The genomically estimated breeding value (GEBV) you received reflects the additive genetic merit of your animal, in relation to differential susceptibility to CWD.

Q1: What exactly do extremely negative GEBVs specifically express or say about an animal? **A1**: The animal possesses an overabundance of desirable alleles that reduce susceptibility to CWD, as compared to a nationwide sample.

Q2: What exactly do extremely positive GEBVs specifically express or say about an animal? **A2**: The animal possesses an overabundance of undesirable alleles that enhance susceptibility to CWD, as compared to a nationwide sample.

Q3: How should I treat or think about the GEBVs of my animals, particularly in comparison to other traits I commonly record and keep track of?
A3: You should essentially consider the GEBV to be a "new trait" that you could not see, record, or track up to the present point. You should also consider it to be a quantitative trait that summarizes SNP effects inside and outside of genes, across the white-tailed deer genome (i.e., across the individual chromosomes). Some SNPs have effects that enhance susceptibility, and some have effects that reduce susceptibility. The GEBV summarizes these effects, cumulatively, for each animal.

Q4: For breeder animals (and their lines) that I find to be very reliable in terms of reproducibility of production traits on the farm (i.e., antler characteristics, early maturity, longevity, durability, etc.), why don't I see the same degree of reproducibility or predictability in the GEBVs of their offspring?
A4: This is a new trait. You have never selectively bred for superior GEBVs until now, and for this reason, you have not yet enriched your breeding lines for all the beneficial additive alleles that lead to superior (extremely negative) GEBVs, and to fawn crops that routinely meet or exceed the recommended cutoff. You cannot assume that the degree of reproducibility you see in production traits will similarly and immediately manifest in the GEBVs of the offspring, especially under certain circumstances described below.

Q5: I thought the GEBVs of my fawns would always be somewhere in the middle of the sire and dam GEBVs, yet I see some that are outside of this bounded range. Why is that?
A5: Fawn GEBVs often do fall somewhere in between those of the sire and the dam, especially when the sire and dam have very dissimilar GEBVs. However, there are instances where the fawns can have GEBVs that outside of the range of the parents. For example, how does this happen:
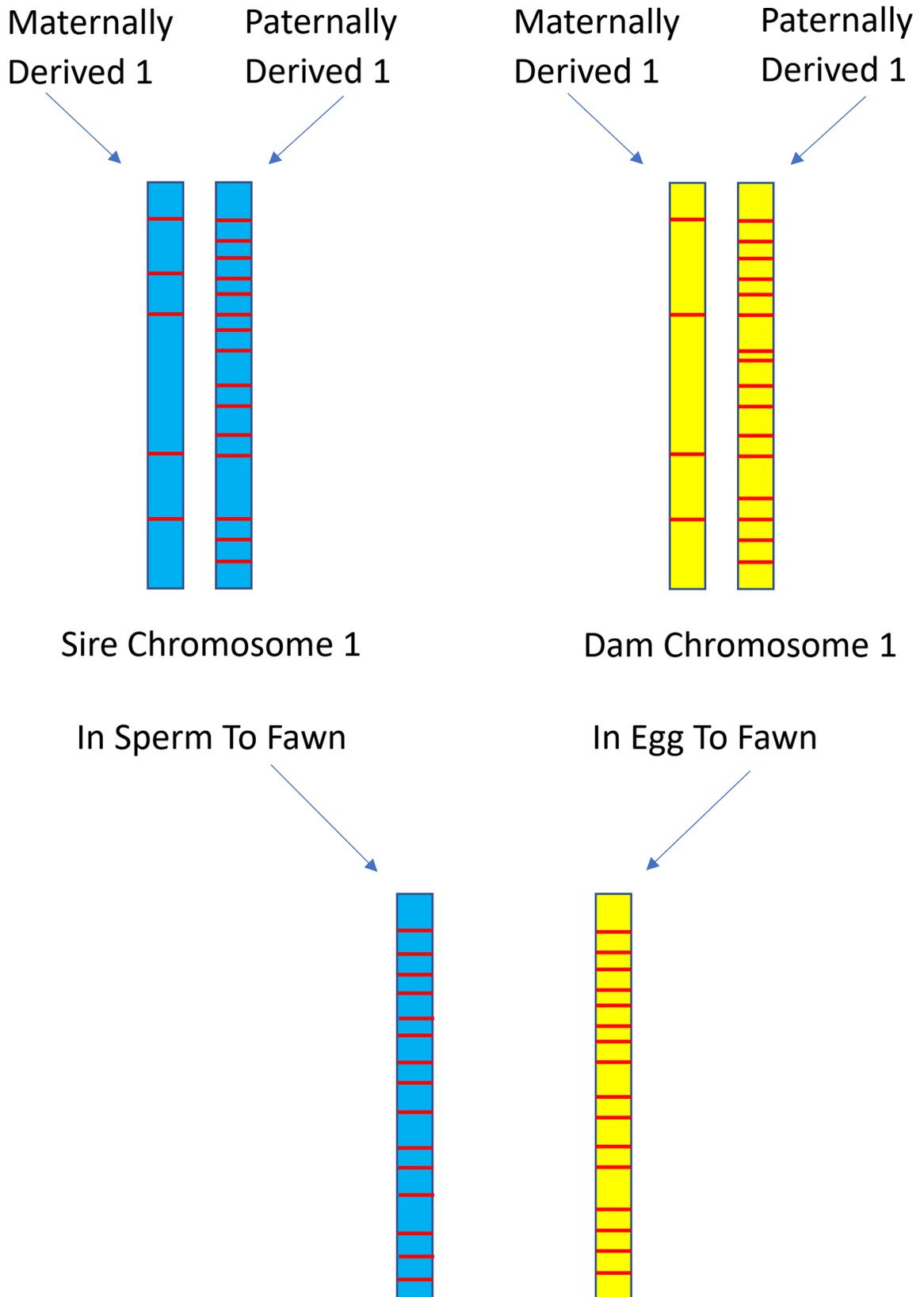
Parentage Verified Sire GEBV = 0.069
Parentage Verified Dam GEBV = -0.024
Parentage Verified Fawn GEBV = 0.157

