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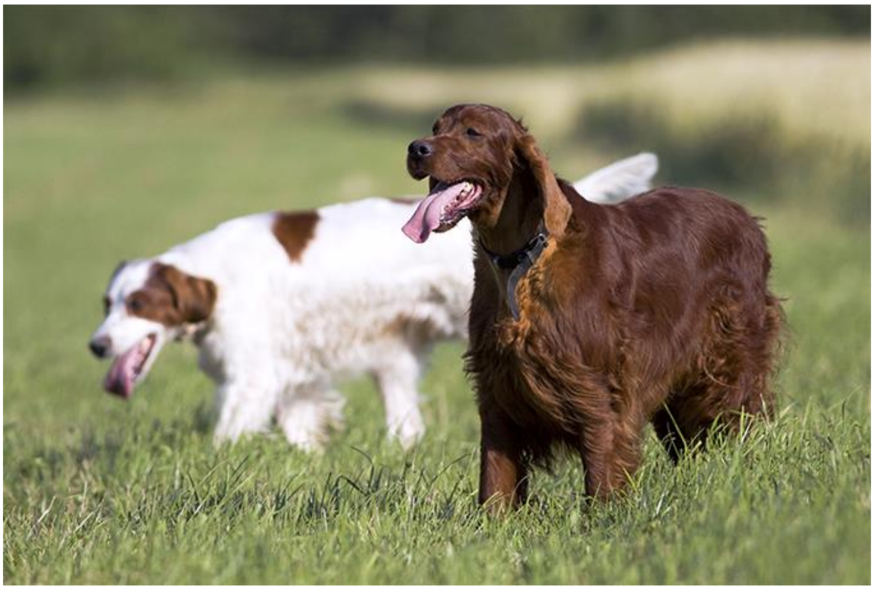

Iris van den Broek

Reg no. 950821128010

Bsc Thesis Animal Breeding and Genetics

June 2017

WAGENINGEN UNIVERSITY
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Supervisor: Jack Windig

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Commissioned by: De Ierse Setter Club

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Preface

What you are reading is a Bachelor thesis comprising a study on inbreeding and kinship in the Irish Red Setter and Irish Red-White Setter. This thesis is written in request of *De Ierse Setter Club* and to complete the Bachelor *Dierwetenschappen* at Wageningen University, The Netherlands. The study was conducted in 2017 at the chair group Animal Breeding and Genetics under supervision of Jack Windig.

During the Bachelor *Dierwetenschappen*, in which I learned a lot about animals on different aspects, the focus was mainly on production animals, such as cows, chickens and pigs. Despite the fact that I really enjoy learning about these species, my real interest is in non-production animals. Because I want to specialize in breeding and genetics and am an enormous lover of dogs, this thesis subject was a logical choice for me to make and I really enjoyed researching it for the past three months.

I would like to thank my supervisor Jack Windig for his profound and constructive feedback and patience in explaining certain matters over and over to me. Next to that I would like to thank *De Ierse Setter Club* for the provision of all necessary data and their time and help with answering questions.

I sincerely hope that this study can help *De Ierse Setter Club* to optimise their breeding program and thereby reduce the rate of inbreeding and preserve the genetic diversity of a special dog breed.

Wageningen, June 2017
Iris van den Broek

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Summary

Breeding purebred dogs comes with several issues. Due to selection for certain characteristics and breeding in a closed population, inbreeding rates increase and genetic diversity gets lost, resulting in genetic disorders. This study analysed inbreeding and kinship in the population of Irish Red Setters and Irish Red-White Setters to formulate breeding recommendations that can support *De Ierse Setter Club* in maintaining genetic diversity and controlling inbreeding. First a pedigree analysis was performed and several population parameters were determined. Next simulations with different measures were carried out to determine the consequences of these measures on the inbreeding rate.

The small population of Irish Setters poses a high risk of inbreeding. Every year on average 40 litters are born in the Irish Red Setter and only 6 in the Irish Red-White Setter. The generation interval of 4.5 and average litter size of 8.4 and 6.5 for the Irish Red Setter and Irish Red-White Setter respectively are high compared to other breeds. In the Irish Red Setter from 1950 to 1989 ΔF_{gen}=1.18% which is classified as a high risk of genetic disorders and even the risk of extinction of the breed exists. From 1990 to 2017 ΔF_{gen}=-0.37%. This rate of inbreeding is very low but to keep it this low in the long term the population size should be large. In the Irish Red-White Setter ΔF_{gen}=4.71% from 1975 to 1996 which poses a great risk of extinction. From 1997 to 2017 the rate of inbreeding approximated zero with ΔF_{gen}=-0.15%. Again the population size should be large to keep the rate of inbreeding low in the long term. The breeding population in the Irish Red Setter is currently estimated on 33 males and 80 females and on 5 males and 11 females in the Irish Red-White Setter. With simulations the best measures to limit the rate of inbreeding were determined. The largest effect was achieved by constraining kinship with the remainder of the breed and at the same time minimising kinship between parents. Next, enlarging the breeding population turned out to be very effective. This can be done by introducing look-alikes or by importing animals from abroad. It is important that these animals are less or not related to the Irish Setter population. In the Irish Red Setter population also more animals from the current population could be used as breeding animals instead of introducing look-alikes or importing animals. The number of litters per sire could also be increased to enlarge the population size without increasing the rate of inbreeding. These sires should have equal chances of producing offspring.

In short, with the current inbreeding rates being close to zero, *De Ierse Setter Club* is already doing well at limiting the rate of inbreeding. However, in the long term it is inevitable that the inbreeding rate will rise due to the small population size. The rate of inbreeding can be limited by implementing the recommended measures in the current breeding program. A detailed description of these recommendations can be found in the conclusion of this study.

Samenvatting

Het fokken van rashonden brengt verschillende problemen met zich mee. Door selectie op bepaalde kenmerken en het fokken binnen een gesloten populatie, stijgt de inteelt en wordt de genetische diversiteit lager, wat resulteert in genetische aandoeningen. Deze studie analyseert inteelt en verwantschap in de populatie Ierse Rode Setters en Ierse Rood-Witte Setters om aanbevelingen op te kunnen stellen, die de Ierse Setter Club kunnen ondersteunen bij het behoud van genetische diversiteit en het controleren van inteelt. Eerst werd een stamboomanalyse uitgevoerd en werden verschillende populatieparameters bepaald. Vervolgens werden simulaties met verschillende fokmaatregelen uitgevoerd om de invloed van deze maatregelen op de inteelt vast te stellen.

De kleine populatie van Ierse Setters zorgt voor een groot risico op inteelt. Jaarlijks worden gemiddeld 40 nesten geboren in de Ierse Rode Setter en slechts 6 nesten in de Ierse Rood-Witte Setter. Het generatie interval van 4,5 en de gemiddelde worpgrootte van 8,4 en 6,5 voor respectievelijk de Ierse Rode Setter en Ierse Rood-Witte Setter zijn hoog in vergelijking met andere rassen. In de Ierse Rode Setter was in de periode van 1950 tot 1989 ΔF_{gen} = 1,18%, waarbij een groot risico op genetische aandoeningen en zelfs het risico op uitsterven van het ras bestaat. Van 1990 tot 2017 was ΔF_{gen} = -0,37%. Deze inteelttoename is erg laag. Om de inteelttoename laag te houden op lange termijn, moet de populatie groot zijn. In de Ierse Rood-Witte Setter is ΔF_{gen} = 4,71% tussen 1975 en 1996, wat een groot risico op uitsterven met zich meebrengt. Vanaf 1997 tot heden wordt de inteelttoename veel lager , namelijk ΔF_{gen} = -0,15%. Opnieuw moet de populatie groot zijn om de inteelttoename laag te houden op lange termijn. De fokpopulatie in de Ierse Rode Setter is momenteel geschat op 33 reuen en 80 teven en op 5 reuen en 11 teven in de Ierse Rood-Witte Setter. Door middel van simulaties werden de beste maatregelen om inteelt te beperken vastgesteld. Het grootste effect werd bereikt door de verwantschap met de rest van het ras te beperken en tegelijkertijd de verwantschap tussen ouders te minimaliseren. Het vergroten van de fokpopulatie bleek ook zeer effectief. Dit kan worden gerealiseerd door *look-alikes* te introduceren of door dieren uit het buitenland te importeren. Het is belangrijk dat deze dieren minder of niet verwant zijn aan de Ierse Setter populatie. Bij de Ierse Rode Setter kunnen ook meer dieren uit de huidige populatie gebruikt worden als fokdieren, in plaats van *look-alikes* of buitenlandse dieren te introduceren. Het aantal nesten per vader kan ook worden verhoogd, om de populatiegrootte toe te laten nemen, zonder dat de inteelttoename per generatie stijgt. Deze vaders moeten gelijke kansen hebben om nakomelingen te produceren.

Kortom, met de huidige inteelttoename van bijna nul over de afgelopen jaren, is de Ierse Setter Club al goed op weg om de inteelttoename te beperken. Op lange termijn is het echter onvermijdelijk dat de inteelttoename zal stijgen, door de kleine populatiegrootte van de Ierse Setter. De inteelttoename kan beperkt worden door de aanbevolen maatregelen in het huidige fokprogramma te implementeren. Een gedetailleerde beschrijving van deze aanbevelingen vindt u bij de conclusies van deze studie.

1. Introduction

1.1 Domestication

The dog (*Canis familiaris*) is the first species to be domesticated by humans. It is clear that the dog originated from the wolf (*Canis lupus*), but its exact history regarding the manner and location of domestication is still subject of discussion. Due to selection on traits that were important for humans, diversification of breeds started around 3000 to 4000 years ago. From around 1800 onwards, the breeding of dogs started to intensify and hundreds of new breeds arose. Registration and pedigrees were introduced to enable breeding in closed populations. Dogs were bred further as guard dogs, to herd cattle, for different hunting purposes, to drag chariots or for companionship (Bosch and van der Poel, 2014).

1.2 Breeding programs and inbreeding

Nowadays, responsible breeding programs do not only look at animals that meet the breeding goal the best, but also take kinship and inbreeding into account. Inbreeding is the result of breeding animals with a common ancestor, thus breeding animals with shared alleles. Non-random mating might increase the chance of offspring getting the same alleles from both parents, resulting in increased homozygosity. Homozygosity causes identical recessive alleles to combine and to express a trait that is otherwise not expressed. In other words inbreeding exposes recessive alleles through the increase of homozygosity (Oldenbroek & van der Waaij, 2015). To get a good image of the inbreeding in a population, the population first has to be monitored.

The rate of inbreeding (ΔF) in a population can be estimated by:

$$\Delta F = \frac{1}{8N_m} + \frac{1}{8N_f}$$

with N_m being the number of breeding males and N_f the number of breeding females. This rate depends on a combination of the proportion of breeding males to females, the number of breeding males and breeding females and fluctuation in population size. In small populations, having a small number of breeding males and females, the rate of inbreeding will be large (Oldenbroek & van der Waaij, 2015). By maximising the number of breeding animals, the rate of inbreeding can be lowered.

The number of litters and pups per father, as well as the average number of offspring per year of birth of the parents both influence the share of genes in the next generation. If the number of offspring per father or mother is very high, this means that their genes are present in larger numbers in the next generation. This results in a higher level of kinship in the next generation, because a large number of individuals descends from the same ancestor.

The rate of inbreeding can become too high and cause problems, even with a responsible breeding goal that not only focusses on the appearance of an animal but also on its behaviour, welfare and health. The advice is to keep the rate of inbreeding below 0.5% per generation. If the rate of inbreeding per generation is below 0.25%, the minimum number of breeding males should exceed 100 to maintain this low rate in the long term (Oldenbroek & Windig, 2012).

Within a breed there are different measures which can be taken to control inbreeding. These measures mainly focus on preventing an animal to get a too high percentage of the offspring which eventually will result in forced inbreeding: having to breed with strongly related animals. The three main measures that might be taken are explained below:

1. Enlarging the breeding population
   Firstly, this can be realised by enlarging the number of dams and sires from which breeding animals are selected, for example by not castrating male pups. A second way to enlarge the breeding population is by importing animals from the same breed from abroad. These breeds have been separately bred for a longer period of time, resulting in less related animals than those in The Netherlands. A third option is to enlarge the population of breeding animals by schematic crossbreeding with animals from another breed.
2. Male and female breeding restrictions
   The rule that one breeding animal should not provide more than 5% of the pups in the next generation is a good measure to limit relatedness of the breed. In general, in The Netherlands the number of litters a pedigreed breeding dam can have is limited to five, while for the sires there is no mandatory limitation yet. A limitation can prevent that one sire gets an enormous share in the next generation. Therefore most breeds have set a maximum to the number of females serviced per male.
3. Breeding policies managing kinship
   Kinship between potential parents can also be looked at, to reduce inbreeding in future generations. One way is to constrain mean kinship with the remainder of the breed. Animals that have high mean kinship with the rest of the breeding animals are excluded from breeding. Another way is to minimise kinship between father and mother.

The effect of the measures listed above can be predicted using a computer simulation. In this simulation a breed will be mimicked with for example the real number of breeding sires and dams. By simulating mating and offspring over several generations, predictions can be made on the effect of breeding restrictions on the process of inbreeding (Oldenbroek & Windig, 2012).

1.3 Breed characteristics and genetic disorders

The Irish Setter descends from the Setting Spaniels, dogs bred for hunting on birds during the time there were no guns, and is the oldest native breed of Ireland. It developed on the spacious flat heaths and soggy peatlands of Ireland to one of the fastest Setter varieties. The early Irish Setters' coats were red and white and those dogs were called the Irish Red-White Setter. The fully red coated ones, which are more show dogs than hunting dogs, arose during the 19th century and were also called Irish Red Setters or Big Red. Nowadays, these two colour varieties – the Irish Red Setter and the Irish Red-White Setter – occur in very different numbers in the Netherlands. Almost all Red-White Setters disappeared for a longer period of time and the Dutch studbook consisted of Red Setters only, until 1975, when the population of Irish Red-White Setters started to grow. The number of Irish Red-White Setters is however still very low compared to the number of Irish Red Setters, and this variety will therefore have a higher chance of inbreeding.

The life expectancy for Irish Setters is 12 to 15 years. The wither height is 58-67 cm for males and 55-62 cm for females. The weight varies from 25 to 30 kg. Its coat is long, especially on the legs, belly and tail. The colour of the coat has to be gold maroon. The character of the dog is very gentle and kind and a bit more lively and impulsive than the English Setter (De Ierse Setter Club, 2015).

