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Genomic selection and its application in livestock improvement

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Abstract

The world population is rising rapidly along with increasing demands and there is huge gap between the population demands and the livestock production. In this situation there is increased pressure on the livestock for more improved production. Conventional breeding methods have contributed significantly towards it but accuracy of selection is not up to the mark. Genomic selection is a new novel approach towards the genetic improvement of livestock, it is a form of marker assisted selection in which genetic markers covering the whole genome are used so that all quantitative trait loci are in linkage disequilibrium with atleast one marker. In genomic selection, selection decisions are based on genomic breeding values (GEBV). The GEBV are calculated as the sum of the effects of dense genetic markers, or haplotypes of these markers, across the entire genome, thereby potentially capturing all the quantitative trait loci (QTL) that contribute to variation in a trait. It is a better and advance way of selection as it can be done at an early age with great accuracy, improved genetic gain with reduced generation interval.

Keywords: Genomic selection, QTL, GEBV, Genome, Generation interval

Introduction

The world population is rising at a significant rate. On the basis of current projections, the world population will reach 9 billion by 2030. Recent estimations by the Food and Agriculture Organization of the United Nations indicate that to meet the increasing demands, food production must double in the next 50 years^[1]. Agriculture production alone cannot meet the increasing demands, so to fulfill the demands of rising population the production from livestock sector must be improved. When the year 2000 is used as a base, projections indicate an increase in global meat consumption of 68% and in global milk consumption of 57% by 2030^[2]. The largest gains will come from innovations that accelerate agriculture productivity while reducing costs and limiting environmental impacts^[3].

Traditional breeding methods have contributed significantly towards the production of superior animals, but the accuracy of selection was not reliable. The breeding values were estimated by combining phenotypic recording of individual performance with the family information. The efficiency of these traditional methods decreases when traits are difficult to measure, have a low heritability, or cannot be quickly, inexpensively, and correctly measured in a large number of animals. Such difficult-to-measure traits are often critically important; they include fertility, longevity, feed efficiency, and disease resistance. Selection for these traits must be achieved through genomic means. The solution to all these problems was provided with the new approach of selection i.e. genomic selection.

2. Traditional Breeding methods

A number of breeding methods have been used for the selection of animals in order to improve the qualitative and quantitative traits in livestock. Traditionally animals were selected based on the phenotypic data of the animals. Thus, the traits difficult to measure, expressed later in life of the animal, sex-limited traits, and the traits with low heritability were difficult to improve by the use of these selection methods.

The Best Linear Unbiased Prediction is a better way that improves the prediction performance of animals by accounting for the systematic effects associated with trait of interest. In addition, it also improves the reliability of EBV by utilization of pedigree information through the numerator relationship matrix to account for the changes in additive genetic variance associated with inbreeding or assortative mating.

