

# Breeding healthy dogs with genomics

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Farewell symposium Kor Oldenbroek



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# Breeding program



- *These are the steps to follow in setting up a breeding program (Course: ABG20306).*

# Breeding program: production system

1. Definition of production system

???

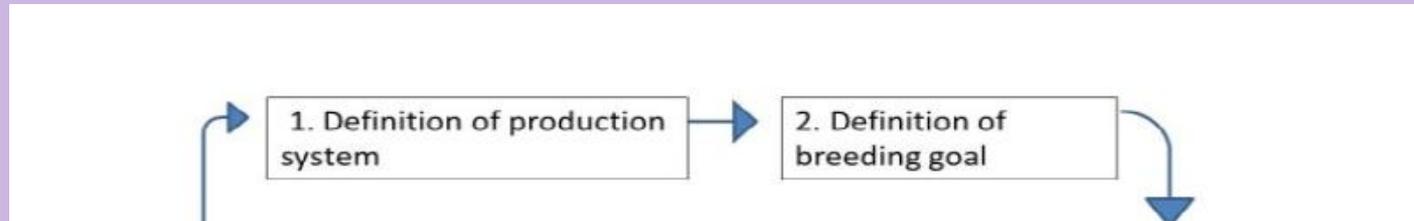
Home:  
Companion  
Friendship  
Status  
...



Ge

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# Breeding program: breeding goal



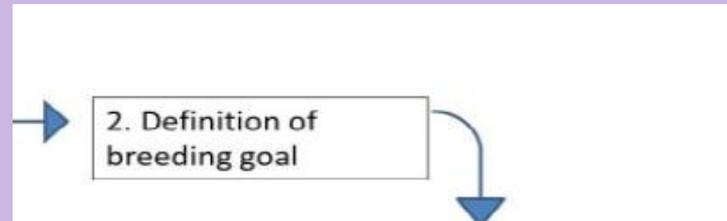
- A good breeding goal is in agreement with the purpose of the breed. So:

1. Excellent health
2. Long life span
3. Good temperament
4. Good looks

**In this order**



# Breeding program: breeding goal



## ■ Breeding goal in practice

1. Good looks (best in show!)

2. Good temperament

3. Good health

**In this order**

## ■ No attention for life span



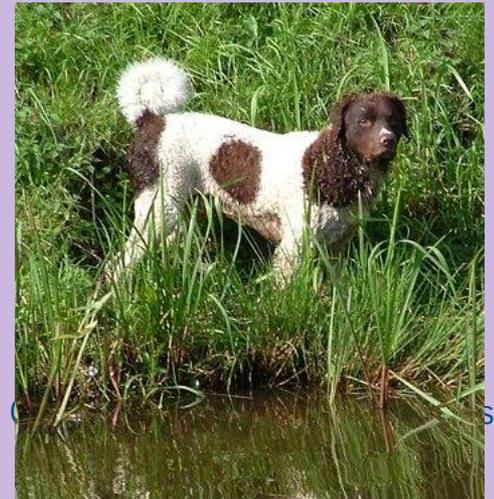
# Dog health: evaluation

- Pedigreed dogs have many inherited health problems
- Genomic information indicates that pedigreed dogs carry 22% more deleterious alleles than wolves (Marsden et al. 2016)
- Each dog carries several lethal mutations
- Lot of negative attention in the media

Species	# disorders - traits*
Dog	678
Cattle	494
Cat	331
Pig	242
Sheep	239
Horse	225
Chicken	212
Rabbit	89
Goat	78
*Omnia.angis.org.au 21/9/2016	

# Genetic Defects and disorders

- Monogenic defects
  - Single recessive deleterious alleles
  - Clear, Carrier, Affected animals
  - Only affected animals if population frequency of deleterious allele is high
- Polygenic diseases
  - Many alleles with small effect
  - Genetic liability varies on a continuous scale
  - Breeding value



# Current practice: Monogenic defects

- Breeding starts when genetic defect becomes apparent
  - frequency of lethal allele is high
- If possible develop DNA test
- Exclude (likely) carriers from breeding
- Barking up the wrong tree
- Mopping up with the tap open



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# Barking up the wrong tree: less deleterious alleles are the long term problem

- Simulated small breed, high inbreeding rate, 250 lethal defects = mean 3.4 defects per dog
  - Frequency went down or allele disappeared altogether because affected animals do not reproduce
  - Breed survived
- Simulated small breed, high inbreeding rate, 250 alleles reducing litter size 10%
  - Part of deleterious alleles got fixed
  - Sometimes breed went extinct



# “Traffic light” inbreeding rate

Inbreeding rate	Risk	Effective population size
>1%	Risk of extinction, accumulation of genetic defects	<50
0.5% - 1%	Genetic defects will most probably occur	50-100
0.25% - 0.5%	Genetic defects can occur	100-200
< 0.25%	Small chance that genetic defects occur	>200

