

Harmonization of Genetic Testing and Breed-Specific Resources

Brenda N. Bonnett

AKC-CHF Parent Club Health Symposium

August 2019





Disclosure Statement

I, Brenda Bonnett have an affiliation with the International Partnership for Dogs (CEO) described in this presentation. We have a grant from AKC-CHF.

IPFD is a non-profit organization.



Brenda N. Bonnett

- Veterinarian, theriogenologist
- Epidemiologist
- Former tenured faculty Ontario Veterinary College
- Research:
 - Population health; many species; breed-specific dog, cat, horse
 - Veterinary communication
 - Human-animal interactions
 - Pet overpopulation
 - Reproduction
- brenda.bonnett@ipfdogs.com

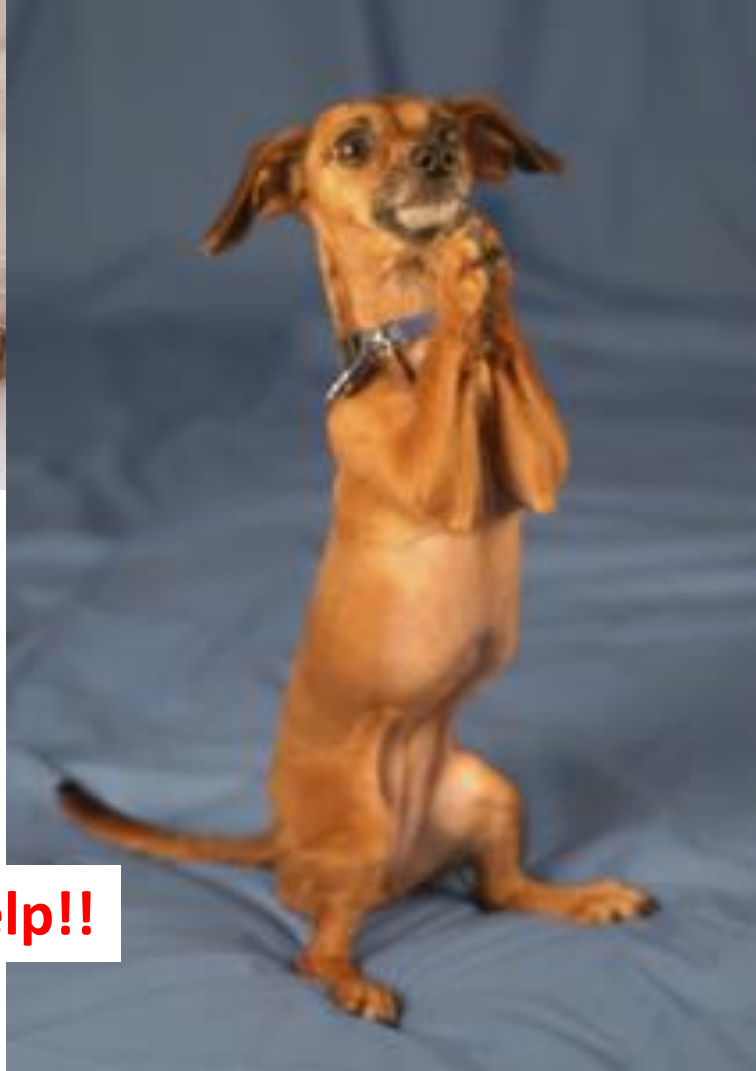


What
the.....
????

Confused!



And asking for help!!



*What I heard from the panel discussion on
Saturday... breed club health committees
are:*

FRUSTRATED!!



International
Partnership
for Dogs



2019
AKC CANINE HEALTH FOUNDATION
NATIONAL PARENT CLUB CANINE HEALTH CONFERENCE

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In spite of us working together to build resources....



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2019
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The world of genetics/genetic testing is complex and messy and there will never be a simple, one-size-fits-all-quick fix – understand and comply with completely.

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IPFD – enhancing the health, well-being and welfare of dogs

- Multi-stakeholder
- International
- Sharing, collaborative
- Participatory

- Arms-length, independent
- Collective evidence and opinion
- Strength in numbers and diversity