Irish Setters are classified as ‘high risk’ on heritable disorders (Rashondenwijzer, 2017). The most common disorders that occur in the Irish Setter are listed below. Especially hip dysplasia is of great concern. This is a painful joint disease for which a recovery operation is expensive. In addition, multiple brain disorders such as epilepsy and cerebellar ataxia, various eye disorders (cataract, PRA, entropion), allergy and stomach twisting (gastric dilatation volvulus) occur in the Irish Setter (Rashondenwijzer, 2017). Many of these can be reduced or eliminated by selective breeding and genetic testing. Inbred individuals are more likely to express autosomal recessive disorders due to homozygosity. Therefore diseases might show up in the future due to inbreeding, that are not yet visible or known to cause any problems. The conditions manifest at a young age.

Table 1. *Conditions with highest risk in The Netherlands (Rashondenwijzer, 2017).*

Condition	**Negative points[1]**	**Risk[2]**
Hip dysplasia – large dogs	(1.5 + 1.5) x 3 = **9**	
Atopy (environmental allergy)	(1.5 + 1.5) x 2 = **6**	
Cerebellar ataxia	(1 + 2) x 2 = **6**	
Stomach-dilatation-volvulus (stomach rotation)	(2 + 1) x 2 = **6**	
Cataract	(0.5 + 0.5) x 2 = **4**	
Epilepsy (‘falling disease’)*	(1 + 1) x 2 = **4**	
Progressive retina atrophy*	(2 + 2) x 1 = **4**	
Mega oesophagus (oesophagus dilatation)	(2 + 1.5) x 1 = **3.5**	
Colour dilution alopecia (baldness with discoloration)	(0.5 + 2) x 1 = **2.5**	
Entropion (inward curling eyelids)	(1.5 + 1) x 1 = **2.5**	
Larynx paralysis (paralysis of vocal cords)	(1 + 1) x 1 = **2**	
Ectropion (outward curling eyelids)	(0.5 + 1) x 1 = **1.5**	
Primary hypothyroidism (deficiency of thyroid hormone)	(0.5 + 0) x 3 = **1.5**	
Cherry eye (swollen third eyelid)	(0.5 + 0) x 2 = **1**	

[1](severity + treatability) x risk:
severity scored as moderately serious (0.5), serious (1) or very serious (2);
treatability scored as good (0), moderate (1) or bad (2);
risk scored as very small or unknown (0), small (1), large (2) or very large (3)
[2]Risk of the condition:
0 negative points: no sign;
0-3 negative points: 1 sign;
3-8 negative points: 2 signs;
8 or more negative points: 3 signs

1.4 Current breeding program

The Iris Setter Club follows the VFR (*verenigingsfokreglement)* since 2013, which is approved by the *Raad van Beheer*. Both colour varieties have their own VFR. The VFR includes several rules on breeding, which are similar for both varieties (Werkgroep Fokkerij & Gezondheid, 2016). The most important ones are the following:

- A dam cannot be mated with her grandfather, her father, her brother, her son or her grandson. The mating between half-brother and half-sister is also not allowed.
- The same combination of parents is only allowed twice.
- A sire and dam have to be at least 22 months of age before they may be used in breeding.
- A sire can only have 3 successful matings per year, with a maximum of 15 successful matings during his entire life. A successful mating is one in which at least one live pup is born (Werkgroep Fokkerij & Gezondheid, 2016).

1.5 Aim and research questions

The aim of this study is to formulate clear recommendations for *De Ierse Setter Club* that provide insight into the genetic diversity of the Irish Setter population. This requires analysis of the current population on population parameters, such as generation interval and number of breeding animals, pedigree completeness and inbreeding and kinship. Different breeding strategies, that show different results on the rate of inbreeding, will be assessed to give recommendations for future breeding. This led to the following research questions:

1. What is the population structure of the Irish Setter in the Netherlands and how did it evolve since the establishment of the studbook?

2. What are the differences between the Irish Red Setter and Irish Red-White Setter with respect to population parameters, pedigree completeness and inbreeding and kinship?

3. What will be the effect of different breeding strategies on the rate of inbreeding and which of these show the best results in the long term?

2. Materials and methods

To get a good impression of the current inbreeding in the population, a program called *inteeltmonitor* was used. The database of the Irish Setter population, received from *De Ierse Setter Club*, was uploaded in the program. This data included the following per animal: number, sex, name, variety, number sire, name sire, number dam, name dam, date of birth. With this data pedigree analysis was performed.

First of all the entire population, including both colour varieties, was monitored. Next to that, the population of Irish Setters was divided into two subpopulations, namely the Irish Red Setter and the Irish Red-White Setter. By doing this, the inbreeding coefficient of the different varieties could be calculated.

2.1 Pedigree analysis

The Irish Setter database contains a total of 36,787 animals, of which 4,175 animals without a year of birth. These 4,175 animals were not included in analyses in which year of birth was a necessary input parameter. Of the remaining 32,612 animals, 31,834 are Irish Red Setters, 768 are Irish Red-White Setters and 10 are Outcross Red x White. Analysis was not performed on the Outcross Red x White, because there were not sufficient animals of this variety to draw any conclusions from with regard to inbreeding. The data was scanned on possible duplicates, animals used as sire and dam (two sexes), animals born before their parents and unrealistic ages of parents. No duplicates were found. Neither were there animals that were born before their parents nor animals that had two sexes. To perform any further analysis *Microsoft Excel* was used.

Population parameters

The following population parameters were calculated and visualised with the use of *Microsoft Excel*:

Age of parents at birth offspring: the number of animals that have fathers and mothers of x years old. Calculated as the difference between date of birth of offspring and parents.

The number of litters per year: equal to the number of dams having bred per year, because each female dog can have only 1 litter per year. Defined as the number of female dogs that have produced offspring in a particular year.

The number of fathers per year: the number of male dogs that have produced offspring in a particular year.

The number of pups per litter: could also be defined as the average litter size in a particular year.

The number of litters per father per year of birth of the offspring: the average number of litters per father that had offspring in a particular year.

The number of pups per father per year of birth of the offspring: the average number of pups per father that had offspring in a particular year.

The average number of offspring per year of birth of the parents: the average number of total offspring per sire or dam per year of birth of the parent. Also the sire and dam with the most offspring were calculated.

Total number of animals per year of birth: number of newly registered dogs per year of birth, comprising new-born pups and founders. Separated intro males and females that were selected for breeding or not. If only a small amount of animals is used for breeding, this will result in a higher rate of inbreeding and a non-equal share of genes in the next generation.

Generation interval: the average age of fathers and mothers at birth of their offspring which will later be used for breeding.

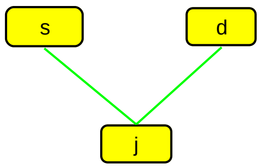
Pedigree completeness

Average generation equivalent: a measure for the completeness of a pedigree. The average generation equivalent is equal to the sum of all known ancestors, where every known ancestor is determined by $\frac{1}{2^n}$. With n being the number of generations between the ancestor and an individual.

Number of fully known ancestral generations: the number of animals that have 1, 2, 3, 4 or more than 5 ancestral generations that are fully known. If the average generation equivalent is low, or a high proportion of animals has less than 5 ancestral generations known, the calculation on kinship is unreliable.

Inbreeding and kinship

The *inbreeding coefficient* (*F*) and *kinship coefficient* (*f*) were calculated by *inteeltmonitor.* The kinship between two individuals is equal to the inbreeding coefficient of their hypothetical offspring. For example in the pedigree on the right the following formula holds: $F_j = f_{s,d}$



The rate of inbreeding in two consecutive years can be calculated with

$$\Delta\bar{F}=(\bar{F}_t-\bar{F}_{t-1})/(1-\bar{F}_{t-1})$$

with $\Delta\bar{F}$ as the inbreeding rate in that year, $\bar{F}_t$ is the average inbreeding coefficient of individuals born in year t and $\bar{F}_{t-1}$ is the average inbreeding coefficient of pups born in the previous year (Oldenbroek & Windig, 2012).

The inbreeding rate over a longer period can be calculated with

$$\Delta\bar{F}= 1 - [(1-\bar{F}_t)/(1-\bar{F}_{t-x})]1/x$$

with F_t the inbreeding in year t and F_{t-x} the average inbreeding x years ago (Oldenbroek & Windig, 2012).

To get the inbreeding rate per generation over this period, the $\Delta\bar{F}$ over this period is first multiplied with 100 to get to a percentage and is next multiplied with the generation interval, because the slope is on a yearly basis. Estimating $\Delta\bar{F}$ with this formula has the disadvantage that it takes only two points (at t-x and t) into account.

If we would like to predict $\bar{F}_x$ in a specific year given a constant inbreeding rate, the formula above can be transformed to the following formula:

$$\bar{F}_x = 1-(1- \Delta\bar{F})^t$$

When we produce a graph of $\bar{F}_x$ against t, the slope at a particular point is equal to the inbreeding rate at that moment. To determine the slope (i.e. get the derivative), a natural log transformation is used which then produces a linear relationship:

$\ln(1-\bar{F}_x) \approx -\Delta\bar{F}\,x + \ln(1-\bar{F}_0)$.

This formula reproduces a linear graph of $\ln(1-\bar{F}_x)$ against t, with the slope being equal to $-\Delta\bar{F}$. The advantage is that it takes the inbreeding levels in each year into account rather than just the start- and endpoint.

2.2 Simulation of possible measures

The Irish Setter population was mimicked with the real number of breeding sires and dams to look at the inbreeding over several generations by simulating mating and offspring. The program *Genetic Management Simulation* was used for this simulation.

The number of years in the future for which the program calculates inbreeding and kinship has to be chosen, as well as the *number of repeats*. Due to variation all calculations have to be repeated for a chosen number of times to get a reliable average calculation. The number of years is set to 25 and the number of repeats to 25 for the Irish Red-White Setter. For the Irish Red Setter the number of years is set to 100 and due to time limitations the number of repeats is set to 10 (because of the large number of Red Setters, it takes longer to perform 25 repeats).

The following parameters were set and first had to be calculated from pedigree analysis data as input for the *Genetic Management Simulation* program.

Population size

The number of breeding males and breeding females in the Irish Red Setter and Irish Red-White Setter have to be entered. These can be calculated with the data on number of litters and number of fathers. The average number of nests between 2010 and 2016 is an indicator for the number of breeding females because every female gets on average one nest every two years. So the number of breeding females will be two times as large as the average number of nests per year. On the other hand, each breeding male gets one or more nests every year. Therefore the number of breeding males is equal to the average amount of fathers per year between 2010 and 2016. The year 2017 is excluded because data are not yet complete.

The number of litters per year will be averaged over the period between 2010 and 2016 as well.

The champion sires are also an important parameter for the program, with its corresponding *percentage of offspring* in the population. This will influence inbreeding, because if the champion sires have a large percentage of offspring, they will have a large share in the next generation and kinship will get higher in this generation, because a large amount of offspring descends from the same father, resulting in inbreeding in the generation after that. The champion sires are calculated over the period of 2007 to 2017.

Biological data

The age structure of the parents is calculated as the number of offspring that has a parent of x years old, divided by the total amount of offspring over the period of 2007 to 2017.

The age of female at her first litter is set to 22 months (Werkgroep Fokkerij & Gezondheid, 2016).

Litter size is calculated by counting the number of pups per unique combination of father, mother and date of birth between the period of 2012 and 2017 in the Irish Red Setter and between the period of 2007 and 2017 in the Irish Red-White Setter.

Breeding policy

Maximum number of females serviced per male per year and per life are entered in the program. By restricting these numbers, one male will be prevented of getting a large share in the population. By lowering the number of serviced females per year, and at the same time making the number of females serviced per life higher, males may be used for a longer period of time.

The maximum number of sons selected as breeding male per male dog is another way to prevent one male from getting a large share in the population. If a father gets a large number of male pups, not all of his pups may be used for breeding and therefore his genes will not get a large share in the population. For this simulation only the maximum number of females serviced per male will we looked at. The maximum number of sons selected will be set to 1000 (no maximum).

The maximum number of litters per female per life is set to 5, which is the current restriction for breeding dams in the Netherlands (Oldenbroek & Windig, 2012). By changing this number the share of genes of mothers in the population can be influenced. Because a mother on average has one litter every 2 years and is only used till the age of 7 or 8, she cannot have a very large number of litters, therefore this is already sort of a restriction. The current restriction of *De Ierse Setter Club* is set to 3 (Werkgroep Fokkerij & Gezondheid, 2016). Effects of this more strict breeding policy on the inbreeding rate will be assessed.

After calculation of the unknown parameters, the program can be run. First the program will be run with the parameters listed in Appendix I. Next the program will be run with different measures:

1. *Enlarging the breeding population*: the number of breeding males and females will be enlarged. More animals will be used for breeding, that are not yet included in the breeding program.
2. *Male and female breeding restrictions*: the number of litters will be spread more evenly over the number of breeding males and females. The maximum number of litters per breeding dam is changed to a less strict and a more strict policy and different values for the maximum number of females serviced per male per year and per life will be assessed.
3. *Breeding policies managing kinship*: animals with the lowest kinship will be crossed over several generations or animals with high mean kinship to the rest of the population are excluded from breeding. A combination of these two measures is also entered in the program.

