**Optimal mating strategies to manage a heterozygous advantage major gene in sheep.**

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**Supplementary material S1**

*Computation of the number of selected parents per sex and genotype:*

The number of selected parents with genotype and sex , , depended on the mating plan: for females, , and for males, where denotes the ratio of the number of males per female and the number of females with genotype mated to a sire with genotype .

*Determination of the single truncation threshold and per sex and genotype and computation of the probability to be selected as a parent for each candidate category.*

Using a numerical approach based on the NAG routines C05ADF and G01EAF (The Numerical Algorithms Group (NAG), Oxford, United Kingdom), the single truncation point for selecting parents with genotype and sex across matings but within sex-genotype categories was determined numerically solving the equation where denotes the probability of a candidate belonging to category at time to be selected as a parent with genotype and sex . Assuming a normal distribution of EBVs in each category (for simplification, ):

Where denotes the probability for an animal belonging to the category to have an EBV at time above the threshold , and the mean EBV and mean accuracy of EBVs of animals belonging to the category .

*Computation of the selection differentials and the proportion of selected parents originating from each candidate**category*(for simplification, )**.**

The selection differential was derived as where denotes the threshold to select parents with genotype g and sex a, and the mean EBV and mean accuracy of EBVs of animals belonging to the category and the genetic standard deviation (polygenic component).

The proportion of selected parents at originating from each candidate category was defined as .

*Computation of the elements of the transition matrix*

By definition, for a given candidate category, all maternal and paternal genetic contribution came from respectively one maternal and one paternal category. Thus the element of ***P*** was derived according to the genetic contribution of candidate categories at t-1 to parental categories. The genetic contribution of the candidate category at time to the candidate category at time was derived as: =0.5\* where denotes the proportion of parents with genotype and sex at time originating from mating at time .

*Computation of the number of lambs per female (phenotypic value of the selected trait) at the nucleus, NLFN, and commercial population level, NLFC, according to the evolution of genetic breeding value*

where denotes the number of weaned lambs per female prior to selection given the genotype , the probability of a candidate belonging to the category at time to be selected as a parent, the number of animals belonging to the category at time , the number of selected females with genotype , the mean EBVs of candidates belonging to the category at time and the selection differential applied to category . In this equation, was the relative proportion of category among transferred females of genotype and their mean EBV. Note that the Genotype effect, GE, was equal to .

**Supplementary material S2**

**Details of**  computing

The genotyping needs depended on the number of parents selected from each type of mating. The genotypes of animals born from [*++/++*] and [*++/mm*] were known without genotyping. For other matings, genotyping needs, computed by sex, depended on the relative number of animals selected of each genotype and originating from the same mating. For example, the number of *++* females born from [*++/m+*] to be genotyped depended both of the number of *++* and *m+* newborns selected. From [*++/m+*]a number of *++* females equal to is selected (is the proportion selected and the number of candidate available). To obtain this number, had to be genotyped. Genotyping needs for females were then equal to . Genotyping needs at time were therefore computed as:

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*Details of computing*

Two modalities for computing were retained. Either *++* and *m+* females born from matings [*m+/m+*] and [*m+/mm*] were (i) genotyped and transferred or (ii) culled. The choice of the modality depended on their relative economic interest.

If i) outperformed ii) then

In this case, additional genotypes were computed.

If ii) outperformed i) then

.

where denotes the number of candidates with sex , genotype and originating from dam and sire with genotype and , the number of selected males, the proportion of selected female () with genotype and originating from dam and sire with genotype and , the number of weaned lambs per transferred female with genotype and the discount rate (the discounted term is only applied on the lambs slaughtered from the commercial population as they were performed one generation later).

*Profit computing*

where denotes the number of lambs slaughtered at time , the number of genotyping at time , the cost of genotyping (expressed as a proportion of the marginal value per lamb slaughtered) and the discount rate.