Tools and Resources



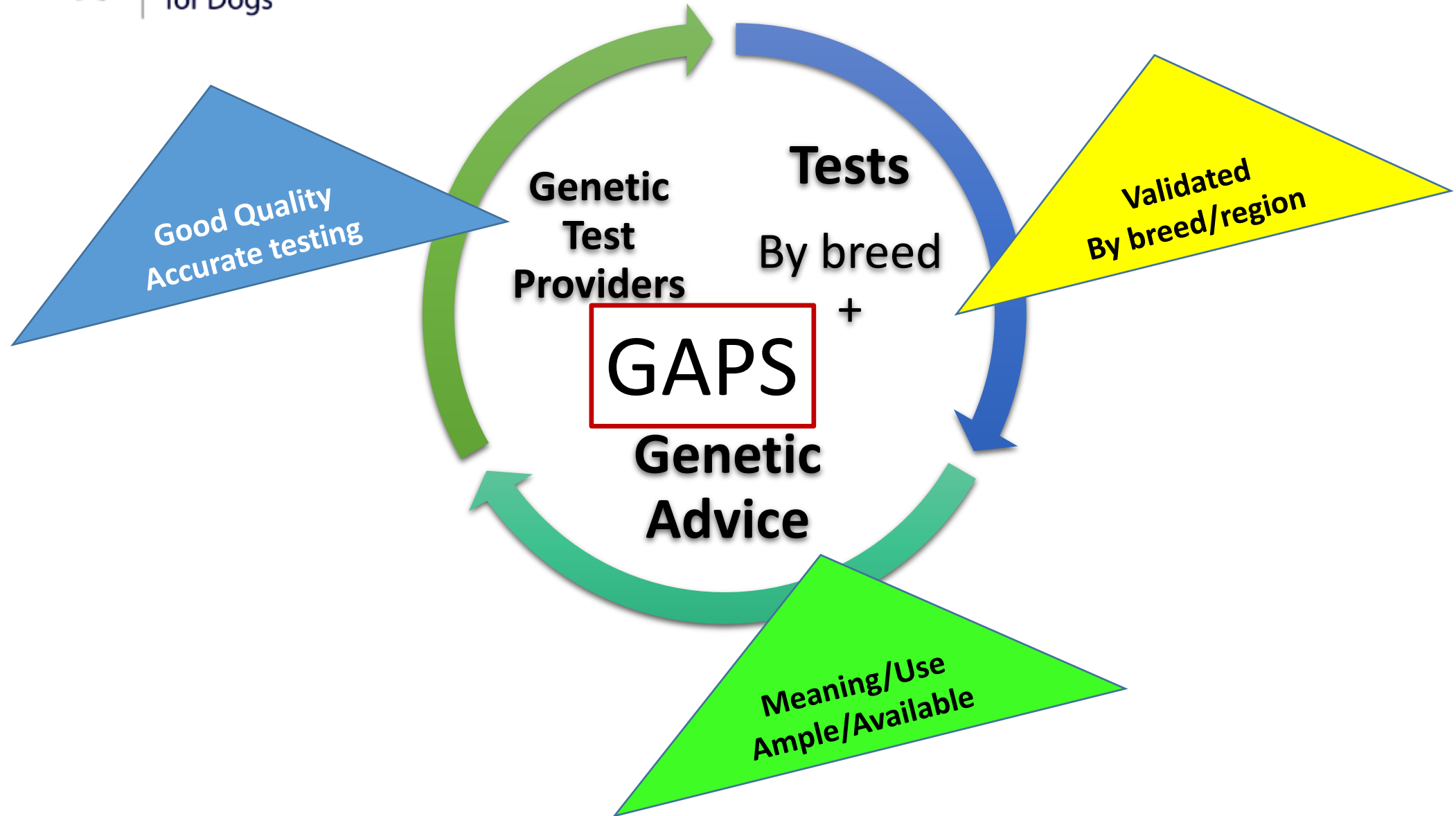
Learning Objectives:

1. **Update on the Harmonization of Genetic Testing resource and new work supporting breed-specific resources.**
2. Describe **impacts and limitations on genetic testing**, e.g. comparative research, direct to consumer testing, and application to individual vs. population health.
3. Demonstrate the need to apply and interpret genetic testing information in the **context of wider aspects of health**, welfare and human-dog interactions.
4. Identify **tools** to support the above.



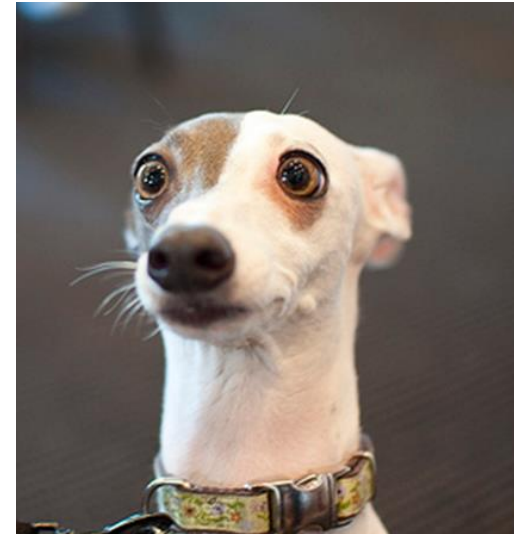
Harmonization of
Genetic Testing
for Dogs

Last time I spoke at CHF I talked about the IDEAL SITUATION...



**There is currently no
quality control system for
DNA testing in veterinary
medicine**

**no standards... no rules
or regulations about who
can offer tests, etc. etc.**



Harmonization of
Genetic Testing
for Dogs

And likely there will never be formal regulation or standards... IPFD together with international participants at the International Dog Health workshop ARE working on exploring various options to address concerns.

5 years ago – 2 years ago

IPFD Harmonization of Genetic Testing for Dogs HGTD

- Too many new DNA testing labs
- Focus on **single gene tests**... AND discovery outpacing:
- **Validation** from discovery to application – not there for many tests.
- Rapid **commercialization**

5 years ago – 2 years ago

IPFD Harmonization of Genetic Testing for Dogs HGTD

- Too many new DNA testing labs

- Focus

- Valid

- Rapid commercialization

People want to know:

What tests are available for my breed?

Which should be used in breeding decisions?

Which Genetic Test Providers can be trusted?

Over the past 5-10 years there has been a relatively quick change from resistance to implementing health strategies/testing ... to

- overemphasis on DNA tests over all other health evaluations.
- 'early adoption of tests without adequate validation for specific breed/disease situation
- *Misunderstanding* of test results &/or inappropriate application

Over the past 5-10 years there has been a relatively quick change from resistance to implementing health strategies/testing ... to

- overemphasis on DNA tests over all other health evaluations.
- 'early adoption of tests without adequate validation for specific breed/disease situation

This has been enhanced and complicated by :

- Decision-making by facebook.

And maybe hesitance of Kennel Clubs to STOP breed clubs from implementing health testing??



PERSONALIZED MEDICINE --- the future!!

