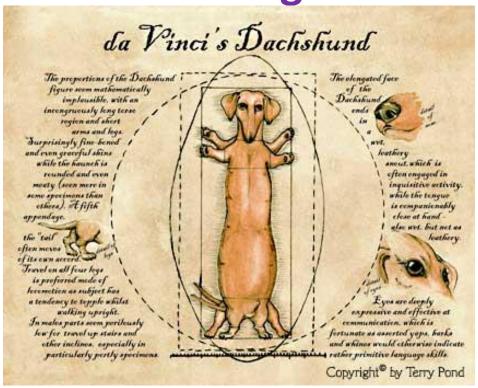
The Dog Health Balancing Act – how to balance health resources for breeding for "whole dog" health



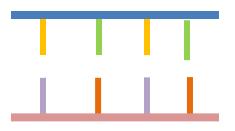
Aimée Llewellyn-Zaidi Head of Health and Research

Today's Talk

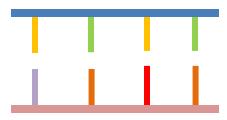
- What resources are available for testing for simple diseases
- A refresher on disease modes of inheritance
- Optimising DNA tests, not all tests are the same!
- Complex inherited disorders help is out there!
- How to eliminate disease with minimum impact on biodiversity
- A dog is more than a test result behaviour and conformation.
- Free resources and information

What is a simple inherited disease?

- A "simple" inherited disease means that there is a single specific gene identified that, when abnormal, can cause disease.
- Two abnormal genes
 (one from each parent)
 must be inherited to
 cause disease
- Many simple diseases have associated DNA tests



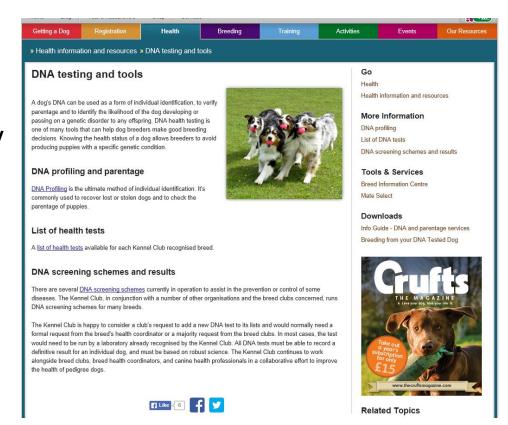
Normal recombination with dam/sire



Abnormal recombination with dam/sire

What tests are available?

- Single-gene mutations are normally breed-specific
- Most are buccal (mouth) swab, saliva, or occasionally blood samples
- Often owners will take and submit samples themselves
- The veterinary practice can help by offering a sampling service, including doublechecking microchip/dog ID
- A summary list of many health-related tests can be found on the KC website



Puppy Seekers

Breeders

Vets

Health Information

You may be aware that some breeds of dog (and crossbreeds too) can be susceptible to inherited disease. Of course you want to be sure that the dog you choose is as healthy as possible, and you would like to know that it has not inherited any undesirable disease-causing genes from its parents. There is some help in that DNA tests for diseases in purebred dogs are available for some conditions in some breeds, but there are not very many such tests just yet! There are also, however, a number of clinical veterinary screening schemes that dog breeders can use to increase the probability of producing healthy puppies.

Details of the various screening schemes, both veterinary and DNA, that are available to breeders in the UK can be found at www.thekennelclub.org.uk/doghealth

Potential dog owners should be aware that, at present, the application of various health screening results to breeding programmes is not always straightforward, and breeders may make choices for various reasons. A responsible breeder though, will always be willing to discuss relevant health issues with you. Breed clubs are often useful sources of breed-specific information.

Schemes or advice relevant to this breed

Kennel Club Assured Breeders must use the following screening schemes for sires and dams

BVA/KC Hip Dysplasia Scheme

BVA/KC/ISDS Eye Scheme

Kennel Club Assured Breeders are strongly recommended to use the following screening schemes and/or advice for sires and dams

BVA/KC Elbow Dysplasia Scheme

DNA test - prcd-PRA

The following other health tests are also available.

DNA test - CNM

DNA test - EIC

The list above is not necessarily comprehensive. Breed clubs and experienced breeders are useful sources of information on health issues in the breed. All breeds have a Breed Health