**Supplementary material S3**

*Overlapping model*

The overlapping generation model was developed according to the OVI-TEST breeding program design. In addition to candidate categories, parental categories, reported on Supplementary Figure S1, were defined according to the dam parity and the age and status of sires (progeny testing sire, proven AI sire and natural mating sire). At each time, 12 000 females were inseminated by AI males (males being progeny tested and proven males) according to the combination of matings assessed, which was constant over time. Following estrus induction, non-pregnant females were mated to *++* natural mating males in multi-sire joining groups to avoid *mm* progeny. No selection differential was considered along the dams-to-breed female pathway, whereas young males were selected among animals born from AI proven sires and sire dams (20% of the best ewes of the nucleus). According to their genotype, young males were selected as described for the discrete model. A fraction of males were progeny tested, and half of these males were then selected as proven sires. Natural mating sires were selected among non-progeny tested males. Non-selected males were slaughtered. Non-selected females within the nucleus were either slaughtered or transferred to the commercial population as parents in accordance with OVI-TEST practice.

*Category definition*. Candidate categories defined for the discrete model were extended by including dam parity, . As shown in Supplementary figure S1, additional categories were defined for adults: 12 categories for females, 1 year old and parity 1-5 (6 ages, 2 genotypes); and 21 categories for males, one-year old males (three genotypes), AI sires (5 ages, 3 genotypes) and natural mating sires (3 ages, one genotype). The number of one-year old males (), males in progeny testing () and proven males () were input parameters (table 1). The number of parity dams depended on the proportion of parity dams where , constant until the maximum age, denotes the proportion of females still present and fertile after each reproductive cycle. The number of weaned lambs in the nucleus was computed as the sum of the initial prolificacy of non-carriers, the GE and the average EBV of the category. The number of animals per candidate category was computed as , where denotes the number of dams with genotype mated to sires with genotype , the proportion of progeny with genotype originating from the mating , , the proportion of parity dams, the female fertility after AI and the number of weaned lambs per nucleus female of parity and genotype at .

*Genetic model.* To estimate EBVs over time, a classical gene flow approach, , was used. To compute elements of the transition matrix and the selection differential for the young and proven male categories, we assumed a within genotype single truncation selection (as described in the discrete model) based on approximate EBV reliabilities. For newborn male candidates, the reliability ( was computed on parental information and depended on their dam’s parity () and the average of their sires’ reliabilities (as proven males reliabilities were close, we only distinguished the paternal genotype but not the age of candidate sire): where and denote the heritability and repeatability of NLF, the genetic contribution of sire category at to the candidate category at , the average number of daughters per sire category . The number of selected young males per genotype was where denotes the total number of young males selected per time. The selected proportion was equal to where indicates the proportion of available candidates for selection (90% of male lambs were culled for non-genetic purposes). The probability that a candidate of z being selected , the proportion of parents selected from , and the selection differential were computed as described in the discrete model. For proven males, the reliability was exclusively computed on progeny information: where denotes the average number of daughters per male in progeny testing. At each time, 50% of males in progeny testing were selected as proven males. For females (), selected newborns were randomly chosen among AI candidates, thus the proportion of selected female for a given candidate category was . The transition matrix was build according to category definition and the selection process implemented.

The element represented the genetic contribution of the category at to the category at . The rows and columns corresponded to:

: female candidate categories at

: male candidate categories at

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| candidates |  |  |  |  |  |
| Males | Females |  |  |  |  |
|  |  |  |  |  |  |
| 103 | 1 | ++/++ |  | 1 | ++ |
| 104 | 2 | ++/m+ |  | | | | |
| 105 | 3 | ++/m+ |  | | | | |
| 106 | 4 | m+/++ |  | | | | |
| 107 | 5 | m+/++ |  | | | | |
| 108 | 6 | m+/mm |  | 1 | ++ |
| 109 | 7 | ++/++ |  | 2 | ++ |
| | | | | | |  | | | | |
| 115 | 12 | m+/mm |  | 2 | ++ |
| | | | | | |  | | | | |
| 133 | 30 | ++/++ |  | 1 | m+ |
| | | | | | |  | | | | |
| 139 | 36 | m+/mm |  | 1 | m+ |
| | | | | | |  | | | | |
| | | | | | |  | | | | |
| 192 | 90 | m+/mm |  | 5 | mm |

++ females from one year old to parity 5 at

: m+ females from one year old to parity 5 at

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| 91 | 0 | ++ | one year old females |
| | | | | | |  |
| 96 | 5 | ++ | females in parity 5 |
| 97 | 0 | m+ | one year old females |
| | | | | | |  |
| 102 | 5 | m+ | females in parity 5 |