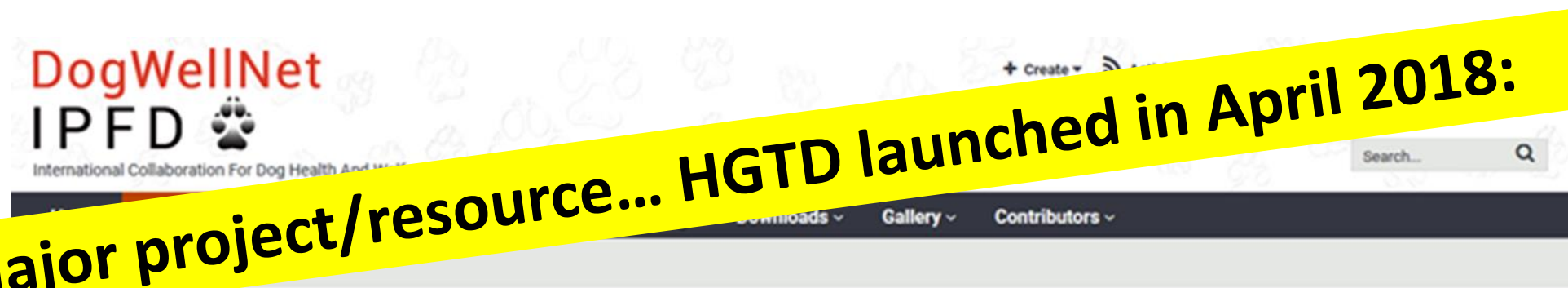
Sounds appealing, but:

*When it began...Tests – albeit markedly fewer than are available today – were ordered through health practitioners – with pre- and post-test counselling.
Now??*

Consumers need help!

Direct To Consumer (DTC)
Popularized thru Social Media
Massive marketing push

Major project/resource... HGTD launched in April 2018:



Harmonization of
Genetic Testing
for Dogs

HGTD GOAL: Improve standardization of, and access to, robust genetic testing to support health improvements and a sustainable future for healthy dogs. The portal for information on Genetic Testing Providers (labs); genetic tests, and tests by breed. There are two major components: the Quality Testing Database and Genetic Counselling resources.

IPFD cannot be held responsible for inaccurate content or any outcome from the use of information or resources found on this site.

[More >>](#)

HGTD Quick Search

[Breed](#)
[Test/Disease](#)
[Lab/GTP](#)

HGTD Database Resources

[How to use the HGTD](#)
[HGTD Quality Indicators](#)
[Acronyms - Mode of Inheritance](#)

FAQs

Accreditation Basics
This brief overview may help you identify what types of accreditation are important to you, when choosing your genetic test provider.

Accreditation and Industry Standards
List of organizations throughout the world that are involved in matters of accreditation and establishing industry standards.

[Choosing a Genetic Test Provider](#)

HGTD - Quality Testing Database



<https://dogwellnet.com/ctp/>

Achievements

HGTD launched April 2018

- **Open-access, sustainable online resource** that catalogues information provided voluntarily by Genteic Test Providers (GTPs)
- **Describes expertise, quality measures, activities and resources of GTPs**
- Includes data from all types of GTPs – commercial, non-profit, academic, test-developers and non-test developers
- **Phene database** is a searchable, easy-access public resource providing extensive information on individual genetic tests
- Steering committee aided development - providing balanced expertise and contributions from a broad-spectrum of stakeholders

Currently:

69 GTPs listed
19 countries
33 volunteering data



300+ Phenotypes,
tests/diseases/
characteristics

PARTNERSHIPS
COLLABORATION
E.G. ... WSAVA



500 plus breeds and
breed-types



HGTD is an initiative of the International Partnership for Dogs with collaborators from kennel clubs, industry, genetic test providers, veterinarians, academics, OMIA and others. The HGTD open access, online resource was launched on DogWellNet.com in April 2018 and currently features work by initiating leadership sponsors and contributors focused on offering quality genetic testing for dogs.

HGTD provides:

- a catalog of quality measures, expertise, activities, resources and information from commercial test providers for genetic testing in dogs;
- access to existing and new resources for genetic counseling and education;
- the foundation for future developments to support GT that is optimal, robust and sustainable in the broadest perspective of pet health;
- GTPs and collaborators should contact us if interested in contributing GT information to the HGTD database.

Identifying challenges and moving forward...

With no existing national or international standards of accreditation, or standardization oversight group, there is a need for guidance on DNA test reliability, laboratory quality assurance, and balanced breeding and test advice.

The **Expert Panel Initiative** will include input from stakeholder groups across breeds, borders and industry to inform and support best practices in the discovery, communication and application of genetic testing to maximize the opportunity to positively impact the health of individual dogs and breeds.

Researchers, genetic advisors and breed experts are welcome to contact us to participate in the initiative.

Contacts: IPFD CEO Brenda.Bonnett@ipfdogs.com or Project Director Aimee.Llewellyn-Zaidi@ipfdogs.com

Benefits of HGTD and our flexible, adaptive platform

- Interactive communication with all stakeholders
- **Identifying gaps/errors**
- Providing balanced responses
- Updating/standardizing terms across stakeholders
- E.g. Chondrodysplasia (dwarfism) and Chondrodystrophy (short-limbs and spinal disc disease)
- **Breeder questions and input**
- **Advice from researchers**

Lots of coverage – some rather sensational - in the media...

Do DNA Tests Work?