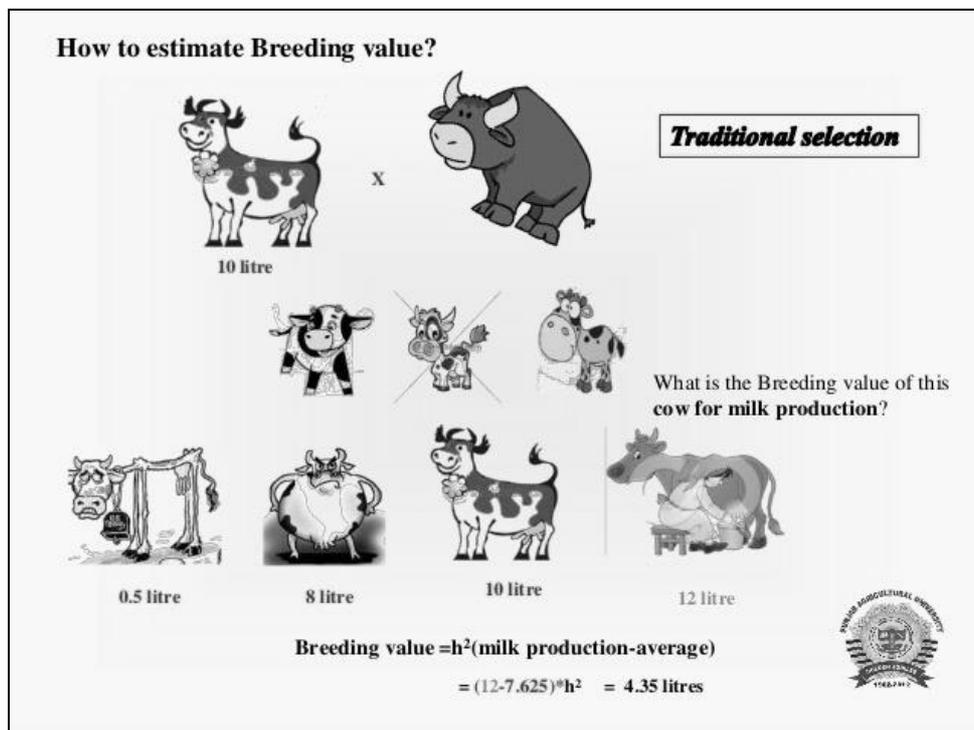


Fig 1: Estimation of breeding value using traditional selection.

3. Marker-Assisted Selection and Genomic Selection

The concept of marker-assisted selection came in the early 1900. It utilizes both phenotypic as well as genotypic information. The selection of animals based on MAS is based on the association between the marker and the linked QTL. The MAS can help us to overcome the limitations of traditional breeding methods i.e. it can be used for the traits with low heritability, sex-limited traits and the traits expressed later in the life of the animals. It also helps to increase the genetic gain by reducing the generation interval. The limitation of MAS is that it requires prior knowledge of gene alleles or markers that are associated with the traits of interest together with quantitative estimates of these

associations in the specific population. It must therefore be implemented within families. Furthermore, MAS explains only a limited part of the genetic differences between individuals. However, with the advancement in quantitative genetics and with the availability of dense panels of SNP markers have opened the new ways for the selection of best-fit animals for breeding program. Genomic selection is one such novel approach, which utilizes both the phenotypic and genotypic data, improves the accuracy and genetic gain, by reducing the generation interval. Thereby improving the technical and economical efficiency of the breeding programs. Thus, these Genomic selection tools are now leading the way to a paradigm shift in animal breeding.