3. Results

3.1 Pedigree analysis

Population parameters

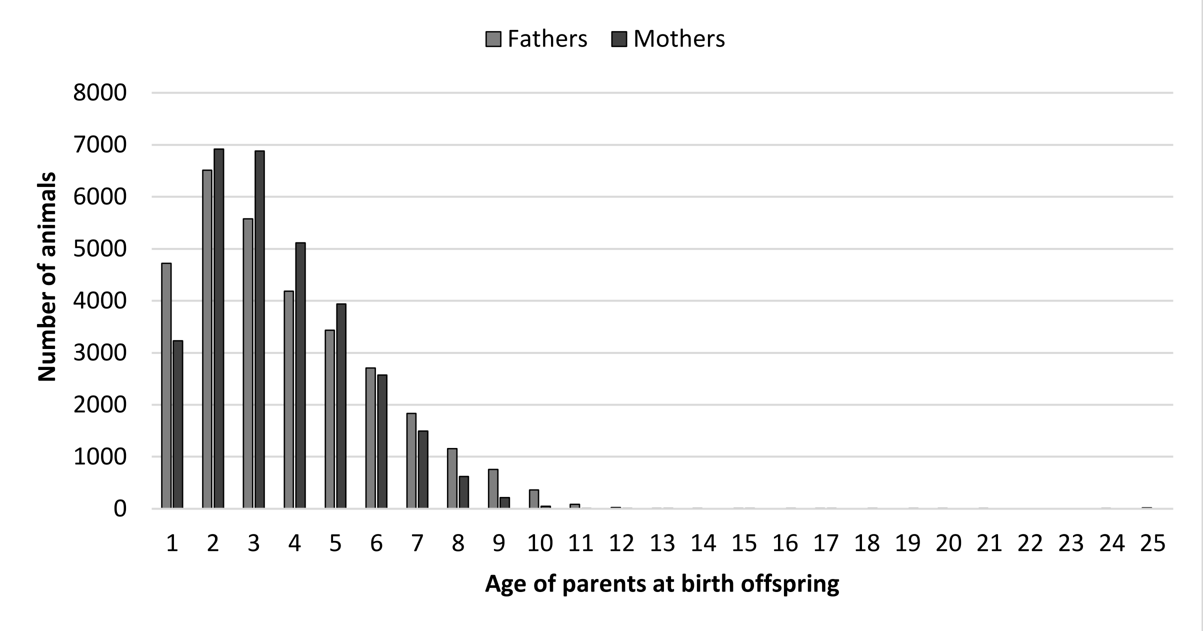


Figure 1. *The number of animals that have fathers and mothers of x years old.*

The life expectancy of Irish Setters is 12 to 15 years. Nowadays, females and males are only allowed to be used in breeding after the age of 22 months. Females may not be used after the age of 70 months if she has not had pups yet, and after the age of 94 months if she has had pups before (Werkgroep Fokkerij & Gezondheid, 2016).This has not always been the case, leading to lots of animals that have parents that are younger or older than allowed (figure 1). Mothers are used for breeding till the age of about 7 to 8 years. There are 280 animals that have a mother that was older than 8 years at time of birth. Some mothers are even used till the age of 19. Figure 1 also shows that 18 animals have a father older than 20 years. This is quite unrealistic, because the life expectancy is only 12 to 15 years. The parents that had offspring at later ages (>15y) are probably due to minor mistakes in notation (of for example date of birth or number sire/dam) in the database or animals that did actually still reproduce offspring at older ages in the past, before the establishment of the VFR. The 15 animals that have a father of 25 years old, are all born in 2000. Their father is Cornevon Westerhuy's Dream (born in 1975), having offspring from 1976 untill 1985 and one litter in 2000. This is most likely a mistake made during entering the sire number. This had no large influence on data analysis.

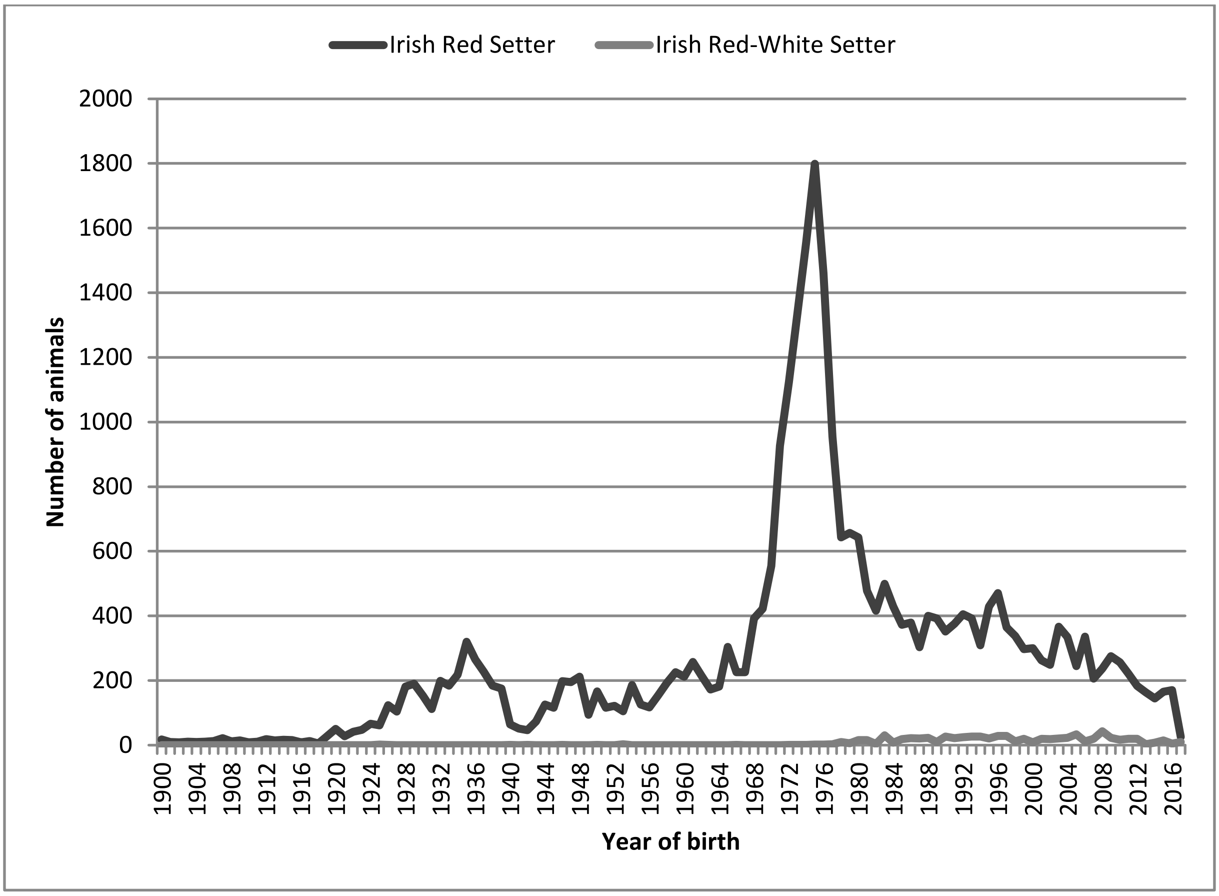


Figure 2. *The total number of Irish Red Setters and Irish Red-White Setters per year of birth from 1900 to 2017, comprising new-born pups and founders.*

In 1926 the number of Irish Red Setters rose above 100 for the first time. This probably is the case because in the beginning of the studbook, only the animals that became parents were registered. The number of Irish Red Setters born peaked in 1975 with a number of 1799 animals. After that the population declined again to 170 animals born in 2016. The number of Irish Red-White Setters started to rise in 1975, with a maximum of 43 animals born in 2008 (figure 2).

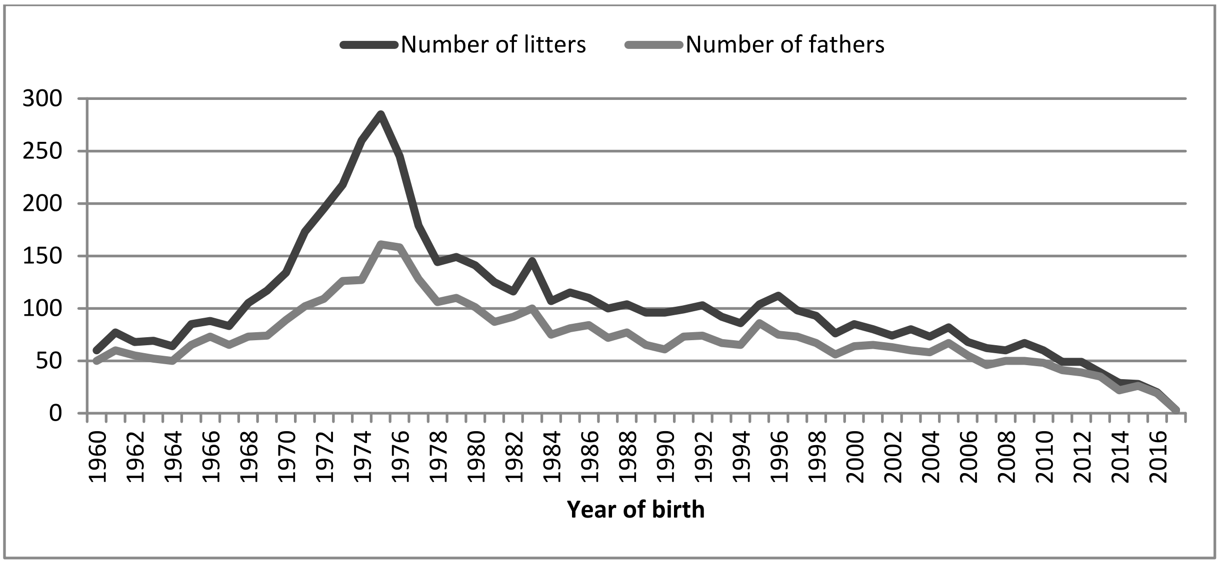


Figure 3. *The number of litters and number of fathers per year of birth of the offspring in the Irish Red Setter from 1960 to 2017.*

The number of litters rose to a maximum in 1975 of 285 litters in one year, the number of fathers also rose to its maximum in that year (figure 3). Because of this rise in fathers, the number of litters per father remained more or less equal during the entire period (figure 4). The number of pups per litter, also defined as litter size, fluctuates over the years. The litter size also peaked in 1975, resulting in more pups per father. These fathers therefore have a larger allele retention in the population. The number of pups per litter and per father is starting to rise again nowadays (figure 4).

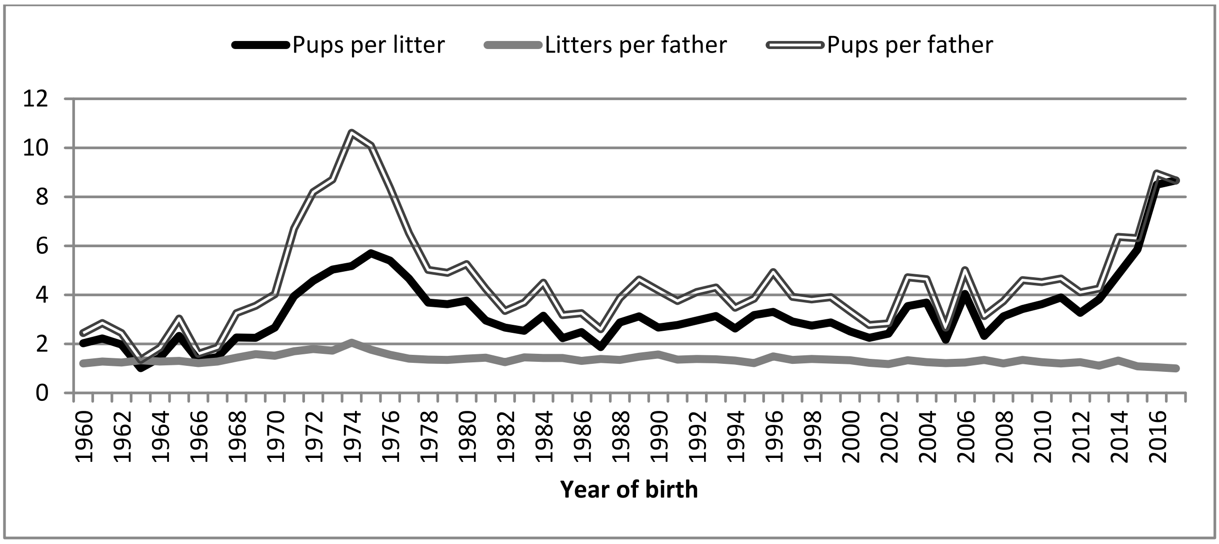


Figure 4. *The number of pups per litter (litter size), the number of litters per father and the total number of pups per father. All per year of birth of the offspring in the Irish Red Setter from 1960 to 2017.*

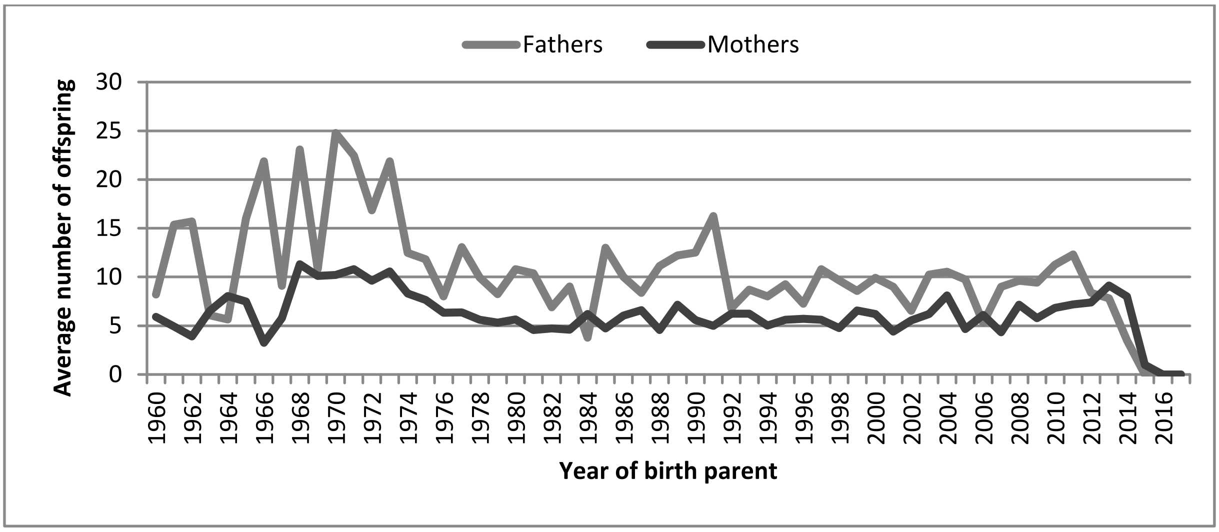


Figure 5. *The average number of offspring per father and per mother, per year of birth of the parents. In the Irish Red Setter from 1960 to 2017.*

The parents born in the period just before 1975, when there was a peak in population size, also show larger average numbers of offspring than parents born in the period before that (figure 5). The father with the most offspring is Harvey of the Hunter's Home, born in 1985, having 288 descendants. The mother with the most offspring is Phydes of the Chestnutgarden, born in 1971, having 70 descendants. Figure 5 shows strong variation over the years due to births of parents that are much more popular than others, resulting in higher average number of offspring (popular sire effect).