Pet genomics medicine runs wild

\$ Big Business €

HOT
TOPIC

nature
International journal of science

The Atlantic

**USA
TODAY**

**IPFD: Genetics and Genomics for
Dogs: Balancing daunting
challenges and great potential**

<https://dogwellnet.com/content/health-and-breeding/screening-tests/dna/dna-tests-for-use-in-breeding-decisions/genetics-and-genomics-for-dogs-balancing-daunting-challenges-and-great-potential-r597/>



IPFD 4th International Dog Health Workshop

DogWellNet
IPFD 



Dates: Thurs. 30 May to Sat. 1 June 2019

Location: Windsor, UK



**Multiple stakeholders –
veterinarians, KC and breed clubs,
advisors, breeders, researchers,
owners, etc.**

[illegible]

Genetic Testing Theme

At the 4th IDHW....

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Harmonization of
Genetic Testing
for Dogs

How do we **know** what tests to use?

Can we **trust** the test results?

How should results be **interpreted**... especially in the context of the **bigger picture of health in the breed?**

Genetic Testing – why is it done?

- **Individual animal**
 - Breed background/ heritage
 - Diagnosis/ prognosis/ therapy
- **Breeding**
 - Risk reduction
 - Selection or avoidance of characteristics
- **Breed/ population**
 - Risk/ prevalence
 - Diversity
- **KCs/ Registries/ Forensics**
 - Dog ID
 - Parentage
- **Veterinarians**
 - Clinical / individual
 - Diagnostic/ therapy
 - Marketing – preventive medicine

What question do you want to answer?
What will you **do with that answer?**



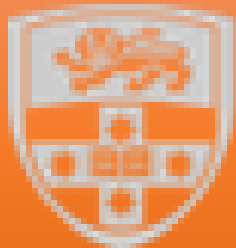
Genetic Testing Theme

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Researcher challenges
impacting genetic test quality

• CLAIRE WADE



THE UNIVERSITY OF
SYDNEY



IPFD had a poster at the 10th ICCFGG meeting in Bern on researcher roles and challenges in genetic testing... and in this poster from Prof. Claire Wade at the 4th IDHW

Why are tests made available without validation?



No funding for the validation process beyond the ability to publish



Different kinds of validation

Assayed differently
Associated
Functional
Penetrant



Population management not required for publication



Most researchers are pure biologists

Why are tests released without publication?



High cost of discovery



Free access by GTP upon publication



Patent application releases method



Inventors seek compensation for effort



Researchers use pre-publication test release as compensation avenue



Issues with peer review

Next Steps: 4th IDHW

- Application/Genetic advice – **IPFD Expert Panel**
- **Validation– IPFD IDHW Validation Matrix**
- Laboratory standards; Proficiency
- *Pre-publication peer review?*

Validation Template

- Definition of 'validation' across the spectrum from discovery to applications and descriptions to underpin genetic counselling.

The genetic test development pathway and levels of validation



Pathway... but ...

Validation Template

- Definition of 'validation' across the spectrum from discovery to applications and descriptions to underpin genetic counselling.

The genetic test development pathway and levels of validation



COMMERCIALIZATION

(should occur after towards the end of this validation pathway... but often tests are sold and applied as soon as they are discovered and without adequate validation.

Validation Template

- Definition of 'validation' across the spectrum of applications and descriptions to underpin genetic testing

***At least we need
TRANSPARENCY!***

The genetic test development pathway and levels of validation



COMMERCIALIZATION

(should occur after towards the end of this validation pathway... but often tests are sold and applied as soon as they are discovered and without adequate validation.

5 years ago – 2 years ago – **now** - future

- Too many new DNA testing labs.... **Maybe too few**

IPFD Harmonization of Genetic Testing for Dogs HGTD

- Rapid commercialization.....
- **All tests on All Breeds**
- Validation from discovery to application – **even more of a problem**
 - **Publication delays... or?**
- **Big Picture of health and disease being lost??**

Next Steps: 4th IDHW

- Application/Genetic advice – **Expert Panel**
- **Validation– IPFD IDHW Validation Matrix**
- Laboratory standards; Proficiency
- *Pre-publication peer review?*
- **Health Strategies Database for Dogs**
- **Get a GRIHP! / breed specific resource package**

IPFD DogWellNet.com resources



HGTD: Catalog of
Genetic Test
Providers (GTPs),
available tests, by
breed

Searchable by
Breed, Test or GTP;
links to research
data and other
information

Quality information
on GTPs, generic
and **breed-specific**
information on
phenes/tests