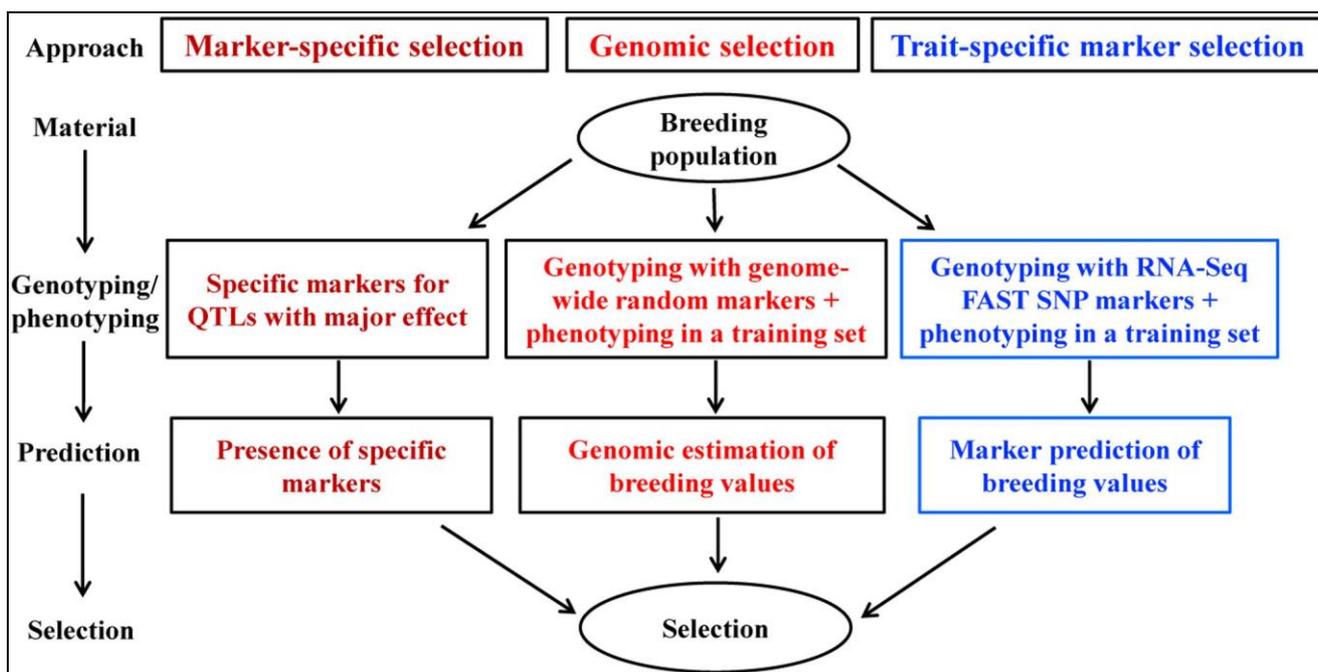


Fig 2: MAS and Genomic selection

4. Genomic Selection

Genomic selection is a form of marker-assisted selection in which genetic markers covering the whole genome are used so that all QTL are in linkage disequilibrium with atleast one marker. In practice, genomic selection refers to selection decisions based on genomic estimated breeding values (GEBV). These GEBV are calculated by estimating SNP effects from prediction equations, which are derived from a subset of animals in the population (i.e., a reference population) that have SNP genotypes and phenotypes for traits of interest.

It utilizes both the phenotypic and the genotypic data from the reference population, and then this data is then used to develop the prediction equation. The prediction equation is then used to estimate the GEBV. These effects are then used for the selection of candidates, with marker genotype information [4]. The genomic selection provides an edge over the conventional breeding methods, with improved accuracy, reduced generation interval and can be used for low heritable traits, sex-limited traits and the traits that are difficult to measure can be improved by genomic selection.

Table 1: Summary of first sequenced genomes for animal species

Species	Genome Size (Gb)	Year
Chicken (<i>Gallus gallus</i>)	1.05	2004
Dog (<i>Canis familiaris</i>)	2.4	2003
Cattle (<i>Bos Taurus</i>)	2.91	2009
Horse (<i>Equus caballus</i>)	2.47	2009
Pig (<i>Sus scrofa</i>)	2.2	2009
Sheep (<i>Ovis aries</i>)	2.78	2008
Camel (<i>Camelus dromedaries</i>)	2.2	2011

4.1. Principle of Genomic Selection

Genomic selection was first described by Theo Meuwissen in

2001 and is based on the fundamental principle that information from a large number of markers could be used to estimate breeding values without having a precise knowledge of where specific genes are located on the genome. With tens of thousands of SNP, well chosen to be representative of the entire genome, it is expected that there will always be an SNP in close proximity to a particular gene or DNA fragment of interest; the existing linkage disequilibrium between one (or several) SNP and a causal mutation will be substantial and can then be used to explain a significant fraction of the variation of the observed trait.