Litters in the Irish Red-White Setter

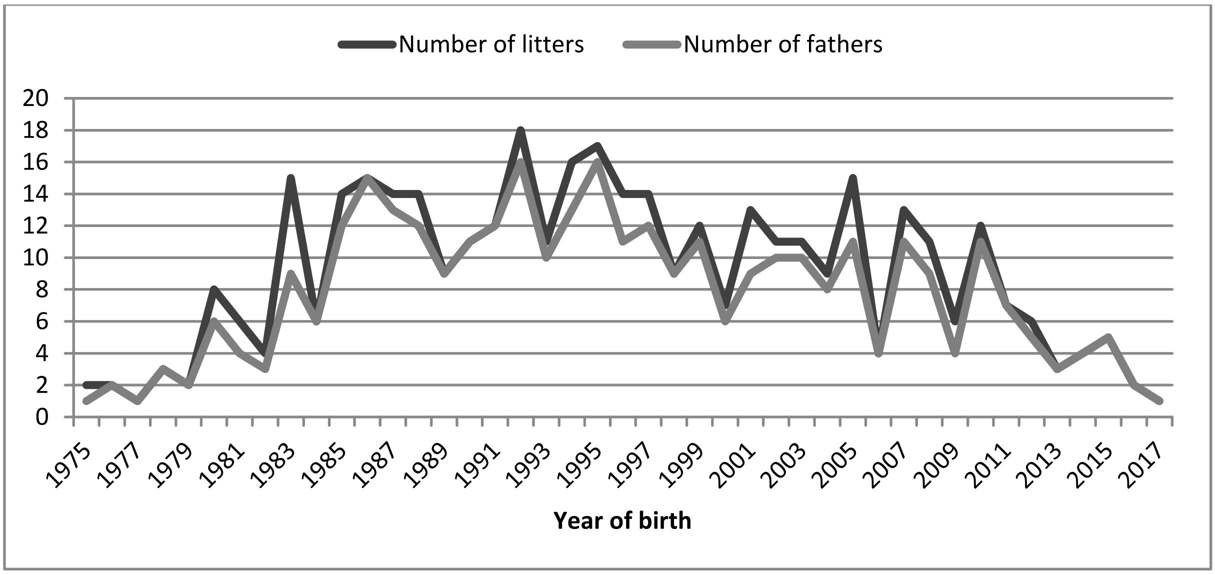


Figure 6. *The number of litters and number of fathers per year of birth of the offspring in the Irish Red-White Setter from 1975 to 2017.*

The number of litters and number of fathers vary equally over the years, resulting in a more or less equal amount of litters per father. Due to the higher amount of pups per litter in some years, these fathers also have a higher number of pups, resulting in a higher allele retention in the population (figure 6 and 7). The father with the most offspring is Yesterday's Hero Woodywoodstock, born in 2003, having 32 descendants. The mother with the most offspring in the population is Corranroo Cartier, born in 2001, having 24 descendants. The litter size is strongly rising since 2007.

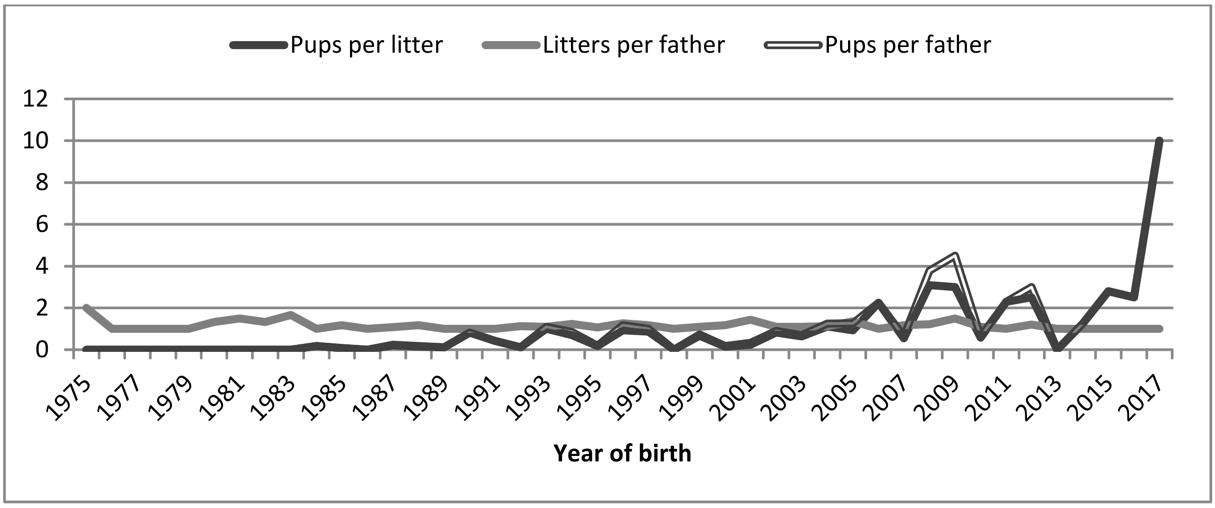


Figure 7. *The number of pups per litter (litter size), the number of litters per father and the total number of pups per father. All per year of birth of the offspring in the Irish Red-White Setter from 1975 to 2017.*

Figure 8 shows strong variation over the years, just like in the Irish Red Setter. This is also due to the fact that some animals are used much more than others, resulting in a higher number of offspring per parent.

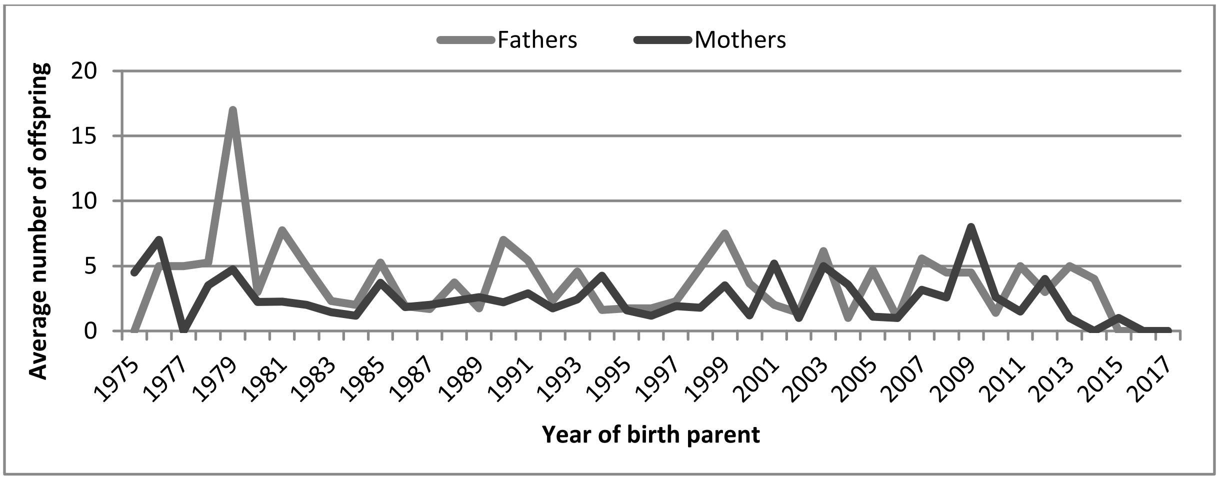


Figure 8. *The average number of offspring per father and per mother, per year of birth of the parents. In the Irish Red-White Setter from 1975 to 2017.*

Breeders in the two different colour varieties

The number of newly registered animals in the Irish Red Setter, comprising of new-born pups and founders, rose until 1975 and started to decline after that (figure 9). Unless the large number of newly registered Irish Red Setters, the number females and males that are selected for breeding is very small, resulting in a non-equal share in the population. In the Irish Red-White Setter however, much more animals are selected for breeding, resulting in a more equal share of genes in the population (figure 10). In both colour varieties, males and females born since 2015 have not been used for breeding yet (except for 1 female in the Irish Red-White Setter).

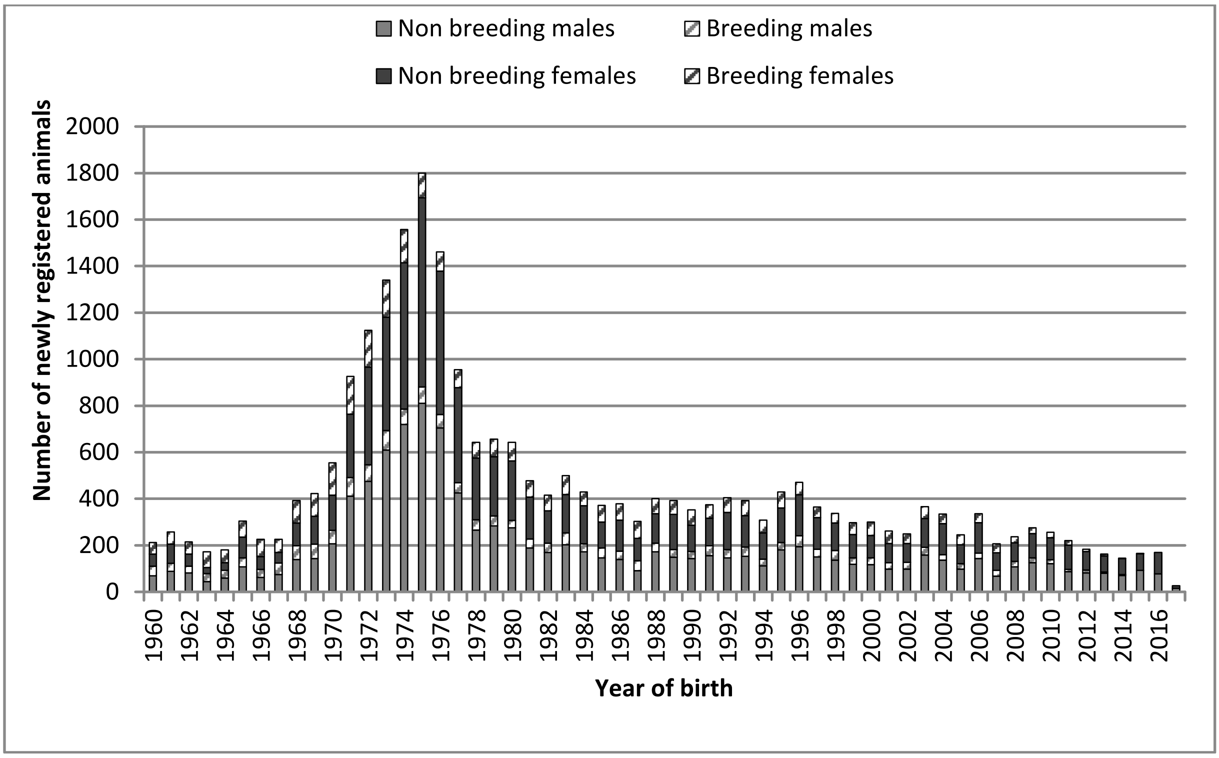


Figure 9. *The number of newly registered Irish Red Setters per year of birth from 1960 to 2017, comprising new-born pups and founders, that were either selected for breeding or not (yet).*

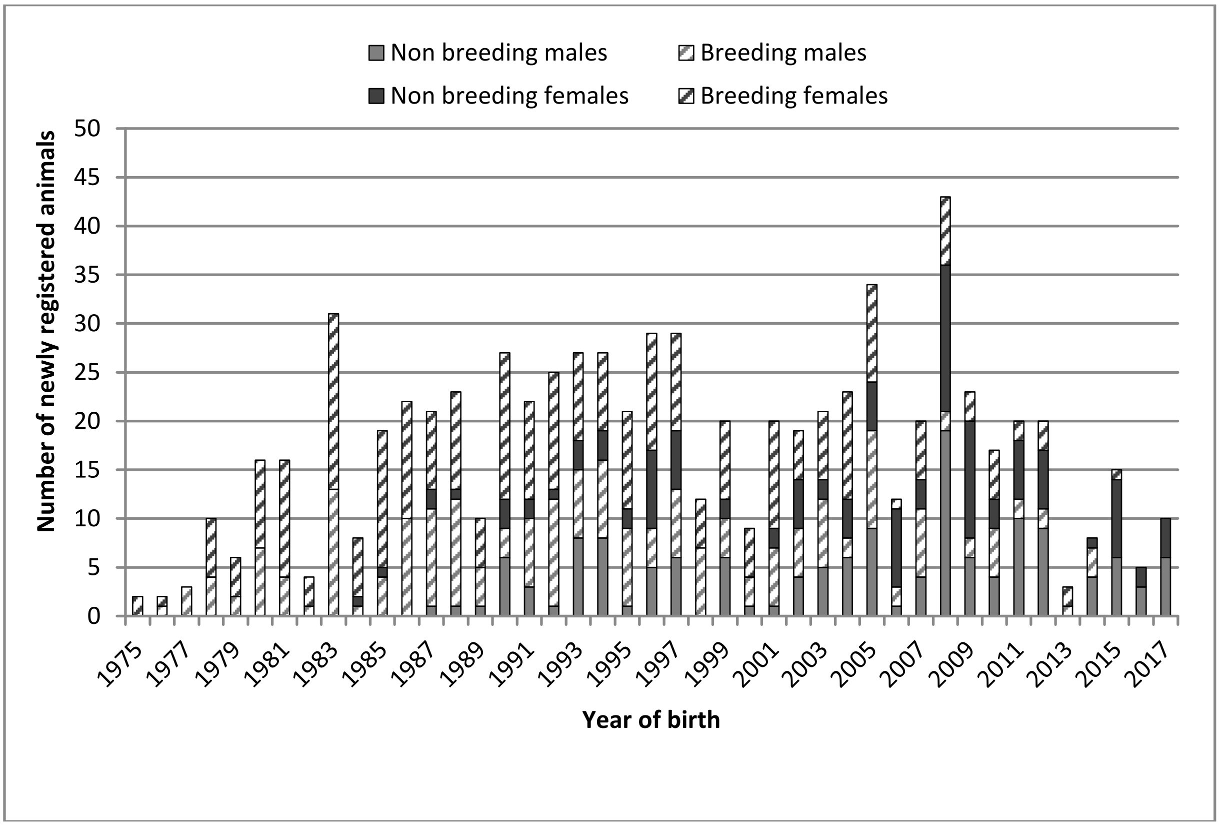


Figure 10. *The number of newly registered Irish Red-White Setters per year of birth from 1975 to 2017, comprising new-born pups and founders, that were either selected for breeding or not (yet).*

Generation interval

The average age of the parents at birth of their offspring fluctuated strongly until 1977, but after that became more or less constant. Therefore the generation interval remained constant over the last years at about 4.5 (figure 11). This value could be interpreted as that every 4.5 years the average generation equivalent should rise by 1, because every 4.5 years a new ancestral generation is known. In the period just before 1975 the generation interval is at its minimum, this is probably because young animals were used for breeding too in these years, resulting in a peak in the population size in 1975 (figure 11).