- Average  $\Delta F$  in 121 UK breeds between 1980-1984: 8%



# Mopping up with the tap open

- Many DNA tests developed
- But strong selection against a defect may increase the inbreeding rate
- If population structure is not changed new defects will keep popping up



- Tap can be turned off
- Compute relatedness of animals with ALL other animals in te breed
  - Not just its (potential) mate
  - And publish these Mean Kinships

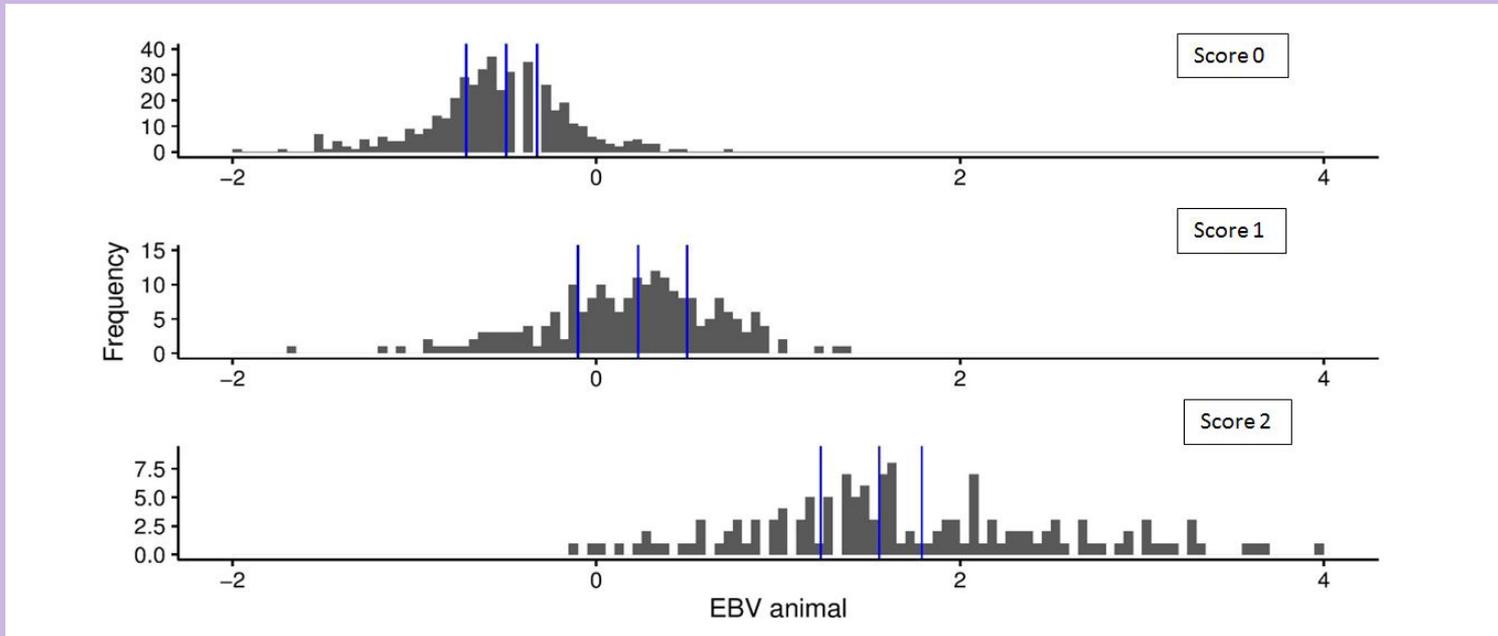
# Polygenic disorders

- Breed standard related
  - Short noses (Brachycephalic Airways Obstruction Syndrome)
  - Etc.
- Other
  - Deafness
  - Hip dysplasia
  - etc.
- Current practice
  - Veterinary test to classify disease
    - E.g. free, mild, moderate, severe (or A,B,C,D,E or ...)
  - Rules by breeding organisations exclude animals for breeding
  - Phenotypic selection is not very effective
    - Environment obscures genetic influence



# Estimated breeding values

From Wijnrocx et al. 2017



- Syringomyelia in Cavalier King Charles Spaniels
  - Overlap in EBVs between categories
  - Large variation within categories



# BV estimation not straight forward

- Needed
  - Systematic recording
  - Reliable pedigree
  - Large number of relatives
- Information from 'Look a likes', across countries and other breeds cannot be used
- Genomic selection combines DNA information with breeding value estimation
  - EBV can be estimated for dogs without (reliable) pedigree, relatives or phenotype
  - Still a lot to do before it can be operational in dogs, but great opportunities



# Strategy for eliminating genetic defects 1

## 1. Monitor breeds for genetic defects

- Systematic recording in registry
- Frequency, severity, breed, sex, age, ancestry etc.