More information on this breed

Go

Breeding Restrictions Assured Breeders

Breed Standard

Accepted Registration Colours

Pictures

Breed Watch

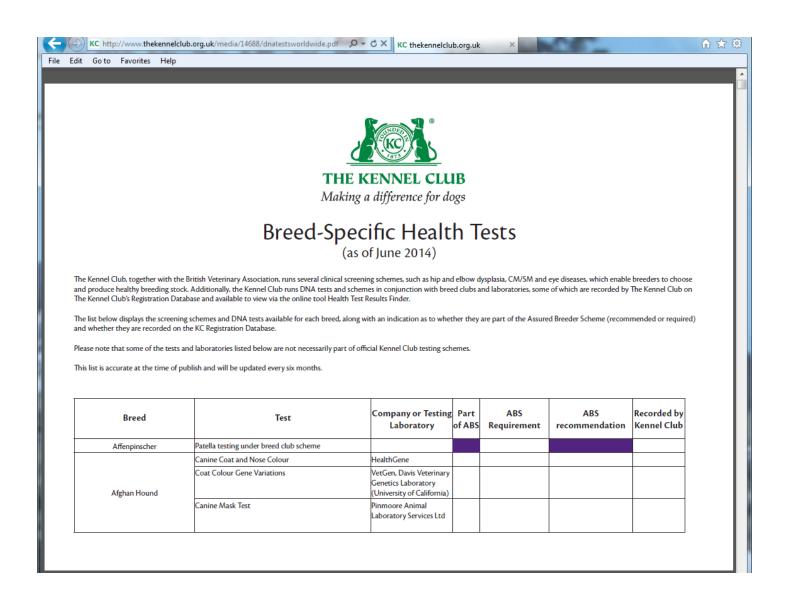
Tools

Information Pack Find A Puppy Find A Rescue Dog Find A Dog Club

More

Other Breeds
Other Breeds in this group

All-breed List



Example of a DNA test result

Owner gets a certificate, which may or may not have advise or information about what the results mean. Often results are sent directly to the KC for recording on Mate Select

Understanding results is **key** to preventing the spread of a specific condition

Just breeding from clear dogs only is *not* good enough

Advise is available



OPTIGEN "ac

for the nepelic advantage

Test Report

1001627232 Paterson 28 Southbrook Road Melksham, Wiltshire, SN12 8DT United Kingdom Optigen Accession #: 13-8346 VIIL#: \$2283 Report issued for: VHL_ID H52283

Ontifien Tost Certificati

Optigen Accession #: 13-8346

Test Performed: CEA/CH test

Registered Name: Loralnian Campbell Clan

Breed: Sheffand Sheepdog

Sex: Malc

Date of Birth: November 30, 2011

Owner(s):

1601627232 Paterson

Test Completed: 08/12/2013 Report Issued: 08/13/2013

Result: Normal

Sample Type: DNA - Blood

Reg#: AP00377503

@#: 985 154 000 377 523

OptiGen Authorized Signature

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email: geleles%optigen.com

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Example of a BVA/KC eye scheme certificate

Performed by opthamalgic specialists from the BVA Eye Panel

Informs on breed-specific diseases known to be inherited (affected/unaffected)

Also provides information on any other visual anomalies in the eye – injury, emerging inherited diseases, non-inherited diseases, adnexa

Currently, only known inherited diseases results are recorded and published – this may change to the future

Results are recorded and published by the KC for inherited disease results only

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Once you know what you should be testing for...

Is it a "simple" gene mutation? i.e. DNA test?

Test result → Health Test Results Finder!

Is it a "complex" condition? i.e. KC/BVA Hip, Elbow scheme?

Scheme result → Health Test Results Finder + EBVs

Informed decisions: Health Schemes and Programs

What is published on Mate Select's Health Test Results Finder

Breed-specific DNA Schemes:

Clear

Carrier

Affected

BVA/KC/ISDS Eye Scheme:

Unaffected

Affected

(cannot identify "carriers")

Other: Complex disease information,

ex: BVA/KC Hip, Elbow, CM/SM

schemes

The importance of publication

- Results available to dog breeders, owners, and puppy-seekers
- Promotes openness and honesty
- Encourages health testing
- Allows breeders to clearly demonstrate good practices

What isn't yet published...

Some recommended testing not currently recorded:

- Breed Club testing recommendations breed specific recommendations Examples: Patella testing, Heart, thyroid, kidney
- Breed Club breeding recommendations

Example: Boxer Breed Clubs recommend "Heart Testing (aortic stenosis)"

Breed-specific breed club recommendations are published, but of course do not have "results"

ex: "bitches under 2 years not to be mated" (many breeds)

Home Mate Select Find A Puppy Transfer Ownership Health Tests Breed Information More Services

Mate Select Health Test Results Finder

Dog Details

Registered Name or Registration/Studbook Number

Miley Twerk en botton





When searching by name you must include the **exact** spelling of the dog's registered name as it appears on the dog's registration certificate and in the BRS.

This tool will allow you to search for any health results for a dog which is registered on the Kennel Club's Breed Register either by its registered name or registration number (or stud book number).

It will display any screening results received and recorded by the Kennel Club from a British Veterinary Association/Kennel Club (BVA/KC) health scheme or an official Kennel Club DNA testing scheme.

Go

Mate Select Home

More information

Glossary of Health Tests Screening Schemes Information Guides

Other services

Breed Information Centre Find A Breed Club

Help

Contact us



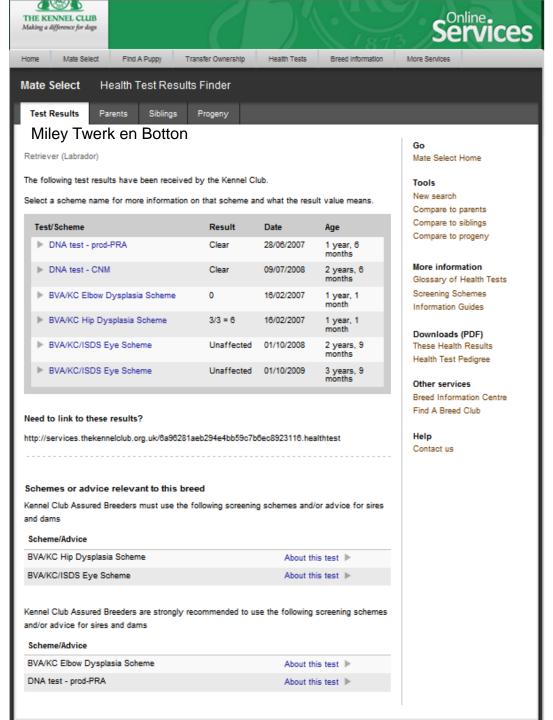
What can I do with the results?