Here we have a sire and a dam, where neither makes the recommended cutoff, and together produce a fawn that also does not meet the cutoff, but appears more susceptible than the parents. The fawn has essentially inherited a lot of the susceptibility alleles (red lines below) from both parents. Let's use deer

chromosome 1 to simply Illustrate this process, knowing that there are 35 pairs of chromosomes in living white-tailed deer (except sperm and eggs). The red lines are alleles that enhance susceptibility to CWD.

Maternally
Derived 1

Paternally
Derived 1

Maternally
Derived 1

Paternally
Derived 1

Sire Chromosome 1

Dam Chromosome 1

In Sperm To Fawn

In Egg To Fawn

Note, upon fertilization, this fawn has inherited the worst paternal and maternal copies of chromosome 1, with the most susceptibility alleles possible, making it cumulatively more susceptible than the parents with respect to chromosome 1. If this occurs with any tangible frequency across multiple chromosomes, it becomes obvious how the fawn can score outside of the range or distance between the parental GEBVs. Note, the "susceptible copies" of the paternal and maternal chromosome 1 above, which were given to the fawn by way of sperm and egg, each contain 4-5 times as many susceptibility alleles as does the other copy of chromosome 1, which also could've been transmitted to the fawn.

Q6: Well, I see this above. I follow it and I understand it, but how do I make breeding decisions to ensure that I have the greatest possibility of meeting or exceeding the cutoff?

A6: You need to treat the GEBV as a new trait you are selecting on, because that is precisely what it is. The greatest insurance for making sure your fawns meet or exceed the recommended cutoff is to engage in more extreme matings. More specifically, the probability that your fawns will meet or exceed the recommended cutoff is maximized by breeding bucks with does where both have more negative breeding values. For example, the probability of fawns meeting or exceeding the recommended cutoff for the following three scenarios is not the same: (Buck1 GEBV = -0.115 x Doe1 GEBV = -0.125 versus Buck2 GEBV = -0.225 x Doe2 GEBV = -0.252 versus Buck3 GEBV = -0.325 x Doe3 GEBV = -0.352. To illustrate this point, I've asked NADR to identify some trios that can be binned in this way with respect to GEBVs, and to then calculate the number of fawns that meet or exceed the recommended cutoff in each scenario. Ideally, I'd like 100 trios for each GEBV bin to be used for the calculations, but we will see what we get.

Q7: Well, I can't do extreme matings because I don't have deer with extremely negative breeding values, so what should I do? I'm frustrated.

