Many of the data sources seem to have a HUGE margin of error (e.g., mean age of 7.26 +/- 3.3 years). Is that a bad thing? How does this impact drawing conclusions from this data? What would need to be done differently to reduce the margin of error?

The numbers following the ± signs are not margins of error, but indicate what is called the “Standard Deviation” (SD). This is a statistical measure that shows how wide or narrow the actual data distribution is. The smaller the SD number, the more narrow the distribution, i.e. the closer the data are gathered around the mean value. This is an inherent feature of the population and cannot be changed through a different way of calculating.

A smaller or bigger Standard Deviation is not in itself a good or bad thing – merely another piece of information about the available data. For instance, when somebody says “these dogs live to 7 years on average”, that does not usually mean that all of them live to 7 and then drop dead instantly; rather, it means that the death ages are scattered around the mean value of 7. The SD allows the reader to assess how narrowly or widely the risk of dying is distributed around that mean age.

Mathematically spoken, SD values are calculated in the way that 68% of dogs die in the age spectrum of mean ± SD, and 95% of them die in the age spectrum of mean ± twice the SD.

When planning a breeding, how important is it (in your opinion) to get information on siblings of direct ancestors and to what generation, and does that vary by (presumed) mode of inheritance for the particular disease?

Given that one usually should consider more than one disease when planning a breeding, every piece of information is valuable. The way in which the information then should be applied to breeding depends indeed on the modes of inheritance of the different diseases.

If we take a simple recessive, like e.g. PSS or PCD, and we know that there was at least one affected full sibling, we know that our clinically healthy potential breeding dog has a two thirds risk of being a carrier. In these cases, it is irrelevant how many other healthy or affected siblings there were, and the breeders can spare themselves the work of researching further siblings for the condition.

If there have been no full siblings diagnosed with the disease, other ancestors and related dogs become important. If our potential stud dog has produced a PSS litter, he is a certain carrier, as is the dam of that litter. If there are half-siblings diagnosed with PSS, our potential breeding animal has a 50% chance of being a carrier. And so on, following classical Mendelian inheritance.

There are some good programs around that help in assessing that risk. One that I can recommend for its simplicity is PedRisk.exe, which is available for free at http://www.azdogs.com/pedrisk.html. And of course, I should also mention the possibility of risk analysis that is being offered by Janis et al. and usually based on more data than the average breeder has access to.
If, on the other hand, we are considering a complex disease like osteosarcoma or bloat, the more information there is, the better the base for a decision. In the absence of a scientific estimation of breeding value (which would require a central database and complicated calculations), the breeder should try and create a pedigree in which the occurrence of these diseases is below-average for the breed. In theory, this includes the siblings of all individuals occurring in there, making it difficult to do in practice. This is why I suggest establishing a central health database and introducing BLUP estimated breeding values (EBV), which would make this much simpler for breeders.

For the breeder, EBV use means that each potential breeding animal is assigned a numeric value for a given disease, which is calculated based on the available health information on the individual, its parents, its siblings and its offspring. When planning a breeding, breeders can then add the EBV’s for each parent and see whether it is more or less than twice the population average.

For instance, let’s say that you have a bitch that has an EBV of 103 for osteosarcoma. The population average is 100. This means that you should use a sire with an EBV of less than 97 on her in order to give the offspring a below-average risk.

As I said, the actual calculation of an EBV is mathematically complex and requires a central database. As you see, however, the practical application of EBV’s by the breeder is extremely simple and could have a huge positive impact on the breed, as it has in other breeds suffering from complex diseases.

What would explain the clinical incidence of PSS being lower than the presumed percentage of carriers should be producing?

After clarification, it seems that the core of this question is that the person asking would like to know how a PSS incidence of about 3% of puppies can indicate a healthy carrier frequency of about 25 to 30%. I should probably point out that the carrier frequency has been calculated using the measured incidence numbers and not vice versa.