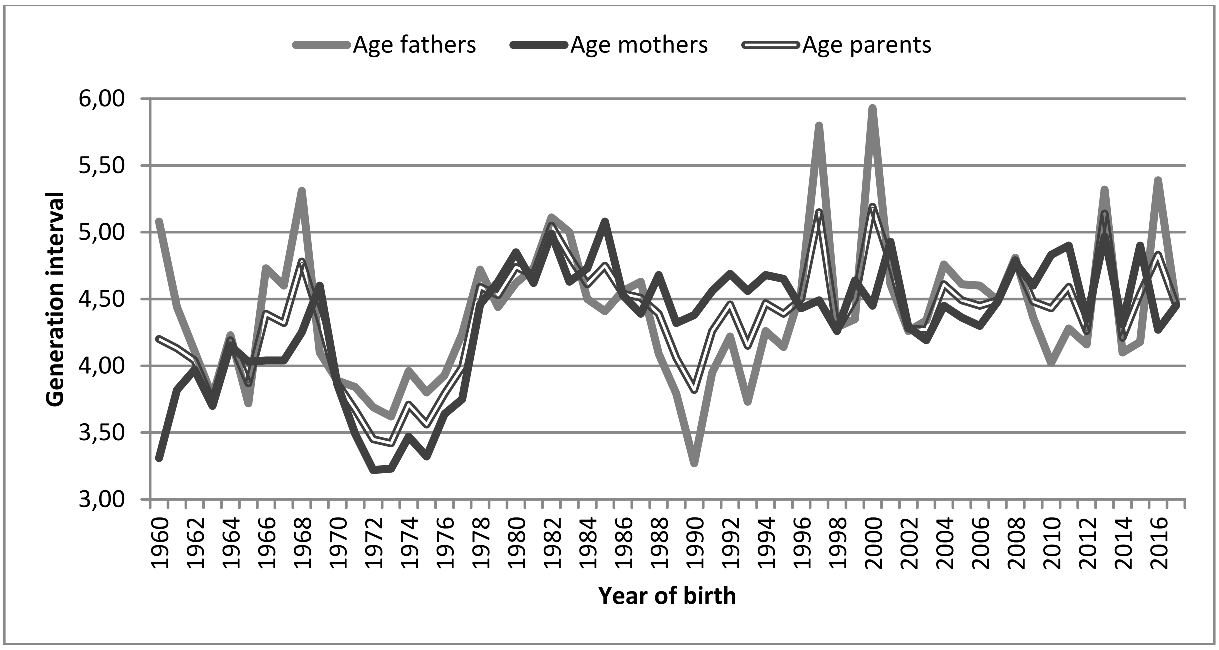


Figure 11. *The average generation interval. With average age of fathers, mothers and parents at birth of their offspring. For the total population from 1960 to 2017.*

Pedigree completeness

As shown in figure 12, the average generation equivalent rises from about 12 in 1950 to about 26 in 2017 in the Irish Red Setter. When adding the trendline, the equation is y = 0.2249x + 12.322. Meaning that every year the average generation equivalent rises by 0.2249. So every 4.5 years the average generation equivalent in the Irish Red Setter rises by 1.01, which is almost equal to the amount expected when looking at the generation interval. In the Irish Red-White Setter the average generation equivalent rises from 9.5 in 1975 to about 20 in 2017. The equation belonging to this trendine is y = 0.229x + 3.0901. So every year the average generation equivalent in the Irish Red-White Setter rises by 0.229. Every 4.5 years this is an increase of 1.03.

Figure 12. *The average generation equivalent in the Irish Red Setter and the Irish Red-White Setter from 1950 to 2017.*

As said before, you would expect that every 4.5 years, one more ancestral generation is completely known. Figure 13 and 14 show the proportion of individuals in the Irish Red Setter and the Irish Red-White Setter with the corresponding number of ancestral generations that are completely known per year. In the Irish Red Setter population, all individuals have more than 5 ancestral generations known nowadays. In the Irish Red-White Setter the pattern is very irregular, in 2013 and 2016 there is a large proportion of individuals that only have 2 and 3 completely known ancestral generations respectively. While in the years before, more than 5 ancestral generations were completely known. This could be due to that new dogs are registered. These dogs' pedigrees only consist of parents, grandparents and great grandparents. Therefore less than five ancestral generations are completely known, while in the years before the registration of the new dogs, more than five generations were completely known.

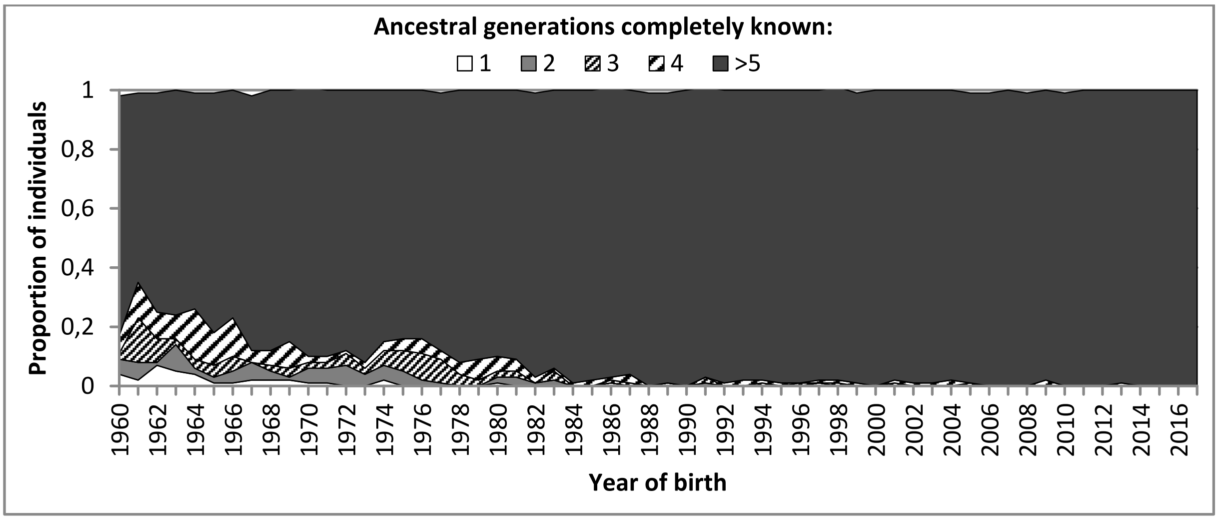


Figure 13. *The proportion of individuals in the Irish Red Setter with x ancestral generations completely known from 1960 to 2017.*

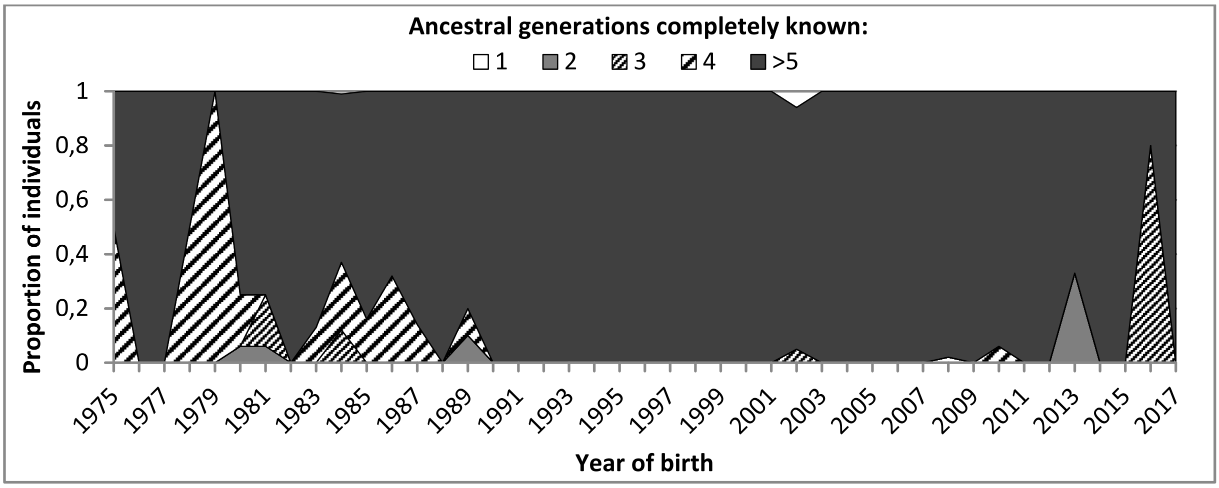


Figure 14. *The proportion of individuals in the Irish Red-White Setter with x ancestral generations completely known from 1975 to 2017.*

Inbreeding and kinship

The inbreeding coefficient and kinship coefficient of the Irish Red Setter and Irish Red-White Setter are shown in figure 15 and 16.

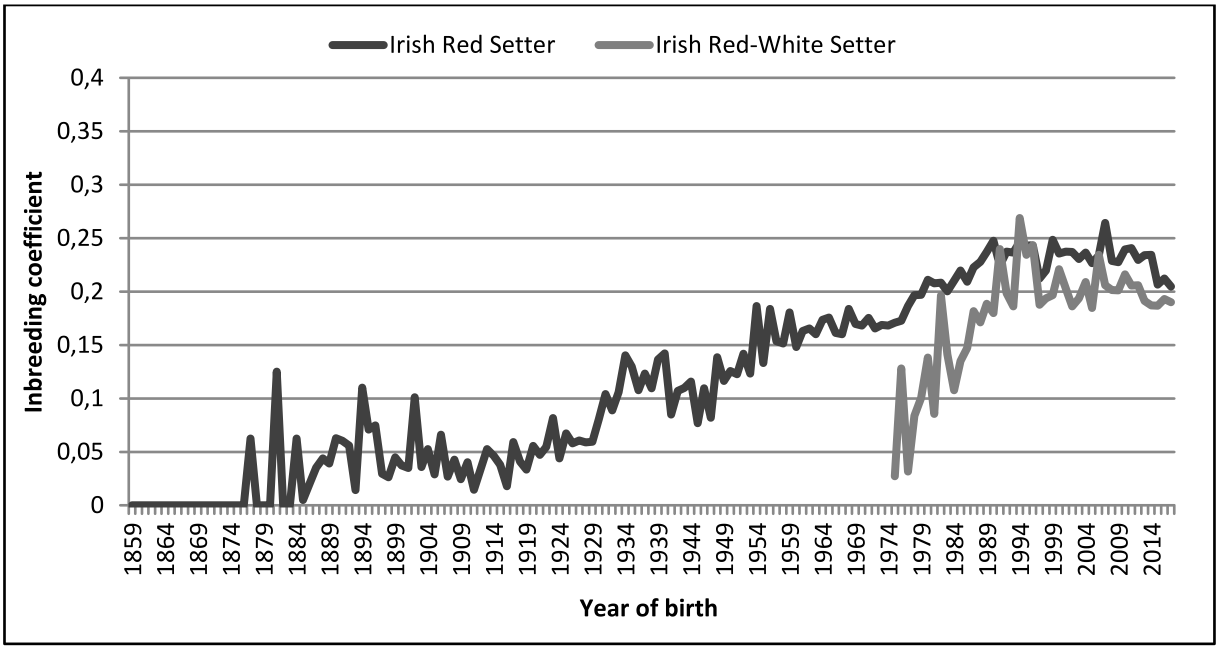


Figure 15. *The average inbreeding coefficient (F) in the Irish Red Setter and Irish Red-White Setter from 1859 to 2017.*

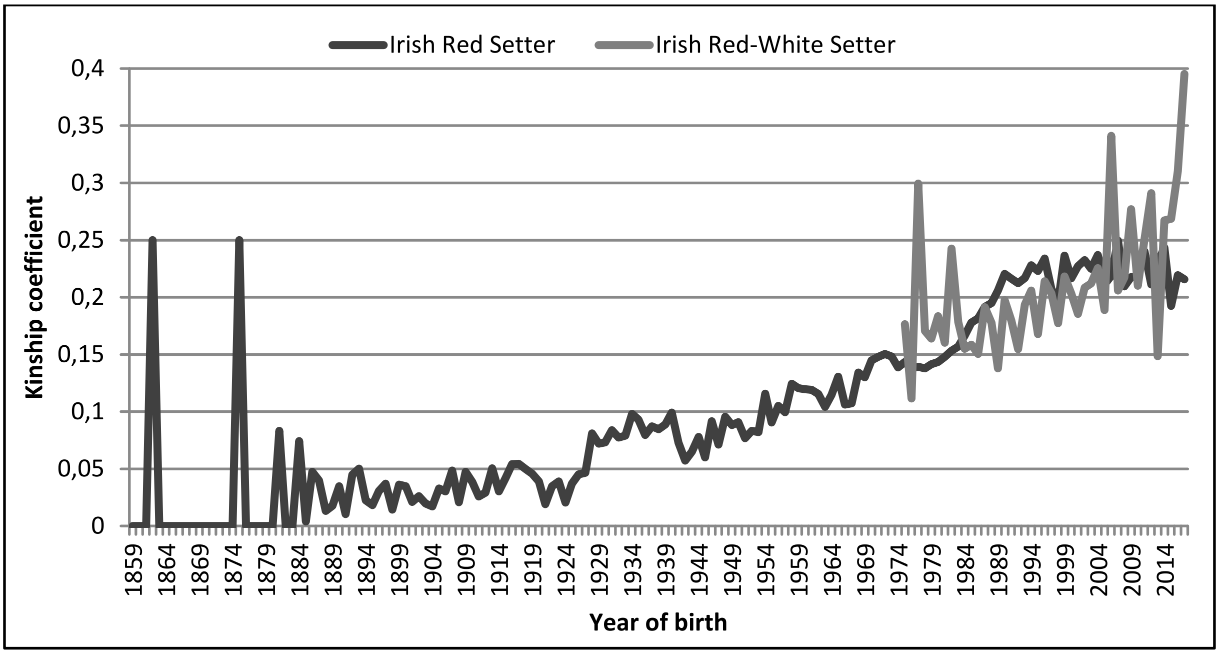


Figure 16. *The average kinship coefficient (f, including self) in the Irish Red Setter and Irish Red-White Setter from 1859 to 2017.*

Inbreeding and kinship in the Irish Red Setter

In the period between 1950 and 1989 F increased with 0.0026*100%*4,5 = 1.18% per generation and Δf was 1.29% per generation. From 1990 to 2017 the inbreeding became quite steady with ΔF being -0.0008*100%*4,5 = -0.37% per generation (figure 17). In the same period also the kinship coefficient remained more or less equal with Δf = 0.04% per generation.