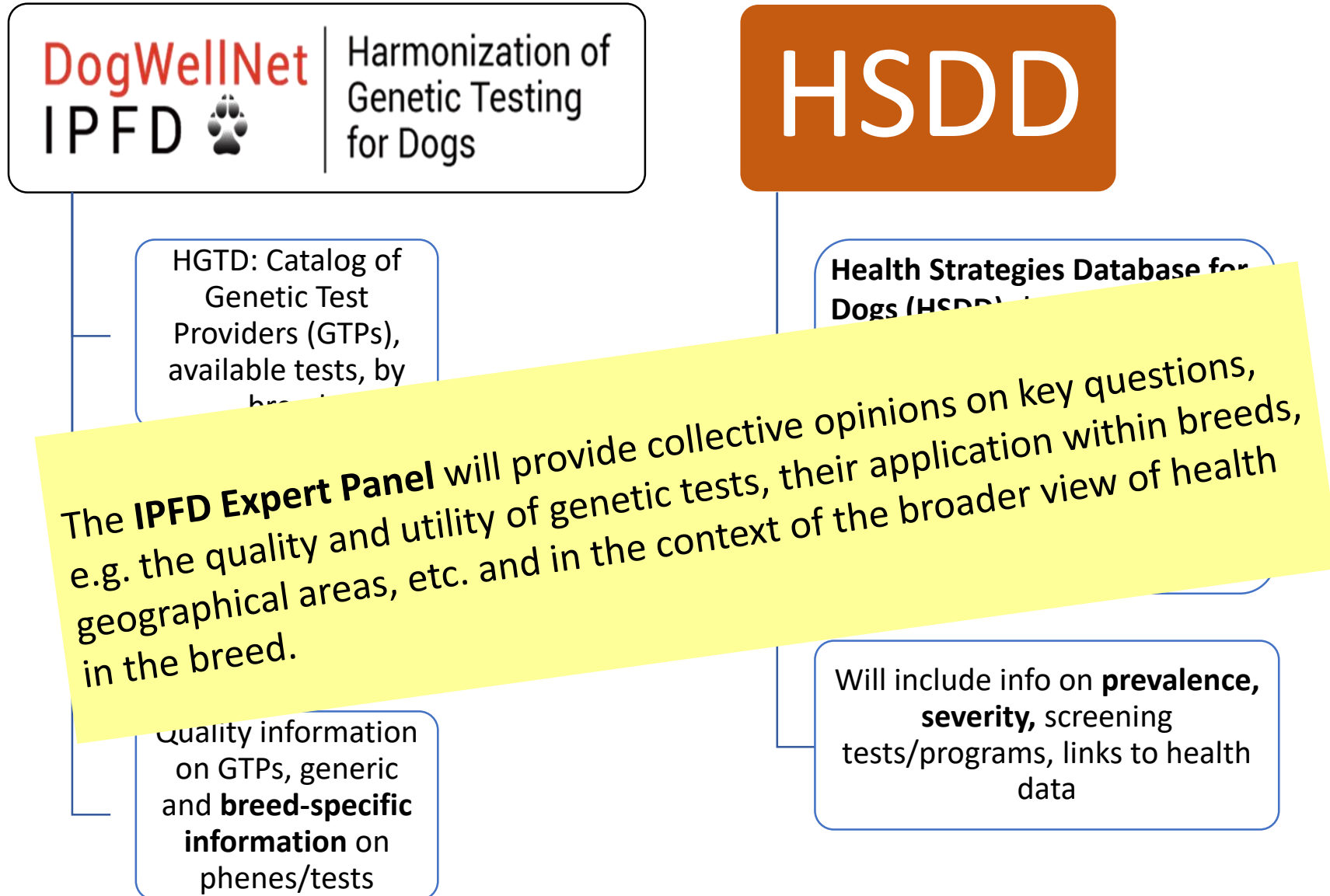
HSDD

**Health Strategies Database for
Dogs (HSDD):** Interactive
resource including conditions
where recommendations have
been made by Health Strategy
Providers (**HSPs**) including kennel
and breed clubs, veterinary orgs.
etc.

'under construction'

Will include info on **prevalence**,
severity, screening
tests/programs, links to health
data

IPFD DogWellNet.com resources





Breed

Golden Retriever x

Search

Home > HSDD > By Breed > Search Results

Search Term: Golden Retriever
For general tests, e.g. identity or coat colours, please search 'ALL'.

Results

Hip Dysplasia Synonym: HD Anatomic Location: hips
Temperament Synonym: Mentality Anatomic Location: N/A
PRA Synonym: Progressive Retinal Atrophy, Anatomic Location: eyes
Elbow Dysplasia Synonym: ED Anatomic Location: Elbow
Eye Disease Synonym: Eye conditions Anatomic Location: eyes and adnex (associated tissues)
Muscular Dystrophy (Duchenne-type, DMD) GRMD Synonym: Golden Retriever Muscular Dystrophy Anatomic Location: muscles
Subvalvular aortic stenosis Synonym: Heart murmur Anatomic Location: heart
Cancer Synonym: Neoplasia Anatomic Location: Any/All
Progressive Retinal Atrophy, PRA1 Synonym: GR PRA 1 Anatomic Location: eyes
Progressive Retinal Atrophy, GR PRA2 Anatomic Location: eyes
Ichthyosis Synonym: Fish Scale Disease Anatomic Location: skin
prcd-PRA Synonym: progressive rod-cone degeneration PRA Anatomic Location: eyes
Pigmentary Uveitis Synonym: Golden Retriever uveitis or pigmentary and cystic glaucoma Anatomic Location: eyes
Multifocal retinal dysplasia Anatomic Location: eyes
Hereditary Cataract Synonym: cataract Anatomic Location: eyes

Not available yet...

Example: Golden Retriever



HSP Name	Golden Retriever Club of America
Alternative HSP Name	GRCA
Type	Parent breed Club Recognized by the AKC
HSP Description	The GRCA promotes the temperament, appearance, soundness, natural retrieving and hunting abilities of the <i>Golden Retriever</i> .
HSP Details	The club supports AKC's conformation and performance events, conducts a rescue program, recognizes regional GR clubs and funds health studies while providing breed-specific educational opportunities for Golden Retriever breeders and owners.
URL	https://www.grca.org/
Country	United States
Year Established	1938
Reporting Group/Committee	GRCA contacts: https://www.grca.org/about-grca/officers-and-contacts/
Breed(s) of Interest	Golden Retriever
Dog Registration	✖
Type of registration	No
Health Database/Registry	✔
Health Database Description	See OFA.
Sources of Health Data	OFA, Breed-specific research/labs; answers to occasional health survey's questions submitted by dog breeders and owners. GRCA - CHIC # GR recommended health screening tests: https://www.ofa.org/recommended-tests?breed=GR Also see The Golden Retriever Foundation's website for breed health and research information: https://goldenretrieverfoundation.org/
Conditions	CancerElbow DysplasiaEye DiseaseHip DysplasiaIchthyosisPigmentary UveitisPRAprcd-PRAProgressive Retinal Atrophy, GR PRA2Progressive Retinal Atrophy, PRA1Subvalvular aortic stenosisTemperament

International
Partnership
for Dogs



Not available yet...