## 2. Determine mode of inheritance

- Monogenic, Polygenic
- Recessive, Dominant, ...
- Heritability, genetic correlation with other traits

## 3. Rank selection candidates

- Monogenic: clear, carrier, affected
- Polygenic: Breeding value
- Multiple defects: make index



# Strategy for eliminating genetic defects 2

4. Evaluate relatedness and inbreeding

5. Select animals

- Breeding organisations have to set rules
  - Threshold Mean kinship
  - Threshold for breeding value(s)
  - Use of carriers



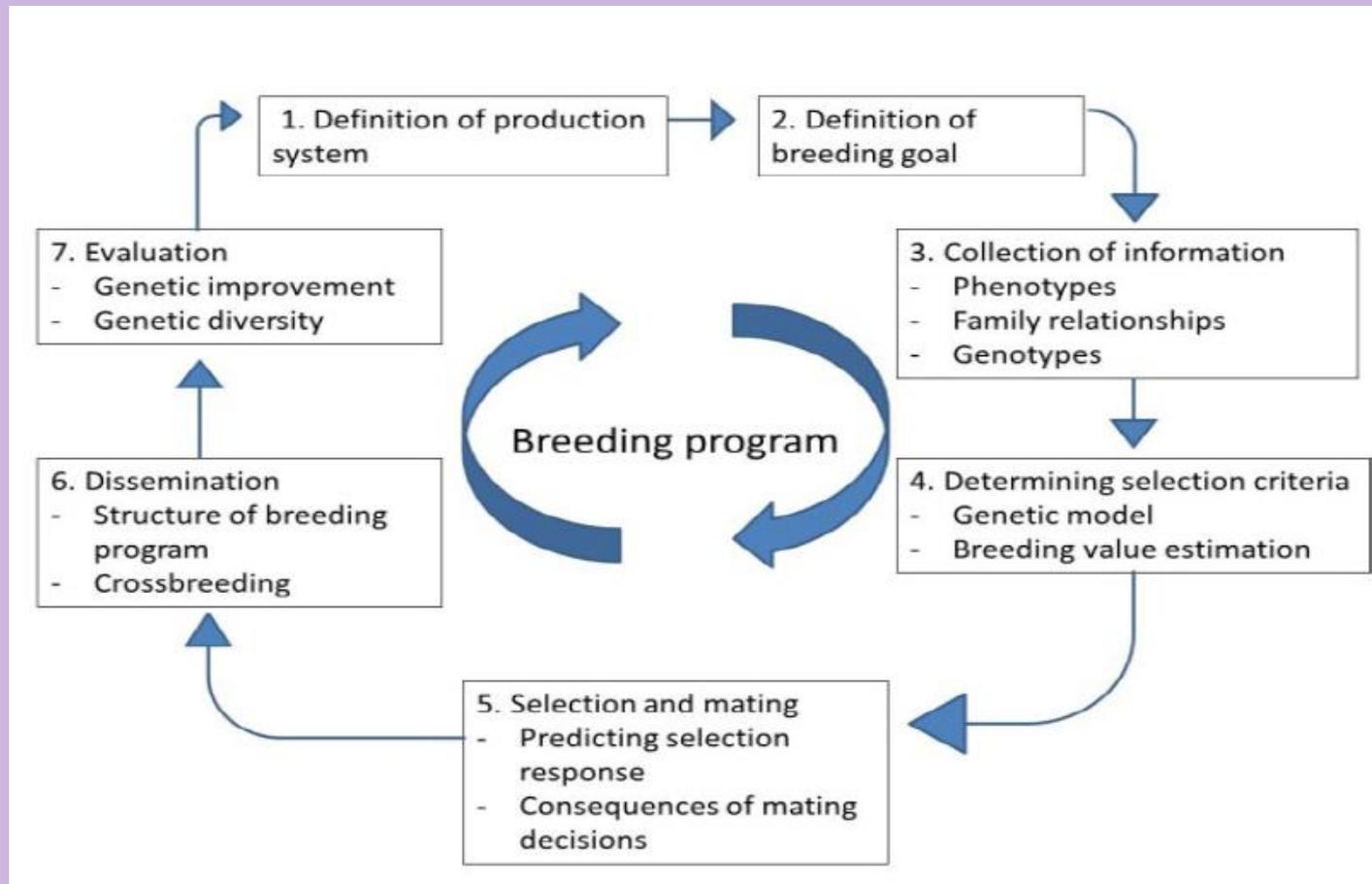
6. Mate selected animals

- Publish for all mating pairs probability of disease
- Level of inbreeding

7. Evaluate frequency of diseases and inbreeding levels each year

8. Keep repeating 1-7

# Breeding program



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# Conclusions

- Dog breeding can and should be improved
- It all starts with a proper breeding goal
- Do not limit breeding to DNA tests
- Monogenic genetic defects need management at the population level
- Polygenic traits need breeding value estimation: Genomic selection can help



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# Thank you

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