All tests/schemes we can record on the database are included

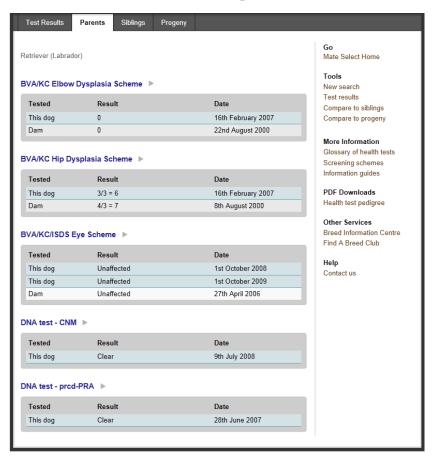
Click on the **links** for more information on the tests/schemes

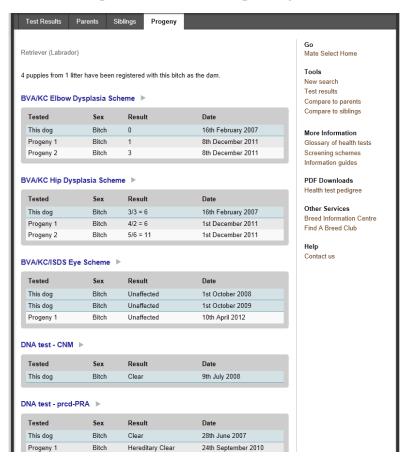
Click on the tabs for health results for Parents, Siblings, and Progeny (where available)

Download, and print-off for your records or for puppy seekers

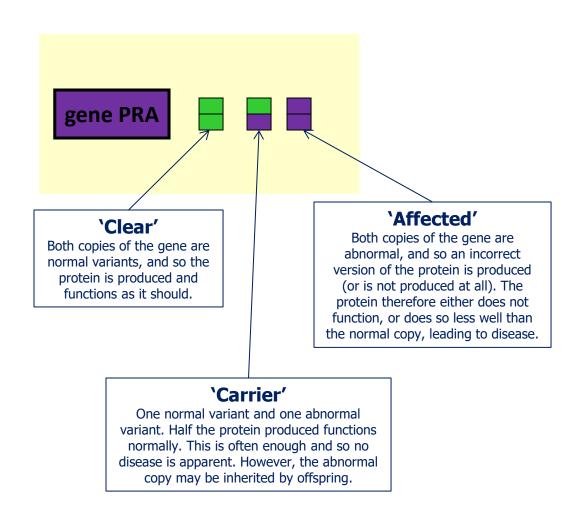


Reviewing results of Parents, Siblings, and Progeny

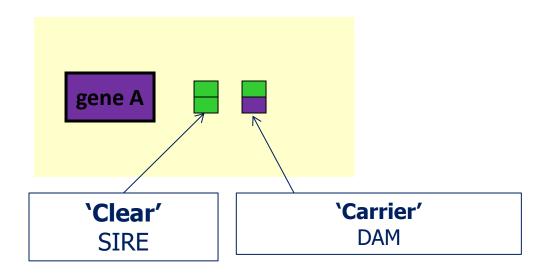




Autosomal recessive conditions (most DNA tests)



Autosomal Recessive conditions (most DNA tests)



Resulting puppies will average 50% carrier, and 50% clear. None will be affected by the specific disease

Simple Disease Prevention – autosomal recessive

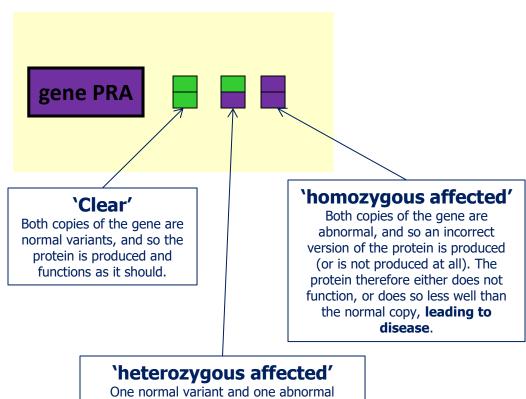
Clear + Clear = ALL Clear

 Clear + Carrier = Some Clear (1 in 2) and Some Carrier (1 in 2)

Clear + Affected = ALL Carrier

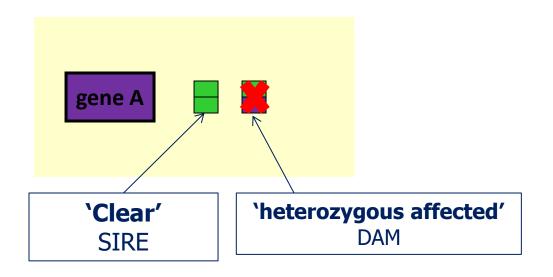
 Carrier + Carrier = Some Clear (1 in 4), Some Carrier (2 in 4), Some Affected (1 in 4)!

Autosomal-dominant conditions (few DNA tests)



One normal variant and one abnormal variant. Half the protein produced does not function normally. The dog will be affected for the disease, and may pass on one abnormal copy to offspring.