: male candidate categories at

: ++, m+, mm 1 year old male categories at

: Natural mating male (aged from 2 to 4) categories at only ++

: male in progeny testing categories at

: male awaiting progeny results categories at

: proven male (age from 4 to 6) categories at

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
| 193 | ++ |  |  | one year old male |
| 194 | m+ | 0 | 0 |
| 195 | mm |  |  |
| 196 | ++ | 0 | 0 | natural mating male, 1st use |
| | | | | 0 | 0 | natural mating male, 2nd use |
| 198 | ++ | 0 | 0 | natural mating male, 3rd use |
| 199 | ++ |  |  | AI male in Progeny Testing |
| | | | | 0.40 | 0 |
| 201 | mm |  |  |
| 202 | ++ |  |  | AI male waiting for Progeny Results |
| | | | | 0 | 0 |
| 204 | mm |  |  |
| 205 | ++ |  |  | AI proven male, 1st use |
| | | | | 0.27 | 0.45 |
| 207 | mm |  |  |
| 208 | ++ |  |  | AI proven male, 2nd use |
| | | | | 0.20 | 0.35 |
| 210 | mm |  |  |
| 211 | ++ |  |  | AI proven male, 3rd use |
| | | | | 0.13 | 0.2 |
| 213 | mm |  |  |

the contribution sire category j of genotype to candidate progeny of sex .

*Contribution of female (j = 92-96, 98-102) categories at t-1 to female (k = 1,90) and male (k = 103,193) candidate categories at t*

Given category definitions, only one dam category contributed to one candidate category. The parental contribution of female category (genotype and parity ) at to candidate category at was equal to for and . For example, the contribution of the female category to candidate category was equal to 0.5 for candidate categories .

*Contribution of male categories at t-1 to female (k = 1,90) and male (k = 103,193) candidate categories at t*

Several sire categories contributed to female (males in progeny testing and proven males) and male (proven males) candidate categories according to their relative use. Therefore, an additional input parameter, was considered as the contribution of sire category j of genotype to candidate progeny of sex .

for

*Contribution of female (male) categories at t-1 to female (male) categories at t.*

One year old females (males) with genotype at came from candidate females (males) with genotype at

and for females ()

, and for males ()

For older female and male categories, the transition matrix reflected aging by having only one element of each row equal to 1. For example, females belonging to the female category with genotype ++ and parity 1 at belonged to the one year old female category with genotype ++ at , .

*Profit function.* The profit function was adapted to the real case of the OVI-TEST breeding program. Non-selected males were slaughtered as well as non-selected females born from matings [*m+/m+*] and [*m+/mm*] to avoid the transfer of *mm* females to the commercial population (no transferred females were genotyped). In accordance with the real proportions observed, half of females born from natural mating sires were transferred to the commercial population and half were slaughtered. Their number, , according their genotype was computed as:

for *++* and

for *m+*

where denotes the fertility on induced estrus, the proportion of females in parity , the number of dams with genotype mated to a sire with genotype , the number of lambs per female of genotype at on natural estrus and the fertility on natural estrus of ewes that failed to become pregnant on induced estrus. We assumed a delta of in prolificacy between natural and induced estrus. The prolificacy, or number of lambs per female, was computed as the sum of initial prolificacy, the genotype effect and half of dam’s EBV (weighted by the parity contribution) and half of sire’s EBV (weighted by the sire contribution to females ). For non-selected females born from AI, 75% were transferred and 25% slaughtered. The genotyping needs and costs as well as the discounted revenues were computed using the methodology described for the discrete model. The profit function was computed from time horizon 2 to 21.

**Supplementary material S4**

*Optimization: description of linear constraints*

As the population was constant over time, the range of variation was from to for each mating. Two types of constraint were defined. First, at any , the sum of matings was equal to the number of females: . Second, for any genotype\*sex , available candidates produced at had to be sufficient to select parents (or replacements) at . The latter constraints were assumed to be linear as we did not consider the increase in prolificacy due to the genetic progress. This resulted in defining a linear inequality linked to each category with sex and genotype : the left term represents the number of parents to be selected and the right term to the number of candidates. For the discrete model, the inequalities were:

for ,

for ,

for ,

for ,

for ,

where denotes the number of dams with genotype mated to a sire with genotype , the proportion of progeny with genotype originating from the mating , the number of weaned lambs prior to selection given the genotype and and the number of dams and sires.

For the overlapping model, we extended these inequalities by multiplying the left term by , the proportion of female in first parity and by computing, in the right term, the number of candidates produced across dam parity categories.