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How to genetically manage inbred populations with a multitude of genetic diseases?

Jack J. Windig, Rita Hoving

Bouvier de Flandres.

Problem

A **multitude of genetic diseases** occur in pedigreed dogs. This is partly due to breeding for conformation traits such as short snouts or small skulls without attention to health, and partly to excessive inbreeding. Nowadays, diagnosis of genetic health problems is extensive, and many DNA tests are available to detect carriers. However, **excluding dogs** that carry or suffer from genetic diseases will limit the breeding pool, will lead to **more inbreeding**, and will induce **new genetic diseases**.

Staby houn.

Case study: Bouviers des Flandres

Multiple genetic diseases occur in the Bouvier des Flandres. Regular screening especially for diseases of the eye has led to the discovery of many affected dogs Table 1).

Table 1. Genetic diseases discovered by screening Bouviers.

Disease	Onset	% positive tests	Genetic background
HD	Variable	Low	Polygenic
ED	Variable	Low	Polygenic
PPM	>6 weeks	17,1%	Recessive, dominant or polygenic?
PHTVL/ PHPV	Unknown	10,6%	Autosomal incomplete dominant
Hereditary cataract	Weeks till months	Congenital: 9,5% Not congenital: 27,6%	Autosomal recessive/dominant?
RD	2-3 moths	8,2%	Autosomal recessive (sex-linked?)
Distichiasis	0,3-9 year	11,6%	Autosomal dominant?
Corneal dystrophy	Variable	9,5%	Sex linked recessive?
PRA	Early: 2-6 wk Late: 2-5 yr	0%	Autosomal recessive
Entropion	4-7 months	4,8%	Polygenic?
Microphthalmia	Unknown	-	Autosomal recessive
Primary Glaucoma	± 7 years	78,4% not ICAA free	Polygenic (?)

Current inbreeding rate (ΔF) is 0.8% (Ne = 56). Computer simulations indicate that will increase to 1.1% (Ne = 45) if 25% of dogs are banned from breeding and to 5.5% (Ne = 9) if all (potentially) diseased dogs are excluded.

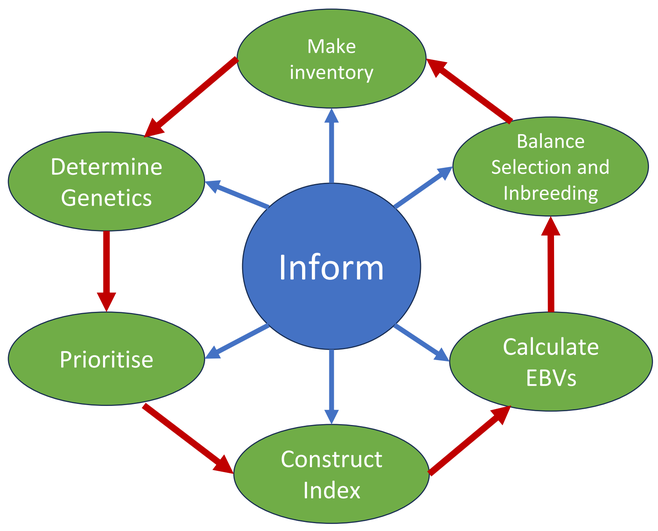

Figure 1. Framework for reducing the burden of multiple genetic diseases in a (dog) breed

Reduction of genetic disease prevalence

The following steps can be taken to tackle a multitude of genetic diseases in (dog) populations (Figure 1).

- Make an inventory of diseases (as in Table 1), including prevalence.
- Determine genetic background: mono/polygenic? Recessive?, Sex linked? etc.
- Prioritize diseases, based on severity, impact on welfare, age of onset and prevalence.
- Construct a genetic health index.
- Estimate Breeding values for health of all dogs.
- Determine scope for selection and select dogs while restricting inbreeding. Use dogs of other breeds (outcross) when needed.
- Repeat cycle regularly to incorporate new diseases and changes in population structure.
- Inform dog breeders, owners and the general public for every step of the process.

Saarloos Wolfdog. F2 hybrid of outcross program.

Construction of a Genetic index

A breeding goal (Health index) can be defined by weighing diseases based on severity and prevalence. Breeding values can be estimated using a BLUP procedure. Note that EBVs can be estimated even for individuals without phenotypic information by using information from relatives. Likewise, EBVs can be estimated even for badly registered traits by using genetically correlated traits such as indicator traits. Classical quantitative selection index theory can be used to determine the accuracy of EBVs of different combination of (indicator) traits and relatives.

Wetterhoun. Breed involved in outcross program.

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Wageningen University & Research
P.O. Box 123, 6700 AB Wageningen
Contact: Jack.Windig@wur.nl
T + 31 (0)317 480 543, M +31 (0)6 1930 4558
www.wur.nl/ web/show/id=542191/langid=2534814