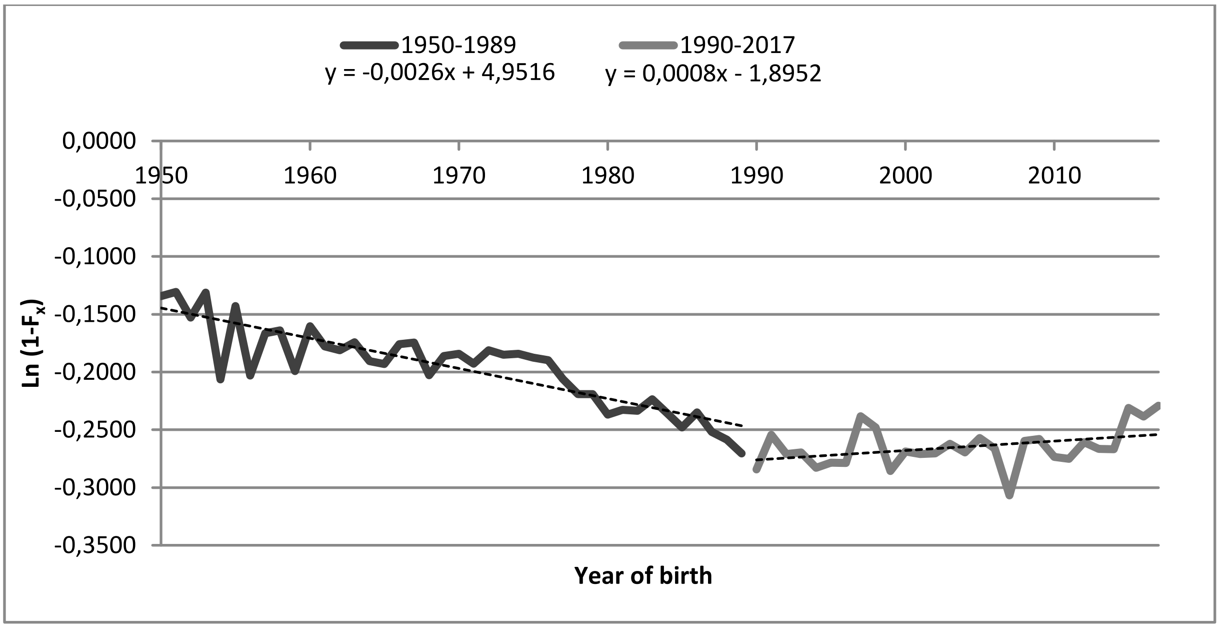


Figure 17. *Logarithmic regression of 1-F_x against the year of birth for the periods 1950-1989 and 1990-2017 for the Irish Red Setter. The slope represents the average inbreeding coefficient per year (-ΔF).*

Inbreeding and kinship in the Irish Red-White Setter

From 1975 onwards the inbreeding coefficient started rising until 1996. After this the rate of inbreeding became more or less equal to zero, while the kinship coefficient rises (figure 15 and 16). In the period between 1975 and 1996 F rises with 0.0105*100%*4,5 = 4.71% per generation and f with -0.02% per generation. From 1997 till now ΔF is equal to -0.0003*100%*4,5 = -0.15% per generation with a corresponding Δf of 3.48% per generation (figure 18).

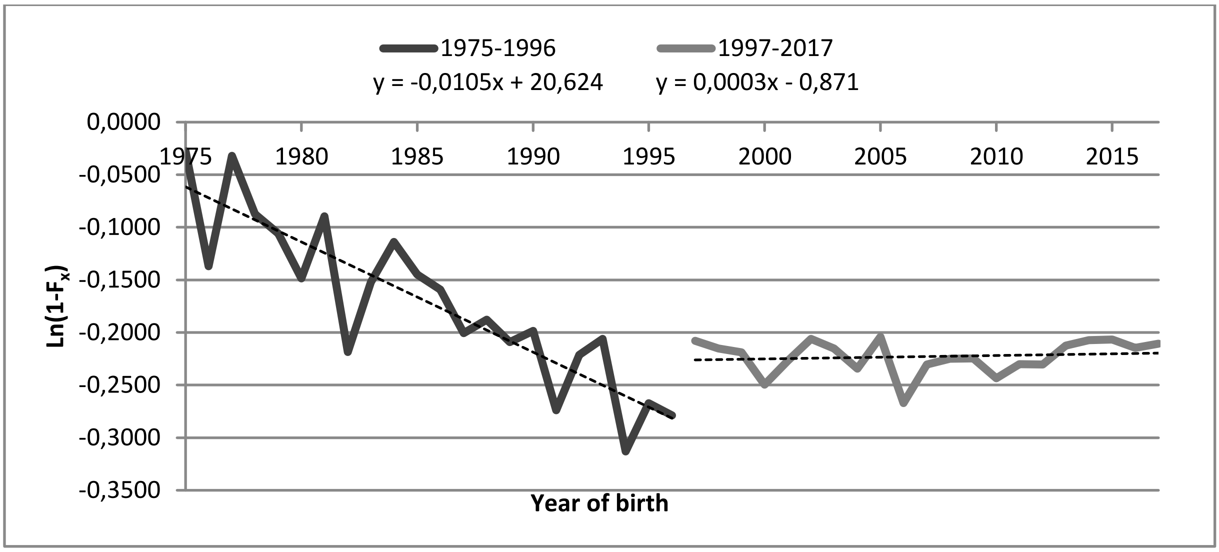


Figure 18. *Logarithmic regression of 1-F_x against the year of birth for the periods 1975-1996 and 1997-2017 for the Irish Red-White Setter. The slope represents the average inbreeding coefficient per year (-ΔF).*

3.2 Simulation of possible measures in the Irish Red Setter

All input parameters that were calculated are included in appendix I. The results of simulating different breeding strategies are presented below. These input parameters are the same over all simulations, unless shown otherwise. By simulating the current population with the current restrictions over a period of 100 years as shown in appendix I, ΔF_{gen} = 0.67% with a minimum of 0.69% and a maximum of 0.84%. This is higher than the above calculated current inbreeding rate of -0.37%.

Enlarging the breeding population

The effect of increasing the breeding population of Irish Red Setters on the inbreeding rate is shown in table 2. By doubling the breeding population (adding 80 females and 33 males) a decrease in ΔF_{gen} of 0.19% to 0.57% can be achieved. By adding 17 males (+50%) ΔF_{gen} decreased with 0.06% and by adding 20 females (+25%) ΔF_{gen} decreased by only 0.02%. So in absolute numbers, increasing the number of breeding males is more effective than increasing the number of breeding females. Likewise, when adding only 33 males (+100%), ΔF_{gen} decreases with 0.14%, while an addition of 80 females (+100%) only results in a decrease of 0.06%.

Table 2. *Effect of increasing the number of available breeding males and females per year on the mean ΔF_{gen} (in %) of 1 simulated population of Irish Red Setters repeated 10 times.*

Males available for breeding	Females available for breeding			
	n = 80 (baseline*)	n = 100 (+25%)	n = 120 (+50%)	n = 160 (+100%)
n = 33 (baseline*)	0.76 (0.69-0.84)	0.74 (0.67-0.80)	0.73 (0.66-0.79)	0.70 (0.64-0.77)
n = 41 (+25%)	0.71 (0.65-0.75)	0.71 (0.65-0.76)	0.66 (0.60-0.71)	0.64 (0.55-0.72)
n = 50 (+50%)	0.70 (0.60-0.80)	0.66 (0.55-0.75)	0.67 (0.60-0.76)	0.56 (0.51-0.62)
n = 66 (+100%)	0.62 (0.58-0.65)	0.60 (0.48-0.67)	0.56 (0.48-0.60)	0.57 (0.52-0.70)

* The estimated number of yearly available breeding individuals for the period 2010-2016.

Male breeding restrictions

Different combinations of year-based and life-based male breeding restrictions were simulated. During these simulations all other input parameters remained unchanged. The effects of these restrictions on the rate of inbreeding per generation are shown in table 3. With the average of 10 simulation runs and minimum and maximum.

Table 3. *Effect of restricting the use of sires per year and life on the mean ΔF_{gen} (in%) of 1 simulated population of Irish Red Setters repeated 10 times with average (minimum-maximum).*

Max no. of females serviced per male/year	Maximum number of females serviced per male/life			
	No	15*	5	3
No	0.83 (0.74-0.91)	-	-	-
15	0.83 (0.74-0.91)	0.84 (0.78-0.94)	-	-
5	0.83 (0.74-0.90)	0.79 (0.71-0.84)	0.78 (0.69-0.88)	-
*3	0.78 (0.70-0.85)	0.76 (0.69-0.84)	0.71 (0.63-0.80)	0.81 (0.73-0.90)

* Current restriction (Werkgroep Fokkerij & Gezondheid, 2016).

The rate of inbreeding remained more or less the same with different restrictions. Only very strict restrictions on the maximum number of females serviced per year in combination with a strict restriction on the maximum number of females serviced per life showed slight change in the inbreeding coefficient. The current restriction (3 per year and 15 per life) showed a lower inbreeding rate than when no restrictions were applied. This difference is 0.07%.

Female breeding restrictions

Also different restrictions on the maximum number of litters per dam per life were assessed. The current restriction of 5 litters per life resulted in a decrease of ΔF_{gen} of 0.03% compared to 7 litters per life, while a more strict restriction of only 3 litters per life resulted in an increase of ΔF_{gen} of 0.02%.

Table 4. *Effect of restricting the total number of litters per dam on the mean ΔF_{gen} (in%) of 1 simulated population of Irish Red Setters repeated 10 times.*

Maximum number of litters per dam per life	3	5*	7
ΔF_{gen}	0.81 (0.75-0.90)	0.76 (0.69-0.84)	0.79 (0.74-0.86)

* Current restriction (Oldenbroek & Windig, 2012).

Breeding policies managing kinship

The inbreeding coefficient is shown over a period of 100 years for different breeding policies in figure 19. With no breeding policy regarding kinship, the inbreeding coefficient will rise to 0.18 in 100 years. First of all the mean kinship with the remainder of the breed is constrained. This has a constant effect over the years. Animals that have the highest mean kinship with the rest of the animals are excluded from breeding. Over 100 years this results in a decrease of the inbreeding coefficient of 0.08 to 0.09. Next kinship between father and mother is minimised. In the first 20 years the inbreeding coefficient remains close to 0. This is because offspring of non-related parents is not inbred. However this offspring might be related (shown in figure 23). Over the years all offspring gets more related and it cannot be avoided that related animals start to reproduce. When this offspring starts reproducing, their offspring will become inbred. In the end, this results in a decrease of the inbreeding coefficient of 0.05 to 0.13. This decrease is lower than when kinship with the remainder of the breed is constrained. Lastly, the combination of constraining mean kinship with the remainder of the breed and minimising kinship between father and mother is looked at. In this case, the inbreeding coefficient starts rising from 20 years onwards and results in the lowest inbreeding coefficient over 100 years of 0.08, with a total difference of 0.1 compared to no breeding policies. This is because only least related parents are crossed while at the same time animals with high kinship to the rest of the breed are excluded from breeding.

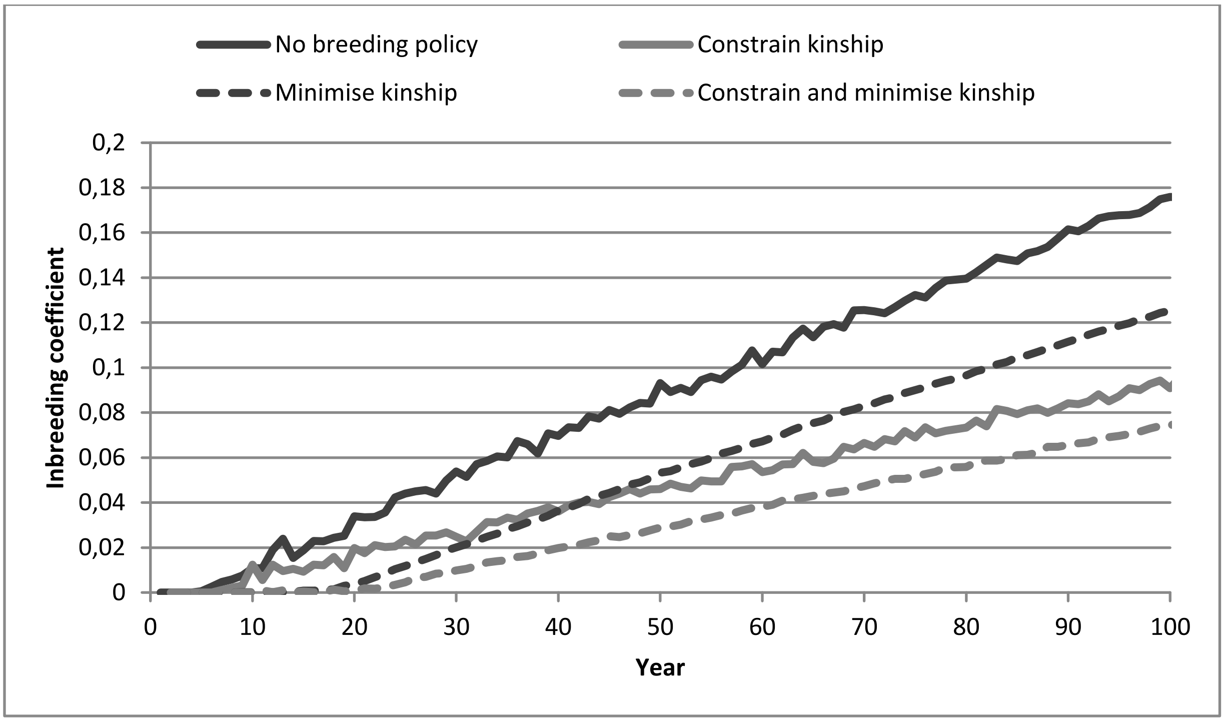


Figure 19. *Effect of various mating programs on mean* ***F*** *of 1 simulated population of Irish Red Setters repeated 10 times over 100 years.*

Effect of best measures

The best measures, with regard to lowering inbreeding, are shown in figure 20 and compared to the current breeding policy. Enlarging the breeding population with +100% had the largest effect on the inbreeding coefficient, compared to enlarging the breeding population with lower percentages. The male breeding restriction in which the maximum number of females serviced per year was set to 3 and per life to 5 had the largest effect on the inbreeding coefficient compared to other maxima. Constraining kinship with the rest of the breeding population and minimising kinship between parents had a larger effect than these measures on its own. When comparing those three measures, it can be said that constraining and minimising kinship has the largest effect in lowering the inbreeding coefficient over time (figure 20). This results in a difference of 0.1 compared to the current policy. Next, enlarging the breeding population has a large effect on lowering the inbreeding coefficient, namely with 0.05. Male breeding restrictions have the smallest effect with a difference of only 0.01 compared to the current policy.

