogs with elbow related veterinary insurance claim, had an official
screening result of normal elbows (figure 7). Out of these observations, the most prominent diagnosis was FCP (86.84%) (figure 9). 73% of dogs diagnosed with FCP, but screened with score 0, were screened between 12-15 months of age and 27% were screened between 16-25 months. They were diagnosed between 10-88 months of age. This indicates that some dogs had a diagnosis of FCP at an age before official screening age, and still got a screening score of 0 (normal). This should not be possible since an ED-related veterinary treatment should be reported at the same time as the official screening result. Perhaps these observations occurred before it became mandatory to report ED-related veterinary treatments at the official screening. However, this was not investigated further.

Figure 10 shows the distribution of the four diagnoses in the insurance data for claims on elbow-related conditions. Fragmented coronoid process is the most predominant diagnosis with almost 80% frequency within the breeds, except for German Shepherd dogs. German Shepherd dogs are instead overrepresented for UAP. Today’s screening with one projection in a flexed lateral position is good for discovering this diagnosis (Cook & Cook, 2009; Gaschen, 2018). According to Gaschen (2018), the best projection to find FCP is in a mediolateral extended position. Perhaps it is better to use a projection that shows the most common diagnosis of FCP.

Because the number of observations with both screening results and insurance claim are quite few, it is important to keep in mind that the results may not be completely representative for the studied breeds in general. However, it can still be an indication that the screening programme may benefit from more projections to accurately diagnose the dogs. On the other hand, more projections expose the dog and personnel for more radiation and is more expensive. Hence, the benefits of more projections should be weighed against the cost.

Most dogs with an elbow-related insurance claim were younger than 12 months of age (figure 6) at the time of the claim. This could be problematic if these individuals are not officially screened later. They will not contribute any information to the genetic evaluation, and the predicted breeding values will get biased with the risk of overestimating the breeding value for the dog itself as well as its relatives. The distribution of screening scores varied in the merged Agria*SKK dataset where dogs with official screening scores tended to have veterinary care after 12 months of age, and dogs with preliminary scores tended to have veterinary care before 12 months of age (figure 7). This is to be expected. It is likely that the dogs with preliminary results were screened before 12 months of age due to clinical symptoms. However, there were 237 dogs with insurance claims but without any recorded screening score, where almost 78% had some elbow related veterinary care before 12 months of age (figure 7). This means that 22% of the 237 dogs without a screening score but with an insurance claim after 12 months of age do not undergo the official screening programme and are therefore lost to the
genetic evaluation. If this were to represent the reality, 22% would be a lot of missed information for the genetic evaluation. One possibility to get more complete information for the screening programme, would be that the insurance companies requires an official evaluation by the SKK panellists, before accepting the claim for reimbursement. This is practiced by some insurance companies with respect to hip dysplasia. However, it is probably of even higher importance with respect to ED since a large proportion of dogs with ED seems to get clinical problems before 12 months of age. By having this kind of collaboration with insurance companies, information about individuals with insurance claims related to ED before 12 months of age will not be lost.

Most dogs with both screening result and an insurance claim, had an official screening score of 3, which is to be expected since that is the most severe grade of ED. However, as mentioned earlier, there was a higher frequency of screening score 0 than expected (figure 8). When combining the preliminary screening scores with respective official screening score, the distribution of ED scores among dogs with insurance claims were more spread out compared to dogs in the screening programme generally SKK dataset (figure 8). However, it is important to point out that dogs that did not have an insurance claim, are not necessarily healthy individuals. They could for example be insured with another insurance company than Agria. Agria, however, does have the highest market share when it comes to dog insurance, and in many cases treatment for ED included surgery, which is expensive, so probably owners do claim their insurance if they have one. A more accurate way to investigate healthy versus clinically affected animals would have been to include all dogs that are insured with Agria during the specified time period, not only the ones with an insurance claim related to ED. That would give a more accurate estimation of the ED score frequencies in healthy versus clinically affected dogs. Because that data was not available for this thesis, it was not possible to calculate the incidence of clinical ED in the studied breeds.

Instead, a non-parametric statistical test was performed to investigate if there was a significant difference in mean ED score between all the screened dogs in the SKK data and those with an insurance claim. The difference was significant within all breeds (table 11). However, also this test would be more accurate if both healthy and clinically affected dogs were included in the insurance data. The reason why a non-parametric statistical test was performed instead of a t-test is because the trait studied is categorical and not normally distributed.

5.3. Other aspects

Even though screening programmes are applied for ED in several breeds in Sweden, it is still necessary to inform and educate breeders how it works. Best
linear unbiased prediction (BLUP) is today used to estimate breeding values (EBVs) for hip and elbow dysplasia in several Swedish breeds. It is an effective method to find the best breeding animals with respect to joint health. However, it could be a challenge to educate the breeders about how it works since the EBV is not a static value, but changes over time as new information about screening records becomes available. A dog can have a good EBV can get a worse EBV after some time. It could be difficult to explain to the breeders how this is possible, and why a dog with normal elbows still might not be the best breeding animal. Educating breeders about EBVs could lead to less selection based only on the dog’s phenotype and thus have a more effective genetic progress. Even though BLUP is a very useful way to evaluate potential breeding animals, it can also be problematic in that way that closely related individuals will have similar breeding values. If not controlled carefully, there is a risk to breed closely related individuals if the EBV is the only criterion. This could, however, be avoided by combining BLUP with optimum contribution selection (OCS). By combining OCS and BLUP, almost the same genetic progress can be achieved, while at the same time reduce or minimize the risk of inbreeding.

In the future, genetic markers can hopefully be used as a selection tool to breed against ED. Today, however, there is no known candidate genes for ED (Temwichitr et al., 2010). It also seems like the different primary lesions have different genes that contribute to the development of ED (Grøndalen & Lingaas, 1991). It may thus be difficult to apply genetic markers as a selection tool for selection against ED.
6. Conclusions

Screening result seems to be a valuable indication of later clinical issues related to ED. However, this thesis indicates that there may be room for improvement of the official screening programme. A larger proportion than expected of dogs with an insurance claim related to ED had an official score of 0 (normal). Most of these dogs were diagnosed with fragmented coronoid process (FCP). Adding one more projection to the screening programme could be beneficial in finding these cases because FCP is the most common diagnosis related to ED according to the insurance data. More investigations are needed to come with a clear conclusion, and benefits and costs should be weighed. In addition, a large proportion of the dogs with an insurance claim related to elbow were less than 12 months of age and have not yet been screened for ED. For a more accurate genetic evaluation, also information from these dogs should be added to the screening data. This might be solved through collaboration between SKK and the insurance companies.

Estimated heritabilities suggest that genetic progress is possible but expected to be slower compared to e.g. hip dysplasia. Suggestions with respect to the statistical model for genetic evaluation could be to include the regressions nested within sex, panellist as fixed effects, and the effect of litter as a random effect.

The results from this thesis should be interpreted carefully since the number of observations were few. Also, there is no guarantee that animals without insurance claims for ED were healthy, as they may have been insured in another company. More research is needed, preferably including all dogs of the selected breeds insured during a certain time period.
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