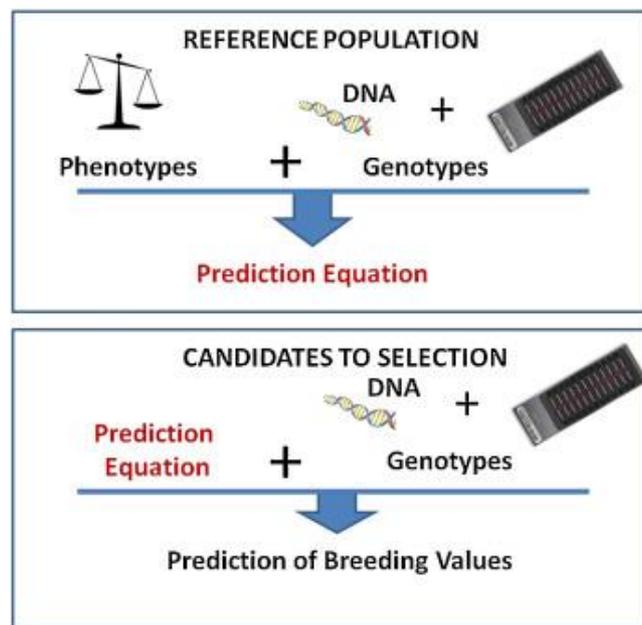


Fig 3: Principle of genomic selection

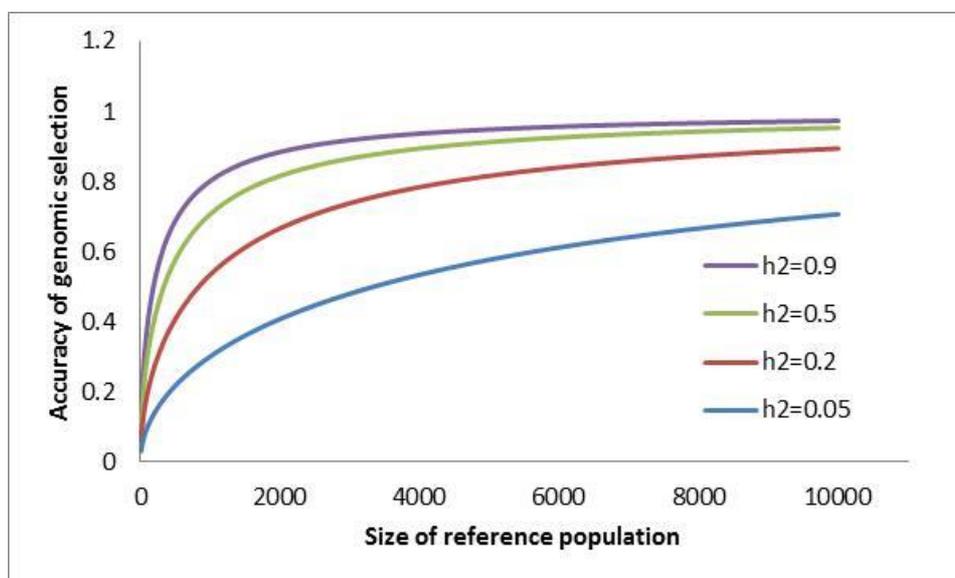


Fig 4: Reference population and accuracy of GS

4.2. Methodology

The first step in the genomic selection process is therefore access to a large group of animals, either a reference or training population with accurate phenotypes for the trait(s). This population should also be genotyped using a whole-genome SNP array. The resulting data will then serve as a reference to develop a statistical model estimating the effect of each SNP with the trait(s) of interest. The result is a

predictive equation to calculate a genomic estimated breeding value (GEBV). After a validation step, the genomic breeding value of new animals can be computed using the prediction equation, based on their genotypes from the SNP array and in the absence of any accurate phenotypes for these animals. The accuracy of the GEBV depends of the size of the population and the heritability of the trait to be considered. In the chicken, a 4-fold increase in GEBV accuracy over the parent

average for feed conversion efficiency [5]. Genomic selection helps to hasten the progeny-testing program. Traditional progeny testing is a time-consuming process, and because breeders want highly reliable EBV when making selection decisions, the generation interval for the SM pathway is extremely long. Genomic selection allows AI companies to make decisions based on GEBV, which are available at a very young age. Therefore, younger bulls can be used as sires of

sons in the SM pathway, and the age at which they can be used is limited only by their sexual maturity. Instead of waiting a minimum of 4.5 years to use progeny-tested bulls as sires of sons, AI companies can use the best DNA-tested young bulls as sires of sons by roughly 1 year of age [6]. This drastically reduces the generation interval in the SM pathway and it could lead to a doubling of the rate of genetic gain.