GET A GRIHP!

Breed-specific **G**lobally **R**elevant **I**ntegrated **H**ealth **P**rofile

The Concept....



What's a GRIHP?

- A **Globally Relevant Integrated Health Profile** is a picture of the health for a breed that incorporates:
 - Information on (all) conditions that are a concern within a breed.
 - Those conditions mentioned in **health strategies** proposed by **kennel clubs, breed clubs, veterinary organizations**, etc. including evidence on the commonness, severity, impact, of these conditions from various sources, e.g. breed-specific studies, insurance statistics, veterinary data, health surveys, etc. and e.g. in the **IPFD HSDD***)
 - For conditions for which there are genetic tests available.
 - Availability and quality sources for genetic tests (from IPFD HGTD*)
 - **Expert Panel** commentaries on the best application of these tests, as well as the overall role of genetic testing for dogs, generally, and specifically for breeds. (**IPFD Expert Panel***)
- (* developments in progress)

Get a *GRIHP* – first breed: Golden Retriever

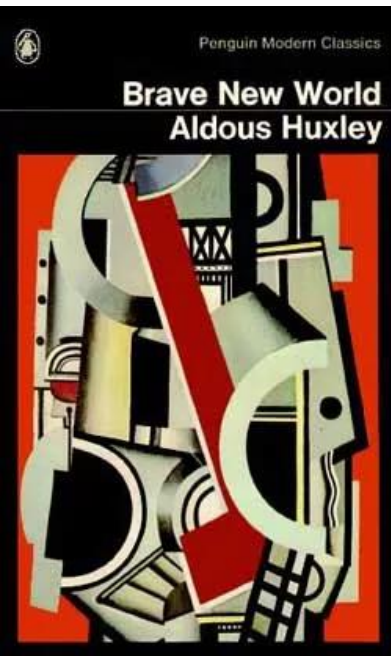
- Project funded by Morris Animal Foundation in coordination with their Golden Retriever Lifetime Study
- Incorporating data from that study, as well as from our IPFD Partner Kennel Clubs and their breed clubs
- Incorporating information and resources from IPFD and DogWellNet.com; including HGTD, Health Strategies Database for Dogs, and Expert Panel.
- Engaging multiple national breed clubs, especially the Golden Retriever Club of America, for advice, input, participation and collaboration
- **Goals:** not only creation of the **profile for the GR** but also a **template for other breeds**

Evolution of Genetic Testing??

Cutting-Edge
Science

And Now??

1920's



Sci Fi

2005



Figure 1. Tasha.
Scientists sequenced
the first canine genome
using DNA from a boxer
named Tasha.

Cutting-Edge
Science

Social
Phenomenon

2005

1920's

Sci Fi

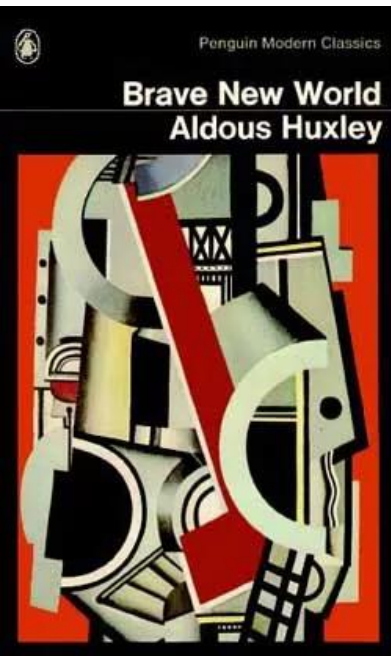


Figure 1. Tasha.
Scientists sequenced
the first canine genome
using DNA from a boxer
named Tasha.



How to Throw a
Dog Breed Reveal Party

<https://petcentral.chewy.com/how-to-throw-a-dog-breed-reveal-party/>

Cutting-Edge
Science

Social
Phenomenon

Human attitudes and behaviors may have a faster and bigger impact than science in how the world of genetic testing evolves