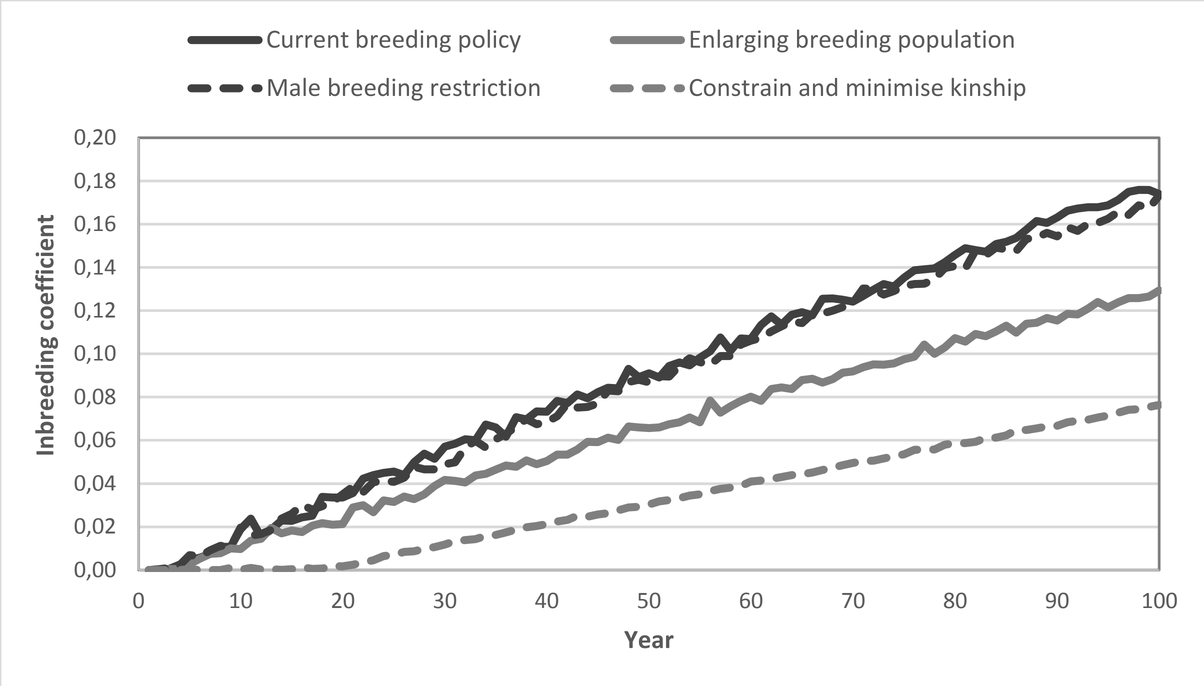


Figure 20. *The effect of enlarging the number of breeding males with +100% and breeding females with +100% (enlarging breeding population), the effect of restricting the maximum number of females serviced per year to 3 and per life to 5 (male breeding restriction) and the effect of constraining kinship with the rest of the breed an minimising kinship between parents (constrain and minimise kinship) on mean F of 1 simulated population of Irish Red-White Setters repeated 10 times over 100 years.*

3.3 Simulation of possible measures in the Irish Red-White Setter

All input parameters that were calculated are included in appendix I. The results of simulating different breeding strategies are presented below. These input parameters are the same over all simulations, unless shown otherwise. By simulating the current population with the current restrictions over 25 years as shown in appendix I, ΔF_{gen} = 4.23% with a minimum of 3.93% and a maximum of 4.55%. This is way higher than the above calculated current inbreeding rate of -0.15%.

Enlarging the breeding population

The effect of increasing the breeding population of Irish Red-White Setters on the inbreeding rate is shown in table 5. An addition of only 5 breeding males (+100%) resulted in a decrease of 0.55%, while an addition of 6 breeding females (+50%) resulted in a decrease of only 0.19%. The largest effect was achieved when the number of breeding animals was doubled. Thus when adding 11 females and 5 males for breeding (+100%) a decrease in ΔF_{gen} of 1.69% was achieved.

Table 5. *Effect of increasing the number of available breeding males and females per year on the mean ΔF_{gen} (in %) of 1 simulated population of Irish Red-White Setters repeated 25 times.*

Males available for breeding	Females available for breeding n = 11 (baseline*)	n = 14 (+25%)	n = 17 (+50%)	n = 22 (+100%)
n = 5 (baseline*)	4.23 (3.93-4.55)	4.02 (3.69-4.36)	4.04 (3.70-4.39)	3.95 (4.60-4.29)
n = 7 (+25%)	4.10 (3.82-4.40)	3.38 (3.06-3.70)	3.24 (2.93-3.55)	3.32 (2.98-3.65)
n = 8 (+50%)	3.71 (3.42-4.00)	3.48 (3.19-3.78)	3.10 (2.83-3.39)	2.95 (2.66-3.24)
n = 10 (+100%)	3.68 (3.35-4.02)	3.32 (3.04-3.60)	3.06 (2.77-3.36)	2.54 (2.34-2.75)

* The estimated number of yearly available breeding individuals for the period 2010-2016.

Male breeding restrictions

Different combinations of year-based and life-based male breeding restrictions were simulated and are shown in table 6. During these simulations all other input parameters remained unchanged.

Table 6. *Effect of restricting the use of sires per year and life on the mean ΔF_{gen} (in%) of 1 simulated population of Irish Red-White Setters repeated 25 times.*

Max no. of females serviced per male/year	Maximum number of females serviced per male/life			
	No	15*	5	3
No	4.10 (3.81-4.40)	-	-	-
15	4.10 (3.81-4.40)	4.10 (3.81-4.40)	-	-
5	4.10 (3.81-4.40)	4.10 (3.81-4.40)	3.80 (3.57-4.04)	-
*3	4.23 (3.93-4.55)	4.23 (3.93-4.55)	4.47 (4.15-4.80)	3.69 (3.49-3.89)

* Current restriction (Werkgroep Fokkerij & Gezondheid, 2016).

It is remarkable that the mean rate of inbreeding per generation rises when stronger restrictions (3/year) on the maximum number of females serviced per year are made. Normally, you would expect it to go down instead of rise, like can be seen in the Irish Red Setter. In this case the inbreeding rate might rise because with a strong restriction per year not all breeding females might get serviced. Other restrictions on the maximum number per year and per life show no effect, except restricting to 5/year and 5/life and to 3/life and 3/year. These restrictions result in a decrease in ΔF_{gen} of 0.3% and 0.41% respectively.

Female breeding restrictions

The effect of restricting the maximum number of litters per dam per life on ΔF_{gen} is shown in table 7. A maximum number of litters per life of 5 results in a decrease of ΔF_{gen} of 0.59% compared to 7 litters per life. When further restricting the number of litters to only 3, ΔF_{gen} rises again with 0.18 compared to 5 litters per life.

Table 7. *Effect of restricting the total number of litters per dam on the mean ΔF_{gen} (in%) of of 1 simulated population of Irish Red-White Setters repeated 25 times.*

Maximum number of litters per dam per life	3	5*	7
ΔF_{gen}	4.41 (4.04-4.80)	4.23 (3.93-4.55)	4.82 (4.48-5.16)

* Current restriction (Oldenbroek & Windig, 2012).

Breeding policies managing kinship

The inbreeding coefficient is shown over a period of 100 years for different breeding policies. With no breeding policy regarding kinship the inbreeding coefficient rises to 0.76 in 100 years. Constraining kinship with the remainder of the breed lowers the inbreeding coefficient with 0.2 to 0.56 over 100 years. Minimising kinship between parents lowers the inbreeding coefficient with 0.09 to 0.67 over 100 years. In this case, the inbreeding coefficient start rising at year 5 when looking at the effects of minimising kinship and constraining and minimising kinship (dotted lines in figure 21). This is because the population of Irish Red-White Setters is very small. The ability to choose animals for breeding that are not related will decline very quickly and therefore the inbreeding coefficient starts rising much sooner than in the Irish Red Setter. Constraining and minimising kinship at the same time has the largest effect. This lowers the inbreeding coefficient with 0.23 to 0.53 over 100 years.

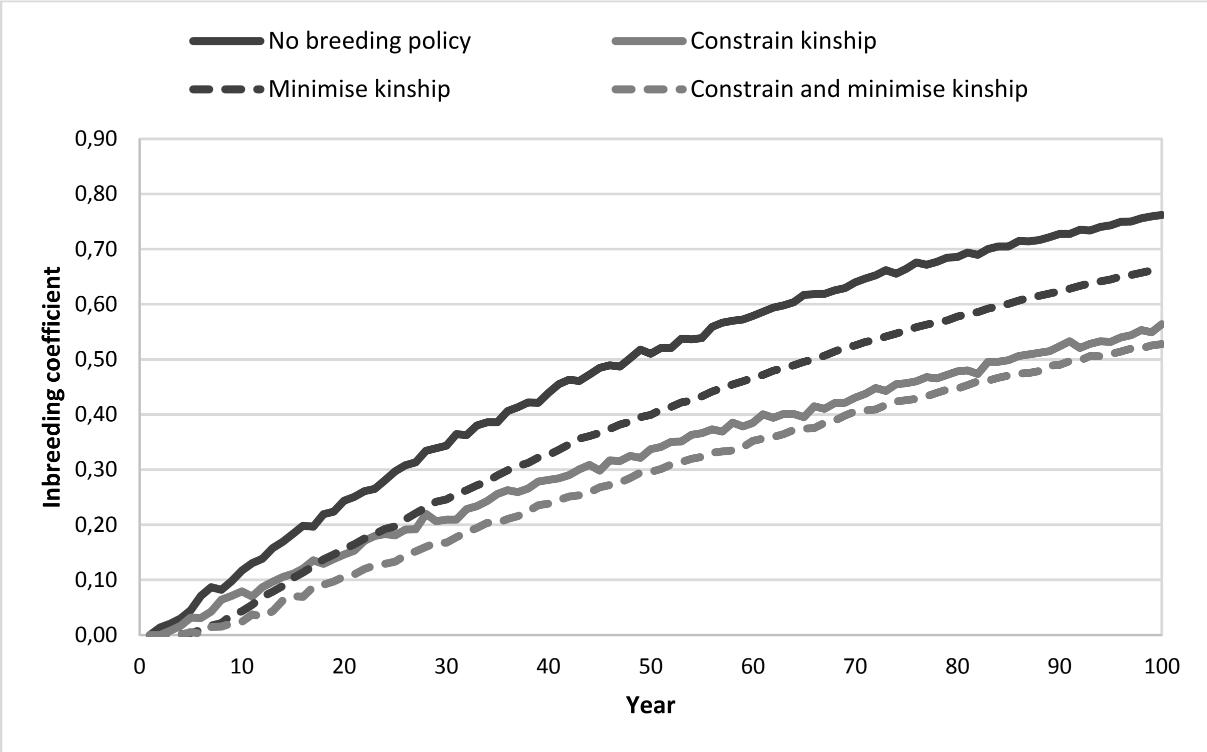


Figure 21. *Effect of various mating programs on mean **F** of 1 simulated population of Irish Red-White Setters repeated 25 times over 100 years.*

Effect of best measures

The best measures, with regard to lowering inbreeding, are shown in figure 22 and compared to the current breeding policy. Enlarging the breeding population with +100% had the largest effect on the inbreeding coefficient, compared to enlarging the breeding population with lower percentages. The male breeding restriction in which the maximum number of females serviced per year was set to 3 and per life to 3 had the largest effect on the inbreeding coefficient compared to other maxima. Constraining kinship with the rest of the breeding population and minimising kinship between parents had a larger effect than these measures on its own. When comparing those three measures, it can be said that constraining and minimising kinship and enlarging the breeding population both have the largest effect on lowering the inbreeding coefficient over time (figure 22). Both these measures result in a decrease in the inbreeding coefficient of 0.23 to 0.53 over 100 years. Male breeding restrictions have the smallest effect, with a decrease of only 0.04 to 0.72 over 100 years.