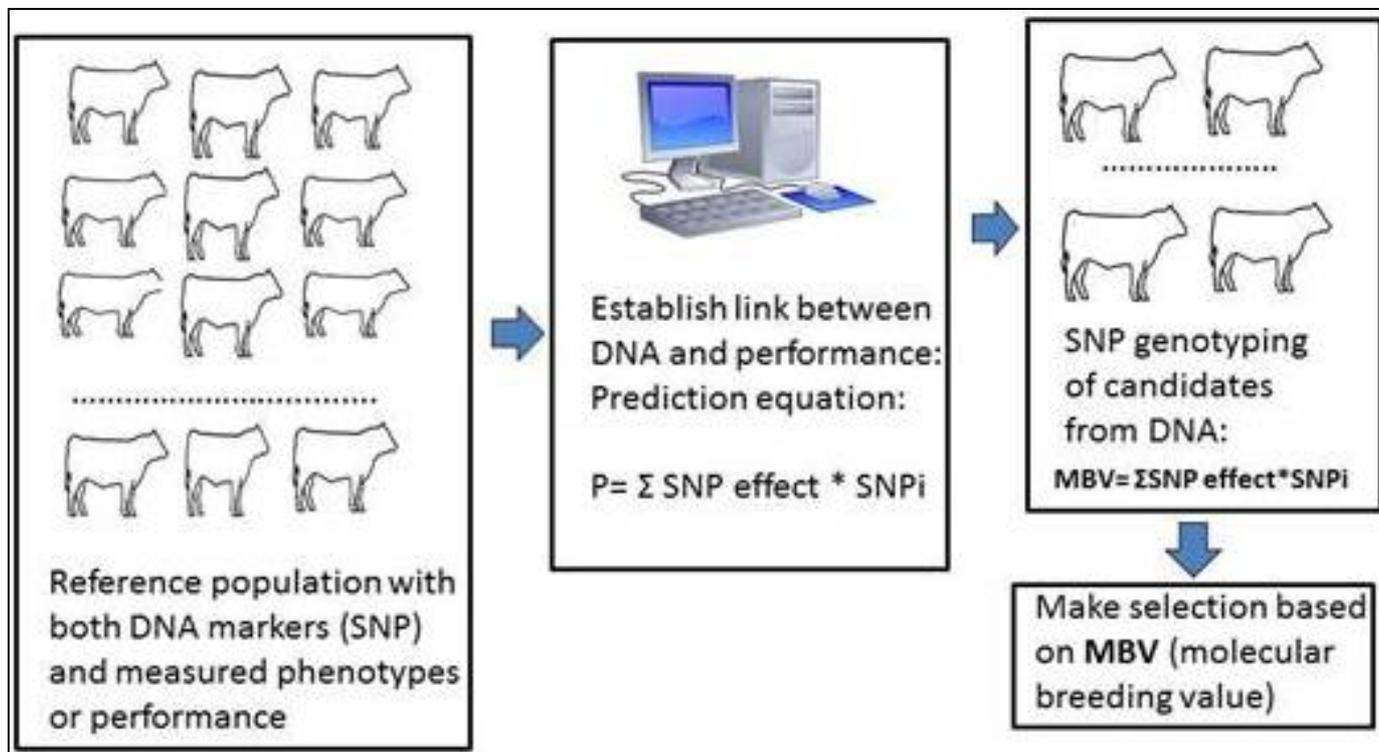


Fig 5: Description of Methodology of Genomic selection

4.3. Advantages of Genomic selection

- Implemented very early in life.
- Not sex limited.
- Can be extended to any traits that are recorded in a reference population.
- Provides for difficult-to-improve traits.
- Better selection accuracy.
- Reducing the generation interval.
- Increasing the intensity of selection.
- Explains a much greater proportion of the genetic variance than MAS.
- Not limited to specific families.

4.4. Genomic selection in Livestock

4.4.1. Genomic selection in dairy cattle

Genomic selection in dairy cattle has been used to discover the markers and improvement of the traits associated with milk production, cow health, udder health, and cow conformation. Australia is the leading country with respect to genomic selection in dairy cows, along with other countries like US, Canada, China also working on the same aspects. The accuracy of genomic prediction in dairy cattle exceeds

0.8 for production traits and 0.7 for fertility, longevity, somatic cell count and other traits [7]. These high accuracies reflect the large reference populations for each breed that have been assembled to enable genomic predictions and the fact that many of the animals in the reference populations are progeny-tested bulls with highly accurate phenotypes from average daughter performance. In addition, the GEBV are often used to predict close relatives of animals in the reference population. A feature of dairy genomic predictions is collaboration between countries to assemble these large reference sets, with three consortiums established (Eurogenomics, including the Netherlands, Germany, France, the Nordic countries, Spain, and Poland; The North American Consortium including USA, Canada, Italy, and Great Britain; and a “rest of the world” consortium consisting of a number of remaining countries).

Up to date, approximately 2 million dairy cattle have now been genotyped Worldwide, for the purposes of genomic prediction. Further it has been suggested that genomic selection has increased the rate of inbreeding per year. Maximizing genetic gain from genomic selection while constraining the rate of inbreeding will therefore be an important topic for future research.