1920's

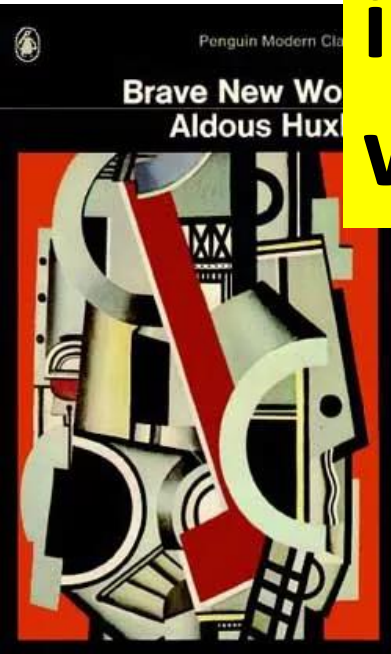
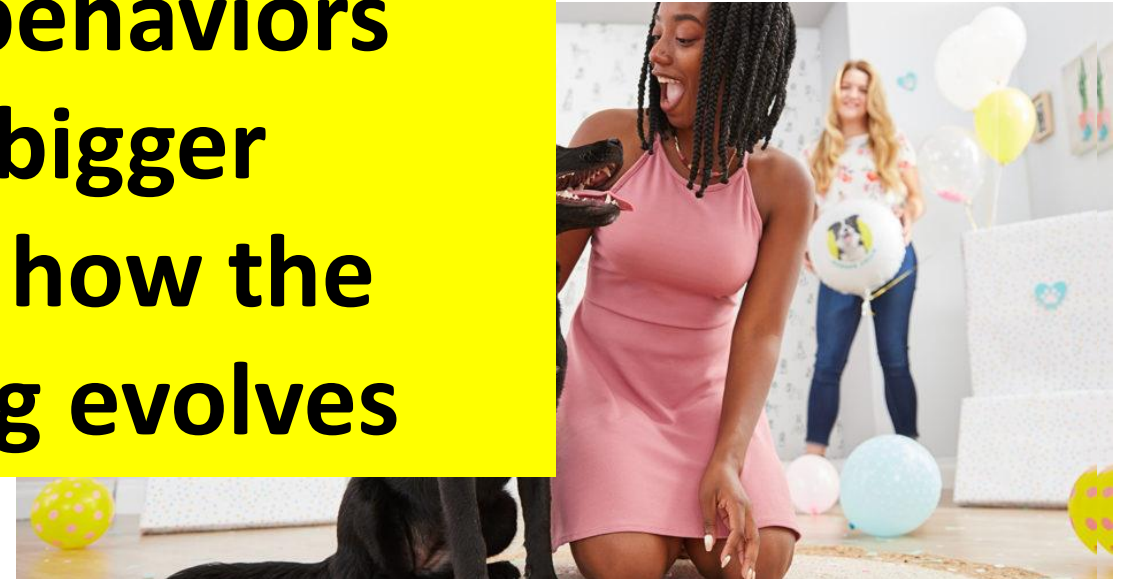


Figure 1. Tasha.
Scientists sequenced the first canine genome using DNA from a boxer named Tasha.



How to Throw a
Dog Breed Reveal Party

<https://petcentral.chewy.com/how-to-throw-a-dog-breed-reveal-party/>

Get a GRIHP on breed health



*Summary of topics to carry forward
from panel discussions...*

1. Diversity... phenotypic reflects genetic...
2. Common sense – what's common is common
3. (DNA) tests are tools not goals or outcomes
4. Standards – do they need to be changed or just applied to include the diversity inherent in the standard?

Think about...

- How did you come to this point of frustration... why so much faith in genetic testing that it derails the 'science and art of breeding'?
- Looking for a magic bullet?
- DNA is always right, holy grail?
- Maybe we need to get back to a bigger picture approach??

Degenerative Myelopathy (DM)

Has **never** been confirmed to occur in
French Bulldogs

... Dr. Jerold Bell

<https://dogwellnet.com/blogs/entry/136-concern-about-genetic-testing-degenerative-myelopathy-dm-in-french-bulldogs/>

So ... there seems to be a testing program for a disease that does not exist in this breed.

Dogs may already have been removed from breeding because of test results.

Is there an even bigger danger???

The following slides present information on testing for Degenerative Myelopathy that were covered in the panel discussion...

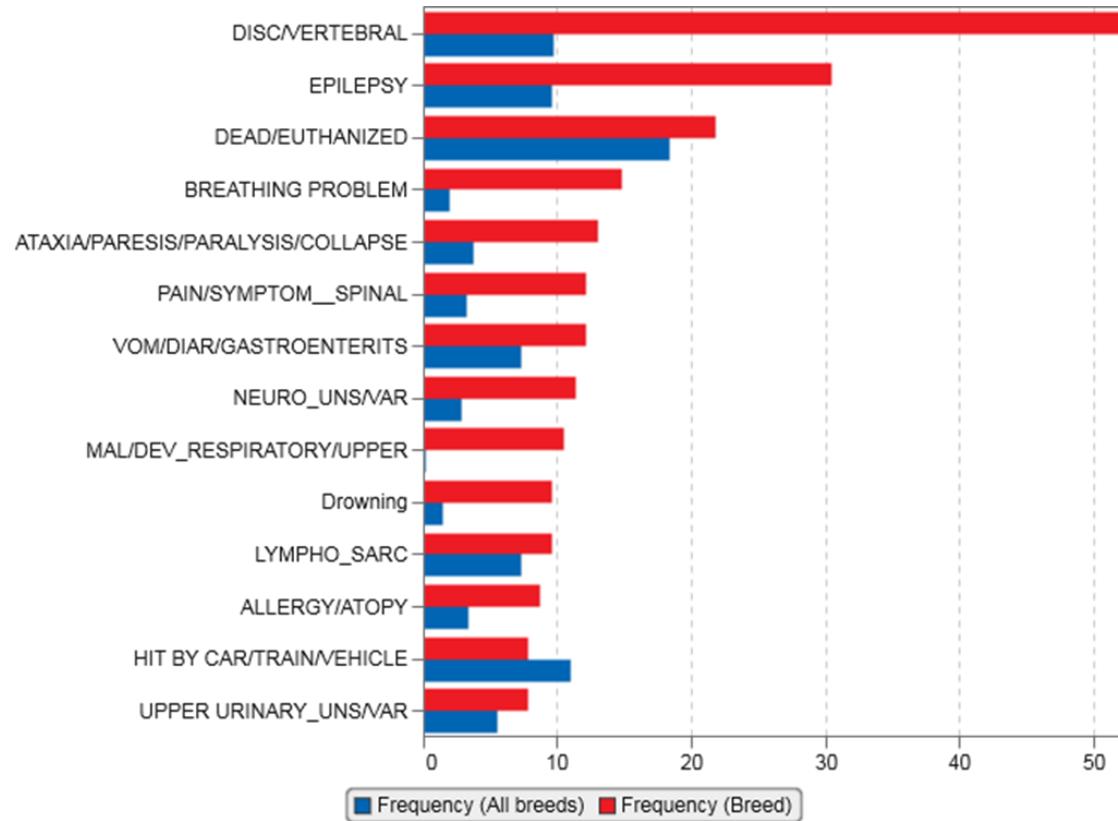
French Bulldogs (FBDs) and Degenerative Myelopathy (DM)