Autosomal Recessive conditions (most DNA tests)



Only two clear tested dogs will produce ONLY disease-free puppies

Simple Disease Prevention – autosomal dominant

Clear + Clear = ALL Clear

Clear + Heterozygous affected = Some Clear (1 in 2) and Some heterozygous affected (1 in 2)

 Clear + Homozygous affected = ALL heterozygous affected

Consider the whole dog!

- There are thousands of genes in a dog around 600,000 SNPs mapped (SNPs = single nucleotide polymorphisms, where the variations in DNA occur)
- There are fewer than 100 single-gene mutation DNA tests across all breeds
- A tested dog is predictable. No test results? Don't assume clear. A known carrier can be safely used, and protects genetic diversity

But what about known complex conditions?

 There could be several/many genes involved (multi-variant)

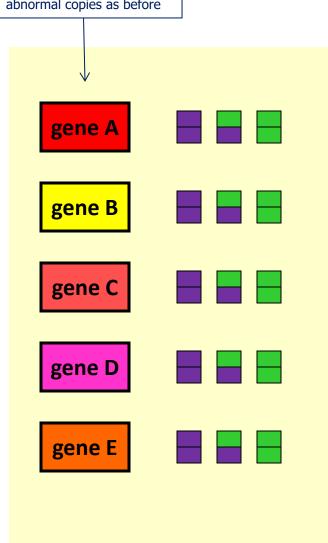
 There could be "outside" influences (environmental factors)

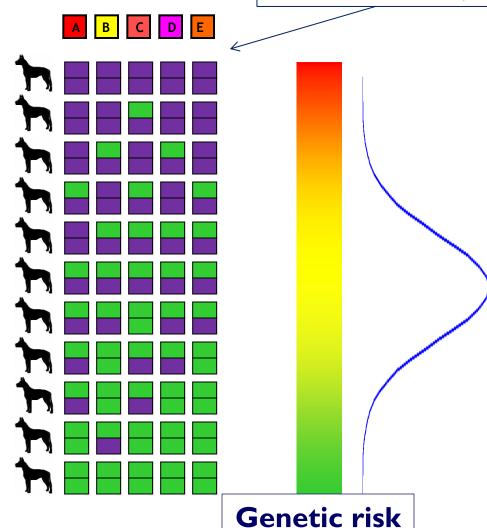
Currently only assessed through "Schemes" –
using these individual scores was the best
option up until now, but harder to predict risk

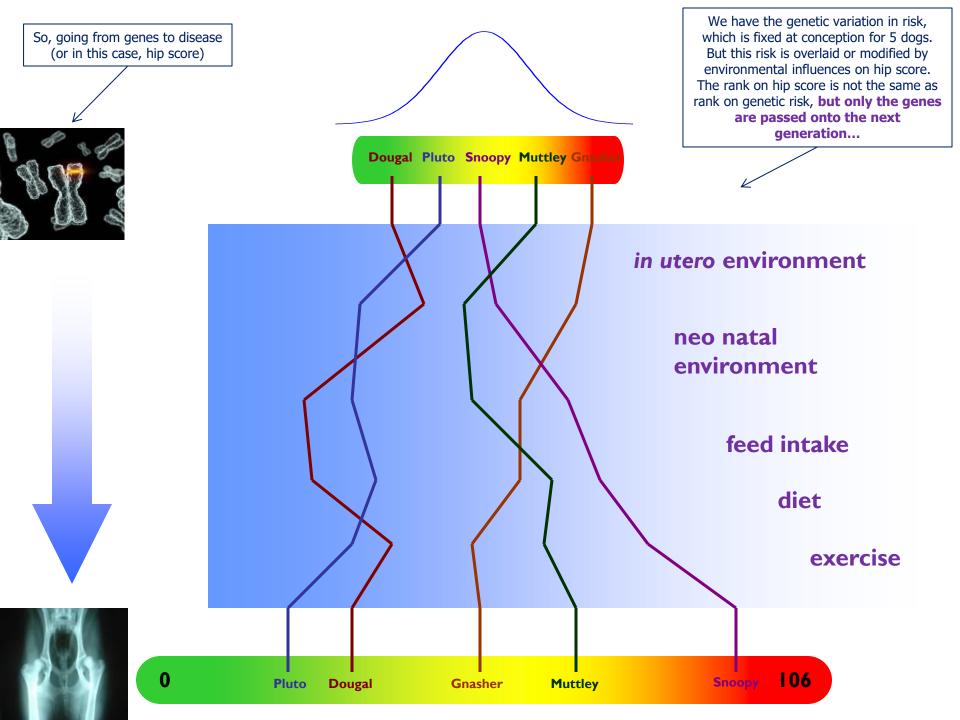
Most traits (and diseases) are affected by multiple genes (often hundreds), each gene adding a small amount of increased or decreased risk. Each gene can have the 3 combinations of normal and abnormal copies as before

Genetic variation

So if we look at a sample of dogs we can see the number of different combinations. This produces genetic variation in the risk of disease. Thus we get a continuous spectrum of genetic risk, which is normally distributed (Bell curve – few at either end, more in the middle)







The Tool: Estimated Breeding Values (EBVs)

- EBVs have been used for many years in other species, and are "tried and tested"
- In principle, you can make an EBV for anything that is measurable: complex conditions, size/shape, yields (i.e. milk in cows), etc.
- 15 breeds with hip or hip + elbow: Akita, BMD, Bearded Collie, Border Collie, Eng. Setter, Flat Coated Retriever, Gordon Setter, GSD, Golden Retriever, Labrador, Newfoundland, Siberian Husky, Rottweiler, Rhodesian Ridgeback, Tibetan Terrier