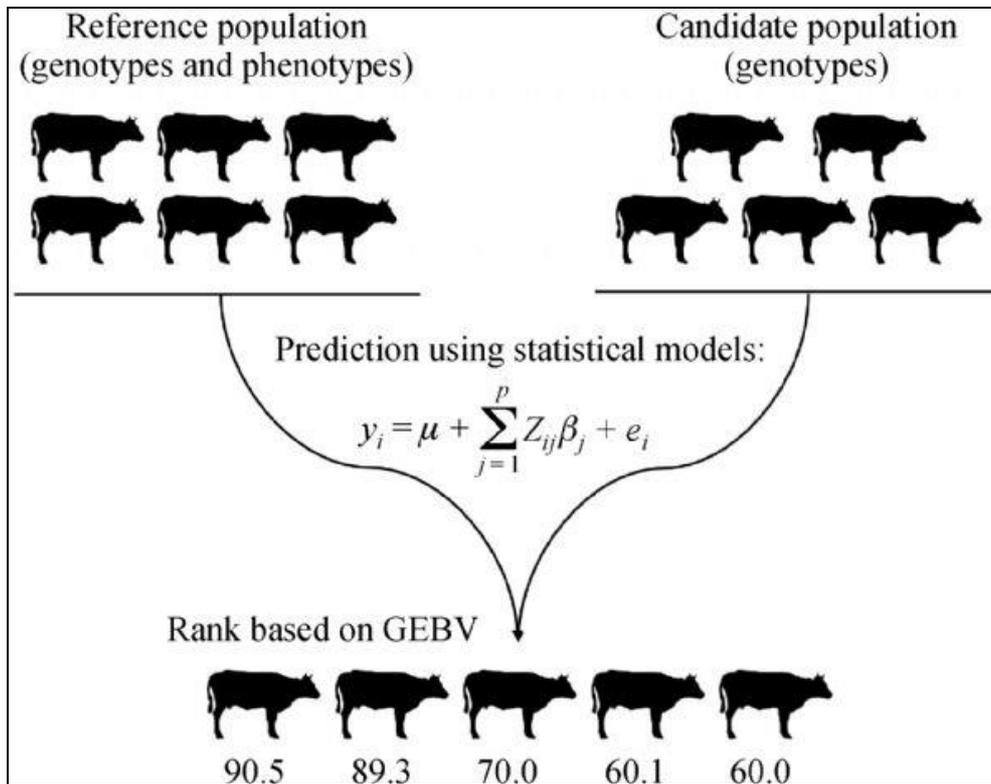


Fig 6: Genomic selection in dairy cattle

4.4.2. Genomic selection in beef cattle

As the generation intervals are more in case of beef cattle so, the beef cattle industry can have more benefits from genomic selection as compared to dairy cattle industry.

In some beef breeds, genomic selection is now applied on a large scale. For example, in the USA, more than 52,000 Angus animals have now been genotyped for GEBV evaluation [8]. But the accuracies of genomic predictions in beef cattle have been lower than in dairy cattle (0.3 to 0.7) [9]. The lower accuracy is because the reference populations are of higher quality in dairy cattle. In beef cattle, the reference population contains fewer animals within a breed, and these animals have not been progeny tested. In addition, the target population and validation animals may be less closely related to the reference population in beef cattle than in dairy cattle.

To compensate for the small number of reference animals within a breed, it is not uncommon to use a multi-breed reference population. This increased accuracy slightly (0.33 to 0.38) but not as much as if the same number of animals had been from the same breed [10]. When a reference population of several pure breeds was used in USA to predict within a crossbred population in Canada, the accuracy was low [11]. If the target breed is not included in the reference population, the accuracy is very low. However Genomic selection has not been adopted as widely in beef as in dairy cattle breeding. This is partly because the accuracy is lower, but also because the economic advantages are not as great.