At the heart of the matter lie two simple equations describing what is called the Hardy-Weinberg equilibrium, which explains the distribution of alleles in a population. PSS being a simple recessive, it is controlled by one gene locus with two alleles. Each allele can take one of two possible values, resulting in three possible genotypes. For this calculation, we shall define the healthy allele as p and the PSS allele as q. Clinically healthy dogs can have a genotype of pp or of pq, while affected dogs have a genotype of qq.

The two equations describing the Hardy-Weinberg equilibrium are as follows:

\[ p + q = 1 \]
\[ p^2 + 2pq + q^2 = 1 \]

Equation (1) describes the distribution of alleles in the gene pool and explains that the sum of allele p and allele q in the gene pool is 1 (100%).
Equation (2) describes the distribution of genotypes in the population, where every dog carries two alleles. In this equation, \( p^2 \) (the same as \( pp \)) is the frequency of healthy dogs, \( 2pq \) is the frequency of healthy carriers, and \( q^2 \) (\( qq \)) is the frequency of affected dogs. Again, their sum is 1 (100% of the population).

Math buffs will remember from when they were taught the binominal formulas that (2) is simply (1) squared. This is because a mating is (aptly, I might add) expressed through a multiplication in this model.

The two equations can be expressed graphically, demonstrating how the frequencies of carriers and free dogs change as the clinical incidence of a disease increases:

As this graph shows, the carrier frequency in a population grows extremely quickly at very low disease incidences. Remember that 1 = 100% for all numbers.

For the mathematically interested, I will demonstrate how to calculate the percentage of healthy carriers based on the percentage of affected dogs using the example of PSS in IWs:

From the literature, we know the frequency of affected puppies to be around 3% (=0.03). According to equation (2), this equals \( q^2 \).

\[
(3) \quad q^2 = 0.03
\]
Now, what we want to know is the frequency of healthy carriers, which is expressed as $2pq$ in equation (2). In order to do this, we need to know the values of $p$ and $q$.

\begin{align*}
q &= \sqrt{q^2} = \sqrt{0.03} = 0.173...
\end{align*}

We use this result on equation (1) and get:

\begin{align*}
p &= 1 - q = 0.827...
\end{align*}

Now that we know the values for both $p$ and $q$, we can calculate the frequency of healthy carriers, $2pq$:

\begin{align*}
2pq &= 2 \times 0.173... \times 0.827... = 0.286... \approx 28.6%
\end{align*}

...et voilà.

**Have there been any other papers published on IW lifespan since yours? Where could a layperson find them?**

To my knowledge, there have been no such papers since my thesis appeared. If you know of any, I would appreciate the references to be sent to my email address, urfer@gmx.net.

Since having written my thesis, I have been made aware of a Swedish IW lifespan study conducted by Anna Blom of Uppsala University and based on data from 1980-2003, which was published in 2004. Unfortunately, it is written in Swedish, which is not a language that I speak. From what I can read of it, it found a lifespan of 6.5 years for bitches and 5.5 years for dogs, but was also tainted with right censored data. I can send anyone interested a PDF.

**Did you have a population of IWs to study for any part of your thesis or is your paper completely based on meta-analysis of other people's studies?**

Apart from the analyses conducted on the data from Bernardi, Prokopenko and Murphy, the thesis also included other IW data collected from various sources. The longer explanation can be found in chapter 4.1, first paragraph.

**What got you interested in IWs in the first place? Why not Great Danes or some other breed?**

I have yet to hear a rational answer to this question from anyone interested in IWs. The decision to become associated with the breed is not one I made consciously. However, it has lead to a lot of interesting travelling, contacts with IW people all over the globe, and provided more than enough material for four years of my professional career so far, so the decision cannot have been that bad.

So, why do I work on IWs? Because they fascinate me, because I love them, and because I want to give them something back.
Did any of your data point to IW lifespan as extraordinarily short in comparison to other giant breeds? Or more disease-prone?

I have not conducted any systematic comparison between IW life expectancy and life expectancies in other giant breeds, so am unable to answer this question. It is likely that specific studies in other large breeds would also be tainted by right censored data, making a standardised comparison more difficult than it may seem at first glance.