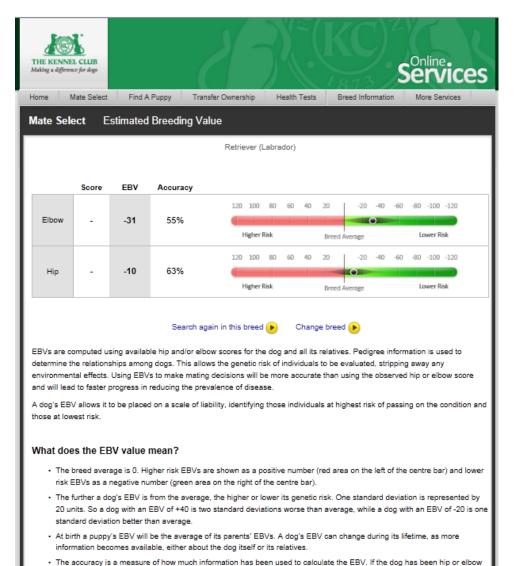
EBVs

EBV stands for: Estimated Breeding Values

They estimate the *genetic* risk of complex diseases

EBVs are a more efficient way to estimate risk, and breed away from undesirable traits more quickly than by individual dog results (phenotypic) alone

EBVs use Health Scheme data for calculation



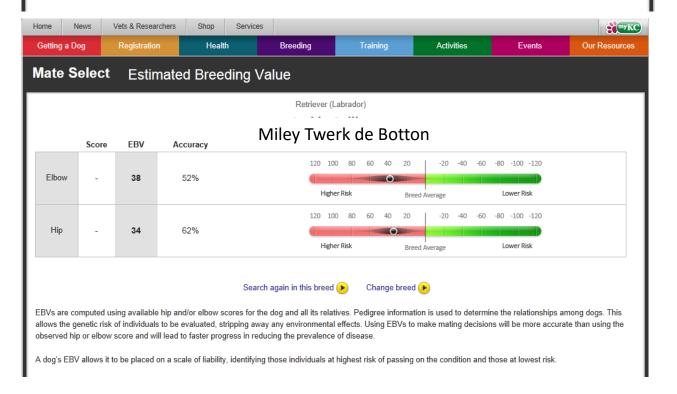
scored itself and has several relatives with scores then the accuracy will be higher than if it has not been scored and has few relatives with scores. Individuals with several scored offspring tend to have high accuracies. Accuracy is the correlation between the estimate of the breeding value and the true value. The more information available the closer the estimate will

be to the true value.

Mate Select **Estimated Breeding Value** Retriever (Labrador) Harry Styles von Floppy Hair Score EBV Accuracy 120 100 80 60 40 20 -20 -40 -60 -80 -100 -120 Elbow 0 45 89% Higher Risk Lower Risk Breed Average 60 40 20 -20 -40 -60 -80 -100 -120 4/3 = 798% Higher Risk Lower Risk Breed Average Search again in this breed () Change breed (> EBVs are computed using available hip and/or elbow scores for the dog and all its relatives. Pedigree information is used to determine the relationships among dogs. This allows the genetic risk of individuals to be evaluated, stripping away any environmental effects. Using EBVs to make mating decisions will be more accurate than using the

observed hip or elbow score and will lead to faster progress in reducing the prevalence of disease.

A dog's EBV allows it to be placed on a scale of liability, identifying those individuals at highest risk of passing on the condition and those at lowest risk.



Mate Select Estimated Breeding Value Retriever (Labrador) Lyndsay Lowhaan **EBV** Score Accuracy -20 -40 -60 -80 -100 -120 Elbow 0 -15 59% Higher Risk Breed Average Lower Risk 120 100 80 60 40 -40 -60 -80 -100 -120 12/5 = 17 Hip 9 81% Higher Risk Lower Risk Breed Average

Search again in this breed 🕨 Change breed 🕨

EBVs are computed using available hip and/or elbow scores for the dog and all its relatives. Pedigree information is used to determine the relationships among dogs. This allows the genetic risk of individuals to be evaluated, stripping away any environmental effects. Using EBVs to make mating decisions will be more accurate than using the observed hip or elbow score and will lead to faster progress in reducing the prevalence of disease.

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Mate Select Estimated Breeding Value

Retriever (Labrador)

Taylor Swifty

	Score	EBV	Accuracy	
Elbow	0	-22	63%	120 100 80 60 40 20 -20 -40 -60 -80 -100 -120
				Higher Risk Breed Average Lower Risk
	8/6 =			120 100 80 60 40 20 -20 -40 -60 -80 -100 -120
Hip	14	-1 82%	82%	
				Higher Risk Breed Average Lower Risk

Search again in this breed () Change breed ()

EBVs are computed using available hip and/or elbow scores for the dog and all its relatives. Pedigree information is used to determine the relationships among dogs. This allows the genetic risk of individuals to be evaluated, stripping away any environmental effects. Using EBVs to make mating decisions will be more accurate than using the observed hip or elbow score and will lead to faster progress in reducing the prevalence of disease.

A dog's EBV allows it to be placed on a scale of liability, identifying those individuals at highest risk of passing on the condition and those at lowest risk.