A7: All you can really do is breed the best to the best, unless you can source materials elsewhere, especially if you need a certain number of animals to maintain your operation this year. However, based on the Q5 figure and explanation above, be advised that matings near the cutoff, with sires and dams that Have GEBVs which are similar (not far apart and closer to zero) will produce fawns outside the GEBV range between the parents. So, you will not be able to predict exactly how many will meet or exceed the cutoff.

Q8: How do I achieve the highest level of predictability in the GEBVs I get in my fawns in terms of meeting or exceeding the cutoff? Give it to me simply.

A8: Try to engage in as many more extreme matings as you can, with your best animals, because that will increase the probability that the fawns will meet or exceed the recommended cutoff, and even do much better than that! Treat the GEBVs like any other trait. Examine your animal records and pedigrees. You will quickly see that some bucks, when bred to certain does, will throw fawns that meet or exceed the recommended GEBV cutoff more times than not; if the parents have more desirable (negative) GEBVs.

Q9: I question the heritability of this because my lines produce reliably for the traits I'm interested in, but from my data so far, I can't predict where the fawns GEBVs will be, or whether they will meet or exceed the recommended cutoff.

A9: The heritability of your production traits has nothing to do with this trait. You've never knowingly selectively bred for this trait. If you're breeding deer with GEBVs that are pretty close together along the number line, the fawns may somewhat often have GEBVs outside the parental range. This problem is exacerbated when you are breeding one animal that barely meets the cutoff to one that doesn't meet the cutoff; or two that barely meet the cutoff, etc. The greatest degree of reproducibility in terms of ensuring

that the fawns meet or exceed the cutoff comes from breeding animals with GEBVs that are more extreme (i.e., not hugging the cutoff). The heritability estimate for differences in susceptibility to CWD is "high" with small standard error (h^2 = 0.611 ± 0.056). This has been confirmed in three different studies, culminating in one new paper currently under review. Notably, the upper limit of the genomic prediction accuracy should be roughly equivalent to the square root of the heritability estimate, and it is, as demonstrated in Table 1 here: https://www.g3journal.org/content/10/4/1433

Q10: Are deer with similar or nearly identical GEBVs really equivalent? More specifically, do they have all the same alleles, and thus will perform the same?
A10: No. Deer can have nearly identical GEBVs, but not necessarily achieved those GEBVs in exactly the same manner. Specifically, all SNPs that enhance susceptibility don't do so in an equal manner. Likewise, all SNPs that reduce susceptibility don't do so in an equal manner. To be precise, some SNPs have small, moderate or large effects on differences in susceptibility. Therefore, a deer could achieve a GEBV of -0.20 by having many desirable small-effect SNPs, and very few moderate or large-effect SNPs that reduce susceptibility. In comparison, another deer could have a GEBV at or near -0.20 by way of having nearly all possible moderate and large-effect SNPs that reduce susceptibility, but fewer small-effect SNPs. These two deer have nearly identical GEBVs, but they didn't achieve them the same way.

Q11: If I run my deer on this test multiple times, will the GEBV always be the same?
A11: No, there will be a little variation in the GEBV when run on the same training data. Two DNA samples from the same deer will not perform identically on the 50K SNP array we use. Additionally, we are currently on CWD training data set 1, and will update those training data with more CWD positive and CWD non-detect deer from positive facilities all over the U.S.

Q12: Why update the CWD training data? I thought my GEBV would last forever (and never change)?
A12: All genomic prediction initiatives for selective breeding of production and health traits should be updated for the following reasons: 1) More trait and genetic data leads to more precise GEBVs; 2) It is desirable to have at least some proportion of the training data that is only one generation away from the animals that you want to predict on (for GEBVs).

Q13: This seems complicated, and like a moving target, how can I most easily understand this?
A13: Genetic improvement for reduced susceptibility to disease in livestock or deer is NOT a single step (i.e., one-time) process. The very best future estimates of any deer's GEBV for CWD will come from increasingly larger training data sets, across time, which accounts for the shared ancestry and genetic change induced by the selective breeding decisions we make now. This is standard practice in commercial/production livestock species. In the simplest terms, it's a work in progress; just as if you were a new breeder trying to consistently create big deer, and reliable does.

Final thoughts: Take the GEBV and consider it as a trait; then select for production quality animals that throw fawns in the desired GEBV range. A codon 96SS layered on top of that is also beneficial.

Thank you and kind regards,

CM Seabury