- Testing and recording of results in several countries
- Testing implemented based on 'allele frequencies' i.e. test results possibly without consideration of actual occurrence of DM in this breed.
- E.g. data from French Kennel Club (SCC):
- **NOTE!! These are allele frequencies – i.e. results of tests not estimates of disease.**

Results for French Bulldog 25/06/2019	
DM1A-1.1 (clear)	324
DM1A-1.2 (carrier)	145
DM1A-2.2 (at risk)	8

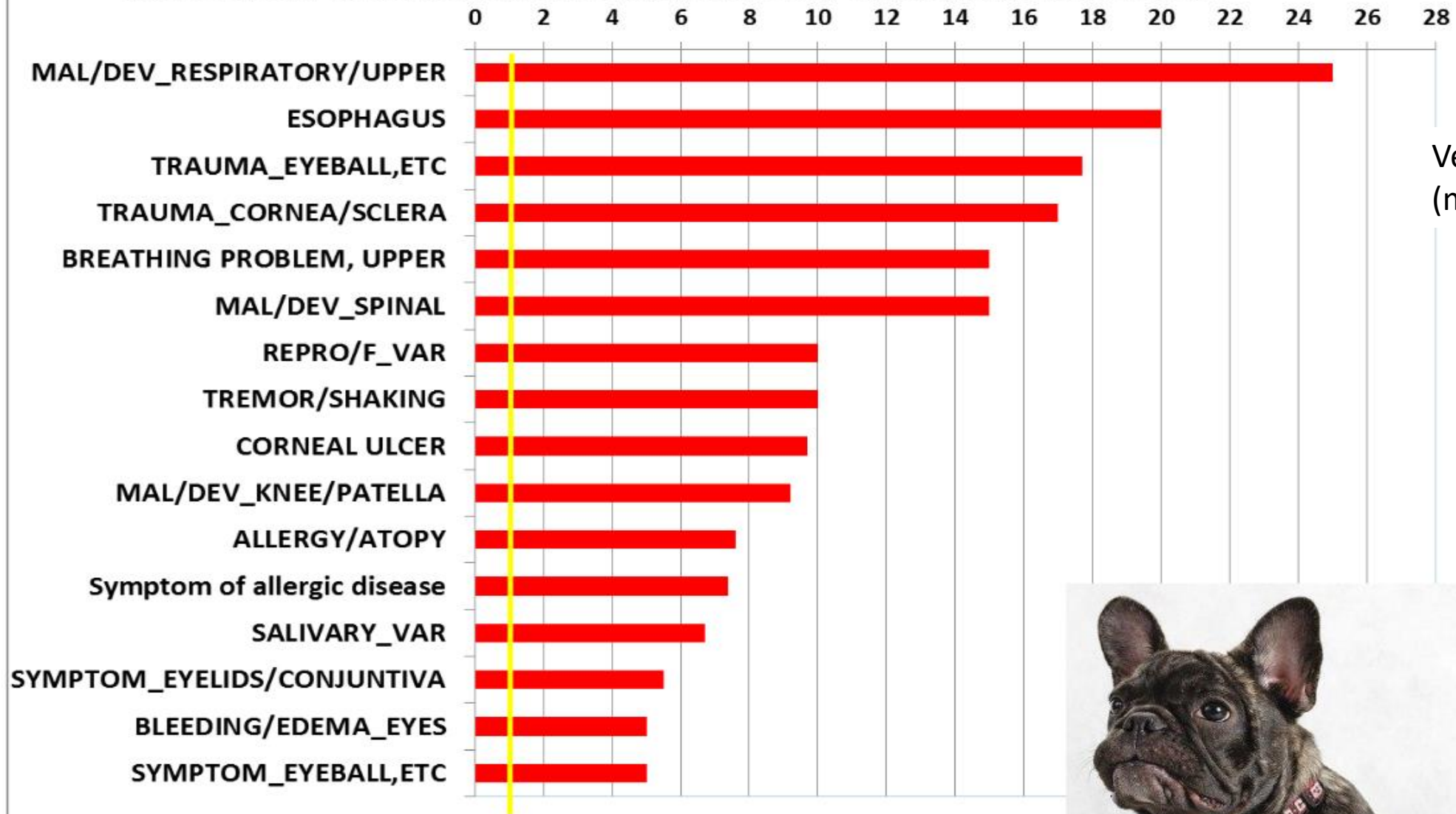
Insurance statistics from Sweden.
Profiles available on [DogWellNet.com](https://dogwellnet.com)
for 2006-2011, with permission.
2011-2016 stats coming soon.

Chart 5: Mortality for Specific Causes (Level 1)
– French Bulldog and All Breeds 2011-2016



Reminder: Categories are shown only if at least 8 animals had that diagnosis.

Specific Causes of VCEs Ordered by Relative Risk: French Bulldog compared to All Breeds 2006-2011



Veterinary Care Events
(morbidity)



These genetic/DNA tests are available, but do they help with the **most important concerns in the French Bulldog?**

- Chondrodysplasia
- Cystinuria Type I-A
- Degenerative Myelopathy
- Congenital Hypothyroidism
- Hyperuricosuria and Hyperuricemia (HUU)
- Canine Multifocal Retinopathy 1 (cmr1)
- Primary Hereditary Cataract (PHC)
- Progressive Retinal Atrophy cord1
- Coat Colour Dilution, Alopecia