Benefits of EBVs to Dog Health and Breeders

- More accurate assessment of a dog's genetic risk
- The lower the EBV, the better but there isn't a need to seek out the very lowest EBV – selecting any animal with a lower risk EBV than average will apply selective pressure to improve hip scores faster than an individual hip score alone
- More flexibility in choosing mates as the EBV measures genetic (heritable) risk, as opposed to the individual score, which measures the risk for that dog
- More flexibility to balance and prioritise health considerations – temperament, DNA test results, health screening results, genetic diversity, conformation, etc...

There isn't a test...

- Get a full diagnosis
- Is the disease actually inherited?
 - Google, PubMed, CGE, PlosOne, Vet Record, In Practice...
 - Peer-reviewed and lots of dogs
- If not inherited...
 - Treat/manage/cure
 - Breeding?

Honesty

- Should these genes continue, to improve the breed?
- How much risk?
- Can I reduce the risk?
 - Family history?
 - Risk-free or low-risk lines?
- Tell the new owners.

Support – You are not alone

- New Inherited disease tests (all breeds) £250,000 (AHT)
- Syringomyelia £2,670 (Bristol)
- Gait studies £13,325 (Bristol)
- Brachycephalic conditions £19,145 (Cambridge)
- Soft-tissue sarcomas £2639 (Glasgow)
- Osteosarcoma (Rotties) £700 (Notts)
- MANY breed clubs
- Karlton Index
- Guide Dogs, Hearing Dogs, BSAVA, BVA
- Kennel Club health section: <u>mateselect@thekennelclub.org.uk</u>
 OR <u>hbs@thekennelclub.org.uk</u>

BRACE YOURSELF! Here comes population genetics...



I promise it will be okay.



Breed Conservation – genetic diversity

- To create a breed, there is a level of inbreeding
- The more in-bred the more shared genes the good and the bad
- Reducing, or slowing the rate of inbreeding, and increasing diversity where possible will give breeders more options and reduce risk across the breed
- Mate Select has an inbreeding calculator for breeds, individual dogs, and matings
- Helps to breed for traits, not relatedness

Selection Pressure

- Every breeder (of any species) has criteria for selection
- For dog, there is known and unknown i.e. assessments available, by observation only, random mutation, false selection (noninherited)
- Every selection pressure alters the available genetic material – not always bad, but must be in balance and done with care!

Selection Pressure – genetic bottlenecks

The Good:

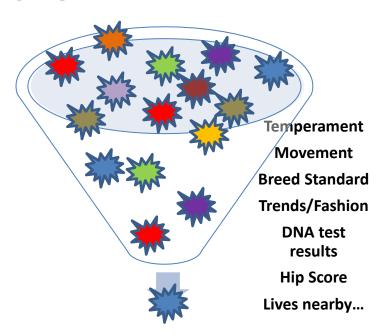
- Elimination of known inherited disease
- Reduced disease risk for *specific* inherited conditions
- Promotion / "fixing" of desirable traits

The Bad:

- Reduced options for *unknown* inherited disease (genetic diversity)
- Inbreeding Coefficients rise
- Effective population size diminished

The Ugly:

Unintended Consequences: Rapist Chickens









Solutions?

- Reduce relatedness of sire to dam TOOL:
 Coefficient of Inbreeding
- Limit numbers of offspring by individual dogs (popular sire)
- Use all available healthy stock (randomise)
- Inner-breed "crossing" (working vs. showing)
- Make use of overseas bloodlines
- Outcross smart ones

Selection Pressure – Every sperm is precious

- Example: Otterhound
- Health (perceived): epilepsy, hips...were they too strict? (1st degree relatives with epy banned, hips suffered)
- Health (actual): NEED MORE DOGS and GENES
 - Low EEPS (28.5 in 2012)
 - Low reg. numbers (42 dogs in 2013)
 - No room to manoeuvre for known inherited diseases
 - Will become extinct NOW
- Outcross?



What is an Inbreeding Coefficient?

- The inbreeding coefficient of an individual is the probability that two copies of the same gene have been inherited from a common founder – that is, an ancestor shared by both parents
- The lower the inbreeding coefficient, the lower the probability (risk) this will happen

Individual Inbreeding Coefficient

Search for an individual KC registered dog using name or registration number

Results compare the dog to the breed average

Result

Inbreeding Coefficient

Retriever (Labrador)

Lady Lass

Breed Average

6%

More information

Health Tests for this dog

Individual Inbreeding Coefficient

What does this value mean?

Mate Select

Inbreeding is defined as the mating of related individuals, whether they are closely
related or more distantly related. The inbreeding coefficient of an individual is the
probability that two copies of the same gene have been inherited from a common
founder, that is an ancestor shared by both parents. The lower the inbreeding
coefficient, the lower the probability (risk) that this will happen.

An inbreeding coefficient of 12.5% means that there is a 1 in 8 chance that a dog will inherit the same version of gene from the same dog that appears in both the sire's and dam's pedigree. The puppies born to a mother/son, father/daughter or brother/sister mating (which the Kennel Club will no longer accept for registration), would be at least 25%. The inbreeding coefficient of puppies born from a grandfather/granddaughter mating would be at least 12.5%.

Find out more about inbreeding...