4.4.3. Genomic selection in small ruminants (sheep and goat)

The genomic selection is not practiced on a large scale in small ruminants and also the genetic gain is low as compared to dairy cattle. Very few studies have been reported about genomic selection in small ruminants. The feasibility of

genomic selection in small ruminants has been evaluated recently in meat sheep in Australia and New Zealand, in dairy sheep in France, and in dairy goats in France and UK [12-15]. One of the most important requirements for genomic selection is that a reference population should be created, whereby dense phenotyping occurs for animals that are genetically related to the wider population to link the genotypic information with the phenotype. Except for New Zealand, which has 13,420 pure (mostly Romney) and crossbred sheep, the reference population sizes are still rather limited when compared with cattle, with around 1,900 Western Pyrenees dairy sheep breeds; around 2,400 and 2,700 UK and French goat populations, respectively; 4,800 Lacaune dairy sheep; and up to 8,000 multi-breed Australian meat sheep [16,17,13]. Within-country reference populations are generally composed of various breeds and crossbreeds.

Purebred populations reached at maximum about 5,300 for New Zealand Romney, 4,000 for Australian Merino, and 4,800 for French Lacaune, with all other populations being in the range of a few hundred to 2,000. Gains in GEBV accuracies were estimated to be on average between 1.05 and 0.10 for carcass traits and meat quality traits in Australian sheep and between 0.05 and 0.27 (mean = 0.13) per breed for meat, fleece, and litter size traits in New Zealand [13]. A similar gain in accuracy between 0.10 and 0.20 was assessed across milk production traits in Lacaune dairy sheep [18]. The gain in GEBV accuracy in the French and UK dairy goat populations amounted to 0.06 for milk yield and 0.14 for fat and protein content the gain in accuracy was well correlated with the reference population size and the genomic heritability of the trait, thus suggesting that accuracy and expected genetic gain can increase in the future if reference populations increase in size.

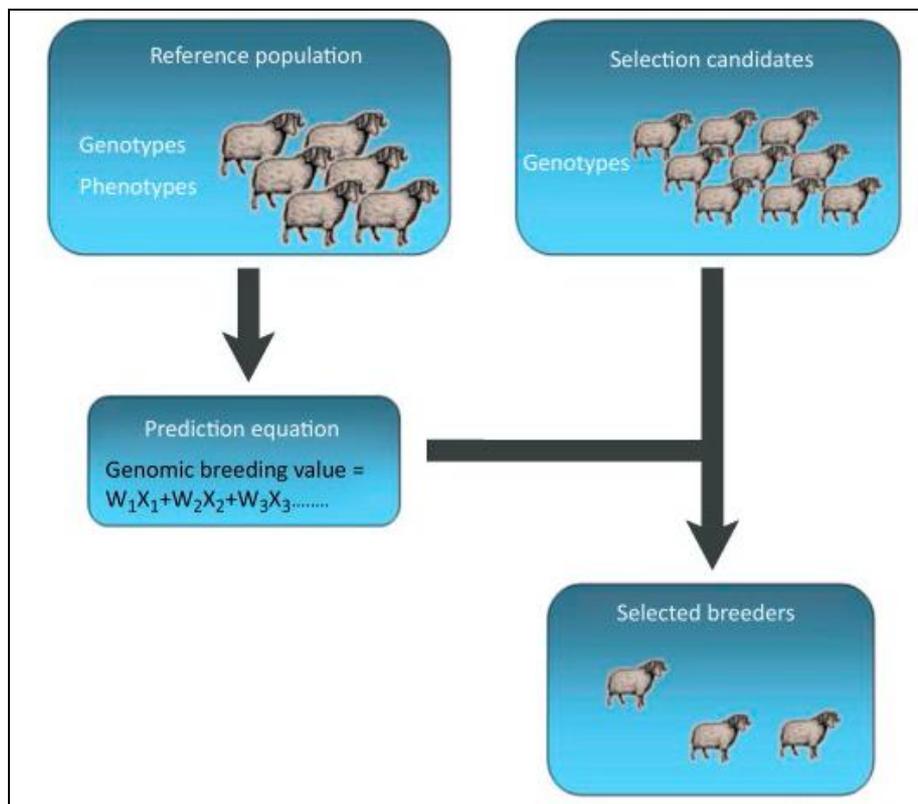


Fig 7: Genomic selection in sheep

4.4.4. Genomic selection in Pig

In 2009 the genome of pig was made available. Genomic selection in pigs can reduce the generation interval by up to 25%, thereby increasing the genetic gain along with improved

accuracy of EBV (up to 50%), particularly for the traits that cannot be improved by traditional breeding methods. Genomic selection in pigs improves the litter size but also increases the pre weaning mortality in piglets.