As for disease incidence, IWs have one of the highest DCM and OS incidences in all breeds. If we look at the data from Dorn (2002) as referenced in my thesis, we arrive at the following table:

<table>
<thead>
<tr>
<th>Heart Disease</th>
<th>Osteosarcoma</th>
<th>Bloat</th>
<th>Hip Dysplasia</th>
<th>OC/OCD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Irish Wolfhound</strong></td>
<td>3.43</td>
<td>27.5</td>
<td>5.52</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Great Dane</strong></td>
<td>1.01</td>
<td>N/A</td>
<td>43.23</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>Newfoundland</strong></td>
<td>1.44</td>
<td>N/A</td>
<td>N/A</td>
<td>2.46</td>
</tr>
<tr>
<td><strong>St. Bernard</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>2.91</td>
<td>2.82</td>
</tr>
<tr>
<td><strong>Great Pyrenees</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>0.76</td>
</tr>
<tr>
<td><strong>Bullmastiff</strong></td>
<td>0.88</td>
<td>N/A</td>
<td>N/A</td>
<td>0.99</td>
</tr>
</tbody>
</table>

These numbers are odds ratios, meaning that the overall dog population has a risk of 1 (=100%) to develop these diseases. As we can see, IWs seem to be over-represented in osteosarcoma and heart disease, occupy a middle ground in bloat and OC/OCD and have a very low risk of hip dysplasia. Unfortunately, Dorn’s data did not include information on Deerhounds.

Was your paper published in a peer-reviewed publication?

I presume that the person asking is referring to Urfer, Gaillard et al. (2007) “Lifespan and disease predispositions in the Irish Wolfhound: A Review”, Vet Q 29(3):102-111, as this is the only publication based on my thesis that has already appeared in print at the moment. It is a condensed version of chapter 3 and parts of chapter 7 of my thesis. The two co-authors, Proff. Claude Gaillard and Andreas Steiger, have been my mentors during my thesis work.

The Veterinary Quarterly (Vet Q), which is published by the Dutch “Euroscience” group at present, is a peer-reviewed journal specialising in veterinary review articles and original descriptions of newly discovered animal diseases. As of 2006, it was ranked in the top 25% of veterinary journals by impact factor. Its highest ranking so far was achieved in 2004, where it ranked second of the 123 journals considered.

I realise that there have been rumours on the Vet Q not being very highly regarded in the veterinary research community. These may be based on the fact that the journal’s impact factor was relatively low before 2002, but has been increasing rapidly since then.
Apart from the review paper published in the Vet Q, another paper based on my thesis (focusing on the statistical aspects) has been accepted for publication by the Veterinary Record, and a third one on population genetics is currently in preparation.

What level of qualification was the thesis for and when was it awarded?

The thesis was a doctorate in the academic sense (i.e. a postgraduate qualification needed to conduct scientific research independently), which was awarded after peer review by the Vetsuisse Faculty of Bern in May 2007, following a bit over 2½ years of postgraduate research. Considering the amount of work that went into it, it is comparable to a PhD in the Anglo-American education system.

Did you know that the University of Bristol (England) vet school records contain some reports of osteo (at least one from the 30's and a few from the 50's)?

You mean of IWs? That would not really be surprising – even though there are none in the Comfort studies, his focus on one single kennel has probably influenced his results to a certain degree. But, to answer the question, I did not know that and would be interested in more information.

Elizabeth Murphy asked for data on show dogs, so those that died young may have been more likely to be excluded (no data sent), as well as any info at all on pets. I don't know how much of a difference that makes in drawing conclusions from it, or whether that makes the data any better or worse than the other self-reported studies.

The Murphy data certainly have a fair share of sampling bias, and I do not think that they are wholly representative for the GB/IRL IW population of the time. I have discussed the possible mechanisms and consequences in my thesis in chapters 3.1.1 and 7.1.3.