Go Mate Select Home

New Calculation Change Breed

Other services

Breed Information Centre Health Test Results Finder

Predict COI of a mating with this dog as the dam

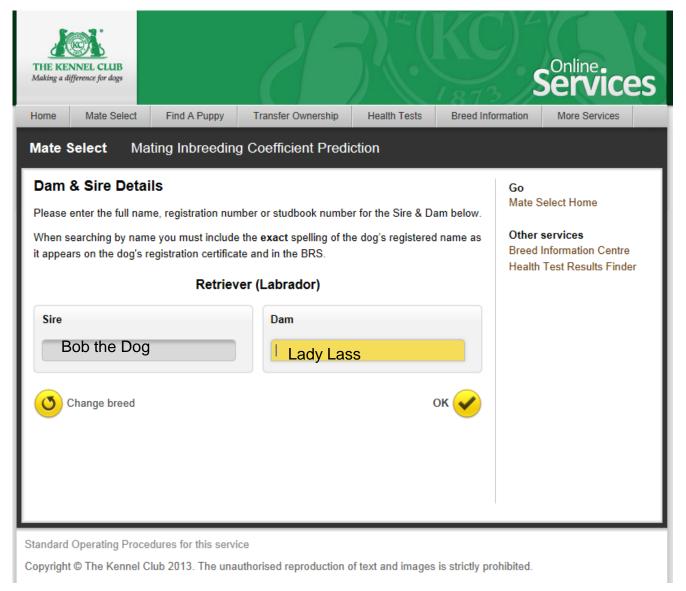
About this calculation

The pedigree data used to calculate this result extended back as far as 19 generations with the first 4 generations being fully complete.

The Mate Select computations are based upon data compiled from pedigree records and data submitted from breeders. As such all information and/or data on the site is provided on an 'as is' basis. Every effort has been made to report information accurately, but the Kennel Club assumes no responsibility for the content or the use or interpretation of the information published.

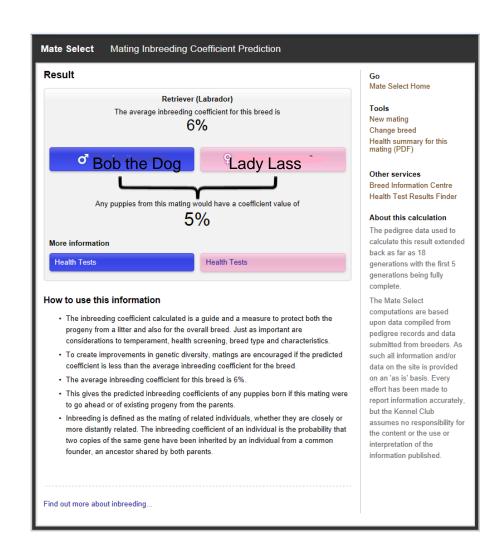
Standard Operating Procedures for this service

Mating Inbreeding Coefficient



Mating Inbreeding Coefficient

- Uses names of dam and sire
- Predicts inbreeding coefficient for resulting puppies
- Breeding for genetic diversity reduces the risk of inherited conditions, and benefits the breed as a whole
- Links to Health Test Results for dam/sire



Individual Inbreeding Coefficient – what would you do?

Mate Select Individual Inbreeding Coefficient

Result

Inbreeding Coefficient

Retriever (Labrador)

Betty

7.2%

More information

Health Tests for this dog

What does this value mean?

Inbreeding is defined as the mating of related individuals, whether they are closely
related or more distantly related. The inbreeding coefficient of an individual is the
probability that two copies of the same gene have been inherited from a common
founder, that is an ancestor shared by both parents. The lower the inbreeding coefficient,
the lower the probability (risk) that this will happen.

An inbreeding coefficient of 12.5% means that there is a 1 in 8 chance that a dog will inherit the same version of gene from the same dog that appears in both the sire's and dam's pedigree. The puppies born to a mother/son, father/daughter or brother/sister mating (which the Kennel Club will no longer accept for registration), would be at least 25%. The inbreeding coefficient of puppies born from a grandfather/granddaughter mating would be at least 12.5%.

Find out more about inbreeding...

Go

Mate Select Home

All results for this session New Calculation Change Breed

Other services

Breed Information Centre Health Test Results Finder

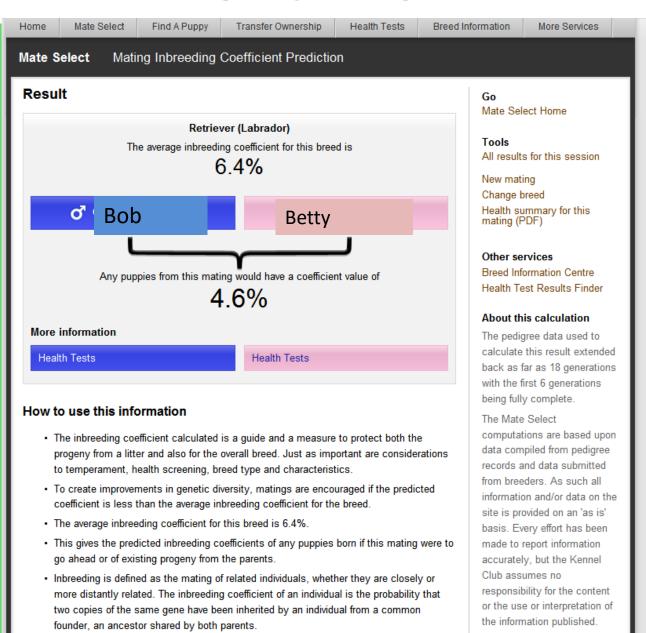
Predict COI of a mating with this dog as the dam

About this calculation

The pedigree data used to calculate this result extended back as far as 18 generations with the first 6 generations being fully complete.