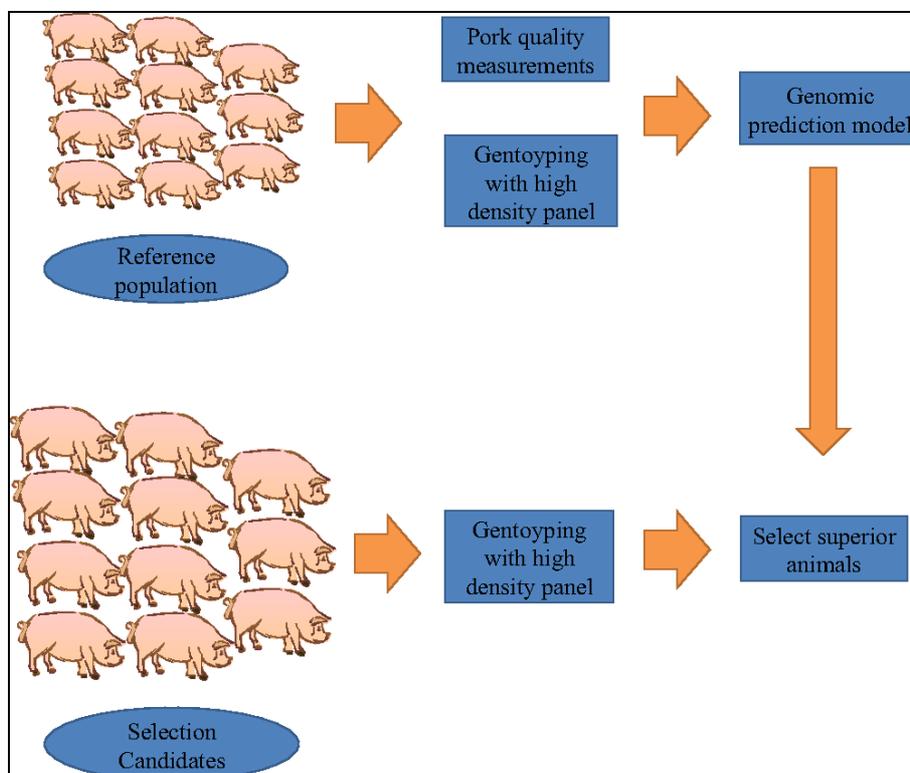


Fig 8: Genomic selection in pigs

4.4.5. Genomic selection in Poultry

The chicken was the first livestock species sequenced and simultaneously, several million SNPs were identified [19, 20].

Although the genetic gain is more than double in chickens as compared to cattle and pigs, due to the larger no of offspring produced by them. However, with the help of genomic

selection, the genetic gain can further be improved by reduced generation interval. In broilers the application of genomic selection is not as large as in layers because most traits can be recorded on both sexes at an early age. Moreover, in broiler chicken, the gain in accuracy for traits like fertility and egg production can range from 20-45 while for highly heritable traits it can be greater than 50%.

4.5. Challenges involved with Genomic selection

- Large training populations are required to obtain acceptable accuracies for breeding values.
- The rate of inbreeding per year will increase.
- The need of continuous phenotyping: Some simulation experiments have shown that accuracy using the same markers is rapidly lost generation after generation and new training populations are required.
- Preselecting bulls in dairy cattle using genomic information can lead to biased predictions with lower accuracy, leading to a decrease in genetic progress and distorting international dairy bulls comparisons.
- SNP estimates calculated from a Holstein-Friesian reference population did not produce accurate GEBV in Jersey bulls, and the correlations ranged from -0.1 to 0.3 when the SNP effects from one breed were used to calculate GEBV in another breed vice versa.
- Implanting GS in current breeding schemes.

4.6. Conclusions

In order to meet the rising demands of the growing population, there is need for a more efficient and rapid method for the genetic improvement of livestock, for the improved production. Genomic selection is a Nobel approach in that area. It has an edge over the conventional breeding methods like it can be practiced at an early age, thereby decreasing the generation interval along with improved genetic gain. It can also be used to improve traits with low heritability and the traits that are difficult to measure. The major drawback that resists the application of genomic selection to all the livestock species is the large sized reference population. Genomic selection is now used on a large scale in dairy cattle industry and with the advancement it may be used for the improvement of all the livestock population.

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