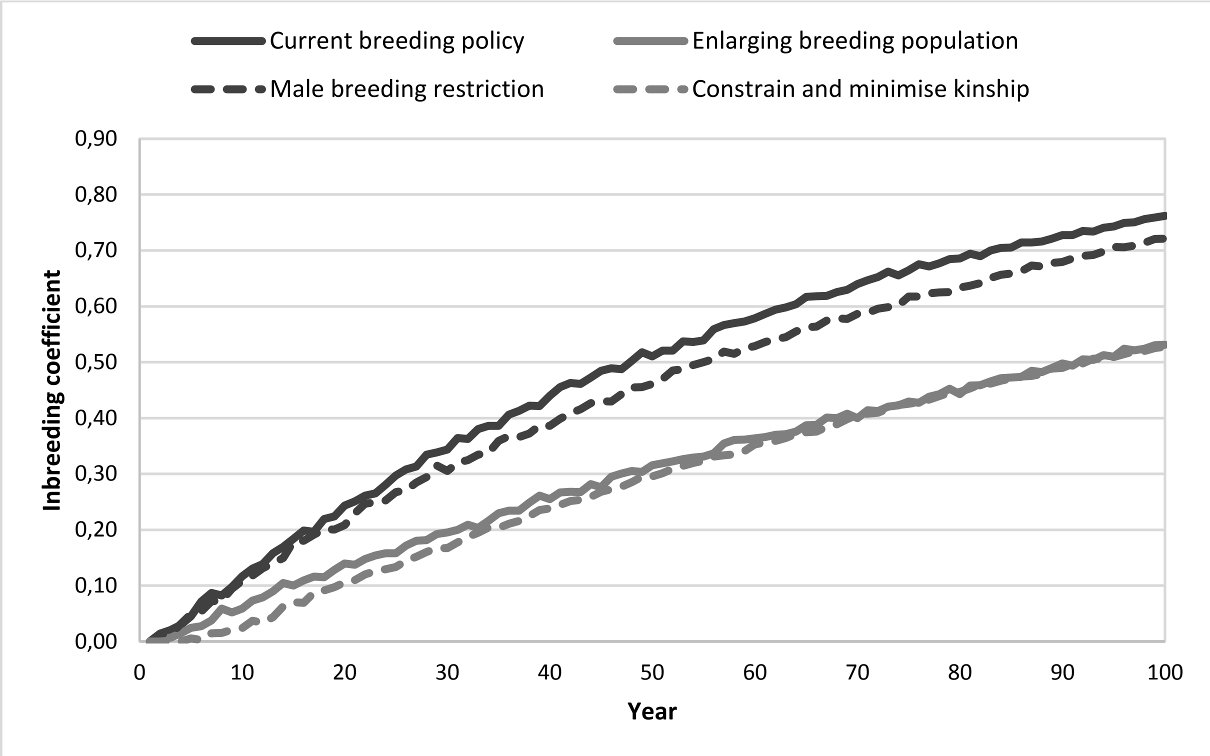


Figure 22. *The effect of enlarging the number of breeding males with +100% and breeding females with +100% (enlarging breeding population), the effect of restricting the maximum number of females serviced per year to 3 and per life to 3 (male breeding restriction) and the effect of constraining kinship with the rest of the breed an minimising kinship between parents (constrain and minimise kinship) on mean F of 1 simulated population of Irish Red-White Setters repeated 25 times over 100 years.*

4. Discussion

Although the inbreeding rate per generation seems to decline from 1990 onwards in the Irish Red Setter with -0.37%, simulations show that it is inevitable to prevent inbreeding in the long term. In the Irish Red-White Setter the rate of inbreeding stabilised from 1997 onwards at a rate of -0.15% per generation, which is below the recommended 0.5% per generation. However, to keep this inbreeding rate low in the long term, a large number of breeding animals should be used (Oldenbroek & Windig, 2012).

Kinship continues to rise in the Irish Red-White Setter, while the inbreeding rate approximates zero. This can be explained with the simple pedigree shown in figure 23. By breeding animals that are not related, there will be no inbreeding in the next generation. However, this offspring is more related and therefore the kinship in this generation is higher. For example a white brother and sister are mated with a black brother and sister. The white male is not related to the black female and the black male is not related to the white female, so their offspring will not be inbred. However, this offspring is related, because they both have DNA from related animals (brothers and sisters). When mating this offspring, the next generation will become inbred again. So in future generations, inbreeding will rise again due to increasing relatedness.

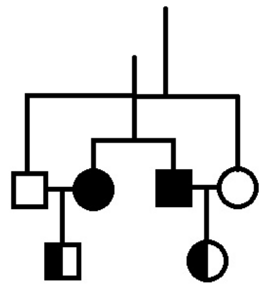


Figure 23. *Pedigree of non-related parents with related offspring.*

The most important cause of inbreeding is the small population size in both varieties. Simulations with the current number of breeding males and females show that ΔF_{gen} will exceed 0.5% in both varieties if no restrictions are applied. To lower inbreeding, it is important to increase the number of breeding animals. Simulations show that the rate of inbreeding decreases if the number of breeding males and females increased. Adding males to the breeding population seemed to be more effective than adding females.

A factor that might limit breed growth is litter size. However for the Irish Red Setter as well as the Irish Red-White Setter, the mean litter site of 8.4 and 6.5 respectively is high compared to the mean litter size of 5.4 for breeds of all sizes (Borge et al., 2011). Therefore this should not be a limiting factor.

In Irish Red Setters only a small fraction of the population is used for breeding. In the Irish Red Setter the number of males used for breeding as a percentage of the total number of males ranges between 10% and 26% between the years 2000-2012, with an average of 17%. The breeding population of Irish Red Setters could therefore be enlarged by using a larger percentage of dogs that are already in the database. Only dogs with a low mean kinship to the population should be selected.

In the Irish Red-White Setter, the number of breeding males ranges from 9% to 86% with an average of 47% between 2000 and 2012. This already is a large part of the population. Due to the small population size of Irish Red-White Setters, only a small number of dogs can be used to breed with, which makes it difficult for the population to increase in size without increasing the relatedness between dogs. By doubling the number of breeding males and females a decrease in ΔF_{gen} of 1.69% was achieved. So using more animals in breeding makes quite a difference with respect to the rate of inbreeding. One possibility to enlarge the breeding population is by outcrossing with look-alikes: dogs that look similar but have different ancestors. In this case, Irish Red Setters might be used as look-alikes, but it is very important that the animals chosen as outcross are not related to the population of Irish Red-White Setters. A second way to enlarge the breeding population is by importing animals from the same breed from abroad. These breeds have been separately bred for a longer period of time, resulting in less related animals than those in The Netherlands. The effectiveness of the use of look-alikes or foreign animals depends on the number of look-alikes or foreign animals used, the kinship amongst the look-alikes or foreign animals and the kinship between the look-alikes or foreign animals and the breeding Irish Red-White Setters. It is wise to test the look-alikes or foreign animals on mean kinship with each other and with the Irish Red-White Setters. If only a small number of look-alikes or foreign animals is available, or if these dogs are too closely related, it should be considered to outcross with a different breed.

Generation interval is another factor that influences the rate of inbreeding. The generation interval in Irish Setters is quite equal to that of other breeds (Leroy et al., 2013; Oldenbroek & Windig, 2012; Lewis et al., 2015). Further increasing the generation interval is not necessary and will not be profitable for dog breeders.

The influence of male as well as female breeding restrictions were analysed in both populations. The current restriction set by the VFR of 3 successful matings per male per year, with a maximum of 15 successful matings during his life results in a decrease in ΔF_{gen} of 0.07% in the Irish Red Setter. Since there is no large popular sire effect in both varieties, restricting the maximum number of females serviced per male per year and per life has no large effect on the rate of inbreeding. Restricting the maximum number of litters per dam per life showed no clear effect either, because a female can already have only 1 litter each 2 years and is used for up to 7-8 years of age.

Breeding males have 1 to 2 litters per life, which is low compared to other breeds (Nielen et al., 2001). By increasing the number of litters per year and per life per breeding male, the population size could be increased, without increasing the number of current breeding males. It is however very important that every male is used an equal amount of times and therefore all males have an equal amount of litters, to prevent the popular sire effect. So every animal should have an equal chance of getting offspring (Oldenbroek & Windig, 2012).

Lastly the effect of different breeding policies was assessed. Constraining mean kinship with the remainder of the breed is effective on the long term, in contrast to minimising kinship between father and mother, which is more effective on short term. By constraining mean kinship with the rest of the breed, animals that have a high chance of producing inbred offspring are excluded and in this way inbreeding is lowered. By minimising kinship between parents, only the next few generations will not be inbred (in this case 20 years in the Irish Red Setter and only 5 years in the Irish Red-White Setter). After this, relatedness of the offspring rises and the rate of inbreeding rises much faster than when constraining mean kinship. Combining these measures is the most effective way to decrease the rate of inbreeding, because highly related animals are excluded from breeding and only parents that are least related are allowed to breed.

Since only 10 populations of Irish Red Setters have been simulated, it is wise to perform further analysis. To decrease the effect of variance, the Irish Red Setter population could better be simulated with 25 populations, but due to time restrictions, this was not possible in this study. Nevertheless the effects of different measures will remain the same (e.g. by increasing the breeding population the rate of inbreeding per generation lowers significantly), only the accuracy of the estimated rate of inbreeding will rise.

Around 1970 to 1976 the popularity of the breed increased enormously, resulting in a peak of 1800 animals in the total number of animals born per year of birth. There was an increase in number of litters to 285 litters in 1975. These 1800 animals descend from 161 fathers. Due to the increase in number of litters, and therefore number of mothers and the increase in number of fathers, probably also related parents were used in breeding, to be able to meet the increasing demand of Irish Setters. This results in an increase of 0.04 in the inbreeding coefficient from 0.17 in 1972 to 0.21 in 1980. However when looking from 1950 to 1989 this increase does not largely affect the slope over this entire period.

From 1975 onwards also the population of Irish Red-White Setters started to arise. In the first 15 years (1975 to 1990) almost all newly registered animals were used for breeding. This might be because only animals that were used for breeding were registered and animals that were born and were not selected for breeding were also not registered.

5. Conclusion and recommendations

Despite the fact that the rate of inbreeding is currently close to zero for both varieties, inevitably inbreeding will rise in the future due to high levels of kinship in the breed and a small population size, especially in the Irish Red-White Setter. Without any further restrictions, simulations show that ΔF_{gen} will exceed 0.5% in both varieties, resulting in a higher risk of genetic disorders and in the long term risk of extinction if ΔF_{gen} permanently exceeds 1.0%.

First of all, to achieve a lower rate of inbreeding in the long term, constraining mean kinship with the remainder of the breed could be applied. In combination with minimising kinship between father and mother, the best result could be achieved.

Another way to lower the inbreeding rate is to increase the breeding population in size. In the Irish Red Setter this can be done by selecting more animals as breeding animals. One important criteria to look at when selecting these animals is that they have low kinship with the rest of the population.

In the Irish Red-White Setter this is not an option. Already about half of all registered animals are used as breeding animals, and due to the small population size it is difficult to increase in size without increasing relatedness at the same time. A way to increase population size in the Irish Red-White Setter is by introducing look-alikes. Irish Red Setters might be used as look-alikes. Another way is by importing animals from abroad. The effectiveness of the introduction of look-alikes or foreign animals depends on the number of look-alikes or foreign animals used, the kinship amongst these animals and the kinship between the look-alikes or foreign animals and the Irish Red-White Setters. If only a small number of look-alikes or foreign animals is available, or if these dogs are too closely related, it might be wise to consider looking at another breed to perform outcrosses with.

Lastly, a way to increase the population size in both varieties is to increase the number of litters per breeding male. Breeding males now only have 1 to 2 litters per life. Increasing the number of litters per male per year or per life does not have a large effect on ΔF_{gen}. Therefore allowing a larger maximum number of litters, will not increase the rate of inbreeding. It is important that all males have an equal amount of litters to prevent the popular sire effect.

By applying above mentioned measures in the breeding program, the rate of inbreeding could be lowered on the long term. Thereby conserving genetic diversity and securing a healthy breed.

Literature

Borge, K. S., Tønnessen, R., Nødtvedt, A., & Indrebø, A. (2011). Litter size at birth in purebred dogs—A retrospective study of 224 breeds. Theriogenology,75(5), 911-919.

Bosch, G. and van der Poel, T. (2014). Historie van de Huisdierensector [Dictaat Introduction Animal Sciences]. Retrieved from https://blackboard.wur.nl/

De Ierse Setter Club. (2015). Rasstandaard Ierse setter Rood. Retrieved from http://www.iersesetterclub.nl/rasstandaard-1/rasstandaard-ierse-setter-rood/

Leroy, G., Mary-Huard, T., Verrier, E., Danvy, S., Charvolin, E., & Danchin-Burge, C. (2013). Methods to estimate effective population size using pedigree data: Examples in dog, sheep, cattle and horse. Genetics Selection Evolution,45(1), 1-10.

Lewis, T. W., Abhayaratne, B. M., & Blott, S. C. (2015). Trends in genetic diversity for all Kennel Club registered pedigree dog breeds. Canine Genetics and Epidemiology, 2, 13.

Nielen, A. L. J., Van Der Beek, S., Ubbink, G. J., & Knol, B. W. (2001). Epidemiology: Population parameters to compare dog breeds: Differences between five dutch purebred populations. Veterinary Quarterly, 23(1), 43-49.

Oldenbroek, J. K., & van der Waaij, E. H. (2015). Leerboek fokkerij en genetica voor het HBO. Centrum voor Genetische Bronnen Nederland en Animal Breeding and Genomics Center (WUR).

Oldenbroek, J. K., & Windig, J. J. (2012). Het fokken van rashonden: omgaan met verwantschap en inteelt. Raad van Beheer op Kynologische Gebied in Nederland.

Rashondenwijzer. (2017). Erfelijke aandoeningen bij de Ierse Setter. Retreived from https://www.rashondenwijzer.nl/rashonden/ierse-setter

Werkgroep Fokkerij & Gezondheid. (2016). Verenigingsfokreglement: Ierse Setter Club [PDF]. Retrieved from http://www.iersesetterclub.nl/gezondheid-abc/verenigingsfokreglement/

Appendix I. Input parameters for Genetic Management Simulation

Table 1. *Number of years and repeats and current breeding policy parameters.*

	Red Setter	Red-White Setter
Number of years	100	25
Number of repeats	10	25
Age female first litter (months)	22	
Maximum number of females serviced per male/year	3	
Maximum number of females serviced per male/life	15	
Maximum number of sons selected as breeding male per male dog	No maximum: 1000	
Maximum number of litters per female/life	5	
Maximum kinship allowed between parents	1	
Maximum inbreeding allowed per animal	1	

Table 2. *Population size parameters in the Irish Red Setter and Irish Red-White Setter.*

	Irish Red Setter	Irish Red-White Setter
Number of breeding males	33	5
Number of breeding females	80	11
Number of litters per year	40	6
Champions sire	3	0
% of offspring	8	0

Table 3. *Age structure parents: percentage of offspring that has a parent of x years old. In the Irish Red Setter and Irish Red-White Setter averaged over 2007 to 2017.*

Age	Irish Red Setter		Irish Red-White Setter	
	Males	**Females**	**Males**	**Females**
1	9	1	16	7
2	21	13	19	12
3	17	26	18	15
4	15	20	15	25
5	15	17	10	16
6	13	12	8	14
7	4	9	6	9
8	4	2	5	2
9	1	0	2	0
10	1	0	1	0

Table 4. *Litter size: number of pups per unique combination of father, mother and date of birth. As percentages of all litters between 2012 and 2017 in the Irish Red Setter and between 2007 and 2017 in the Irish Red-White Setter.*

	Irish Red Setter	**Irish Red-White Setter**
1	1	1
2	1	2
3	2	5
4	5	8
5	7	13
6	8	17
7	10	22
8	11	16
9	14	10
10	16	5
11	17	1
12	8	0