The Mate Select computations are based upon data compiled from pedigree records and data submitted from breeders. As such all information and/or data on the site is provided on an 'as is' basis. Every effort has been made to report information accurately, but the Kennel Club assumes no responsibility for the content or the use or interpretation of the information published.

Choose the right paring!



Get Involved?

Kennel Club support and funding

The collection of scientific data is of the highest importance, helping to:

- Identify the prevalence of canine and breed specific health conditions
- Understand the heritability of specific disorders
- Classify the genetic status of dogs for known conditions
- Provide evidence based advice on how to breed away from particular disorders
- Develop new or more effective treatments for health conditions

To help achieve this, the Kennel Club regularly assists and collaborates with research facilities, Universities, veterinary organisations and charities to further our knowledge of canine health and welfare.

How the Kennel Club helps with your research

The Kennel Club can help researchers in a number of different ways, which can include providing contributions towards funding, assisting with the recruitment of dogs and owners for your study and providing you with data from the Kennel Club Ratabase

International Canine Health Awards

The Kennel Club Charitable Trust International Canine Health Awards, which are the largest veterinary awards in Europe, have been orested to recognise innovative researchers, veterinary scientists and students from around the world, who have carried out research that has helped to improve the health and wellbeing of dogs.

The Awards, which are underwritten by a major gift from the Vernon and Shirley Hill Family Foundation, will identify and encourage visionary thinking, ambition and life-changing accomplishments. Those who receive the awards will be passionate about making a difference for dogs. Each award provides a large funding programme to the recipient, which rewards them for their dedication and innovation in the field of canine health and welfare and invests in helping them to continue making a difference for dogs.

The Kennel Club Charitable Trust

This dog charity helps to look after the health and welfare of all dogs and makes a difference by funding a wide variety of work, ranging from supporting research into canine diseases, dog welfare organisations and the promotion of support dogs, all of which give dogs a healthier, happier life.

Founded in 1987, it has donated almost £6 million to support these initiatives through various dog charity grants, and is able to provide its support through the generosity of our donors.

Recruitment and publicising

On your behalf the Kennel Club may be able to promote your study or encourage people to participate in your study

- An e-mail sent to all registered owners of a particular breed
- Social media (Facebook and Twitter)
- The "Events, seminars and surveys" section on the Kennel Club website
- The Kennel Scope (a newsletter for veterinary practices)
- A press release
- An e-mail sent to all, or selected Breed Health Co-ordinators, who may in turn be able to publicise your study

Bio-Acquisition Research Collaboration

The Kennel Club has created this facility to help bring researchers and olinicians together with regards to research projects, making it easier to form a collaboration of different ideas and information. It will also act as a central platform for researchers to request samples they need to undertake their current research. If you wish to submit any information regarding sample requirements for a research project, please fill in this form and email it to Bonnie Abhayarstne.

Sample information required:

- What the samples are intended for/what is being investigated
- Breed(s) that you would like samples from
- Health status (for example, samples from healthy dogs and/or samples from dogs with a diagnosed condition)
- Type of sample (for example, blood, cheek swab, tissue)
- Sample preservation method
- Where to send samples and contact information
- Other specific requirements (for example, age/sex, additional clinical information)

Please contact us when you no longer require samples.

Current exchange requests

If you are able to help by contributing samples, or have any queries about the research being undertaken, or would like more information, please contact the researchers directly.

Date Added	Breed/Type	Research	Sample Information	Contact
8th April	Pugs French Bulldogs Bulldogs	Non-invasive respiratory function assessment in brachycephalic dogs	Measurements taken from healthy and diagnosed dogs with brachycephalic	Miss Nai-Chieh Liu Tel: 01223 337621
		Aims to characterize respiratory function in brachycephalic dogs and to	obstructive airway syndrome (BOAS) as well as dogs whose	Queen's Veterinary School Hospital, University of Cambridge
		investigate the genetic and anatomical markers that are related to brachycephalic obstructive airway syndrome. Apart from baseline measurement of	BOAS status is currently uncertain (>2 years of age and hasn't undergone any upper ainway surgery).	(measurements taken at this venue but investigators can come to you where there is the opportunity to take measurements from many dogs at once)
		each included breeds, we are also studying the respiratory function before and after upper airway corrective surgery	Following measurements are taken by the study investigator (appointment required): (1) Respiratory flow trace measurement; (2) DNA sample collections from cheek swabs; (3) head/body dimension measurement	Click <u>here</u> for more information



Meet the Health Team

- Aimée Llewellyn –Manager, genetics
- Dr Tom Lewis Quantitative Genetics, Mate Select development
- Nick Sutton Vet communication, health communication, toxicology/poisons, Mate Select, health queries
- Bonnie-Marie Abhayaratne –
 Breed Health Coordinators, web,
 Mate Select, health queries
- Bonnie Wiles Surveys, data, health queries
- Charlotte McNamara High Profile breeds, Breed Watch



From L-R: Aimee, Nick, Charlotte, Tom, Bonnie-Marie, Bonnie

Partners and Thank-yous

- Dr Cathryn Mellersh and the KCGC at the AHT team,
 Dr Tom Lewis, Dr Sarah Blott
- Health Team <u>mateselect@thekennelclub.org.uk</u>

















