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1 **TITLE**

2 **Functional longevity in five rabbit lines founded on different criteria:**
3 **Comparison at foundation and at fixed times after selection**

4
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28 **Running Head (Short title):** COMPARING FIVE RABBIT LINES IN TERMS OF
29 LONGEVITY.

30

31

ABSTRACT

32
33 The enhancement of rabbit female functional longevity, i.e. the ability to avoid voluntary
34 culling, is a paramount aspect for the sustainability of meat rabbit production; this trait
35 represents a direct indicator of female robustness. The objective of our study was to
36 compare the functional longevity of five rabbit lines at their foundation and at fixed
37 times during their selection processes. Four of them are maternal lines (A, V, H and
38 LP) selected for litter size at weaning. The fifth line is the paternal line R, founded and
39 selected for post-weaning daily gain from 28 to 63d. The comparison at foundation
40 involved the complete data set (from March 1980 to March 2013; records of 15670
41 does) and pedigree (19405 animals). Latter comparisons were made when all lines
42 shared the same environmental and management conditions, from March 1997 to
43 September 1998 and from March 2011 to September 2012. In these second
44 comparisons, the same model as that used in the comparison at foundation was used,
45 but now the additive effect was excluded, only data from the corresponding periods
46 were considered. At their foundation, lines V, H and LP showed larger functional
47 longevity than lines A and R, being LP line that with the longest productive life. In the
48 latter comparisons, lines A and R still showing the lowest functional longevity.
49 However, as the selection process evolves, the differences between these two lines
50 and the others were reduced. It could be concluded that the average longevity of a
51 population greatly depends on the criteria followed for its foundation. In addition, along
52 the selection for litter size, the differences of longevity between lines tend to decrease,
53 this is due to an unintended selection for functional longevity, since only offspring from
54 females reaching 3 parturitions are selected as breeding animals for the next
55 generation.

56 **KEYWORDS:** line foundation, selection, functional longevity, maternal lines, survival
57 analysis, rabbits.

58

INTRODUCTION

59 The success of any selection experiment could be limited by the criteria and procedure
60 used to recruit animals in the base generation, i.e. foundation, this holds for any
61 species and trait, and it is particularly relevant in rabbit lines. One way to quantify the
62 consequences of considering different foundation criteria is to compare, for the desired
63 traits, performances of lines sharing the same environmental and management
64 conditions at different moments of the selection processes, for example at their origin
65 and after some generations of selection.

66 Longevity is a functional trait directly related to farm profitability; thus, selective
67 breeding to increase the length of productive life could help to reduce costs attributed
68 to replacements, considering that the annual replacement rate in meat rabbits is about
69 120% (Ramon and Rafel 2002) with nearly 50% of the dead or culled does replaced
70 during their first three parities (Rosell, 2003). The economic weight of doe replacement
71 rate as an estimation of the economic weight of longevity is relatively low (–
72 0.29 €/percentage unit) compared to other traits like, for example, efficiency in the use
73 of feed or prolificacy (Cartuche et al., 2014). However, until now, in the computation of
74 this weight, some relevant factors associated with management, welfare and ethics
75 are not properly defined in the farm benefit function (EL Nagar et al., 2020). With the
76 aim of creating a maternal line outstanding for its longevity, Sanchez et al. (2008)
77 recruited, from commercial farms, females showing an extraordinary length of
78 productive life (over 25 parturitions) but maintaining a prolificacy performance above
79 the mean prolificacy of the Spanish rabbit commercial population. This selection
80 procedure was chosen because traditional breeding methods, based on limited
81 selection pressure within close populations, were not expected to be successful since
82 the time required to obtain relevant information for accurately ranking the animals

83 within each generation would be rather long (Larzul et al., 2014). The aim of this study
84 was to compare the functional longevity of the aforementioned line, with others raised
85 in the same selection farm. Four of these lines have been selected for litter size at
86 weaning and one is selected for post-weaning daily gain. As the comparisons between
87 the functional longevity of the lines are made at their foundation and also at fixed time
88 periods of the selection process of the lines it is possible to assess how the initial
89 genetic differences evolve as a consequence of the different selection procedures
90 implemented for each line.

91

92

MATERIALS AND METHODS

Ethical statement

94 Animal manipulations and the experimental procedures were approved by the Ethical
95 Committee of the Polytechnic University of Valencia, according to Council Directives
96 98/58/EC (European Economic Community, 1998).

Animals and Management

98 Data used in the present study were collected from five Spanish lines of rabbits, four
99 of them are maternal (A, V, H, LP) and the fifth is a paternal line (R). These lines are
100 reared at a selection nucleus located in the farm of the Institute for Animal Science and
101 Technology, Universitat Politècnica de València. The records were collected along the
102 generations of selection of these lines from March 1980 to March 2013.

103 The process of foundation of line A began in 1976, sampling New Zealand White
104 (NZW) rabbits, reared by farmers near Valencia (Spain). After three generations
105 without selection, the line has been selected since 1980 using a family index based on
106 litter size at weaning (Estany et al., 1989). Line V was founded in 1980 as a synthetic
107 line, mating crossbred animals that were progeny of four specialized maternal lines,

108 after three generations without selection, the line has been selected (Estany et al.,
109 1989) to increase litter size at weaning since 1982. Line H was founded applying
110 hyperprolific selection and embryo cryopreservation techniques (García-Ximénez et
111 al., 1996; Cifre et al., 1998). Hyperprolific does were assembled from a large
112 commercial population, spread over different Spanish farms. This line was kept since
113 its foundation in 1996 at the nucleus of selection until May, 2004 (10th generation of
114 selection). Since its foundation, this line has been selected to increase litter size at
115 weaning (Ragab and Baselga, 2011). Line LP was founded selecting females from
116 commercial farms that showed extremely long productive lives and prolificacy near or
117 above the average of the Spanish commercial rabbit population (Sánchez et al., 2008).
118 This line has been selected since 2003 to increase litter size at weaning. In V, H and
119 LP, animals were evaluated for litter size using a repeatability animal model. Line R
120 came from the fusion of two paternal lines, one founded in 1976 with California rabbits
121 reared by Valencian farmers and the other founded in 1981 with rabbits belonging to
122 specialized paternal lines (Estany et al., 1992). The method of selection has always
123 been individual selection on post-weaning daily gain.

124 The farm where the rabbits were housed had isolated roofs and the ventilation was
125 controlled depending on the indoor temperature. The cages for does (90 cm long, 50
126 cm wide and 40 cm high) and progeny (80 cm long, 50 cm wide and 30 cm high) were
127 standard flat deck. Management of animals in the different lines was the same, using
128 natural mating; bucks and does began reproduction from 17 to 18 weeks of age. On
129 day 12 post-mating, each doe was tested for pregnancy by abdominal palpation, and
130 non-pregnant does were mated back. Does were mated 11 days after kindling, usually
131 one female was always mated to the same buck; litters were examined each morning
132 during the suckling period to remove dead kits. Kits were reared by their own dam and

133 weaned at 28 days post kindling. Then animals were individually identified by a number
134 tattooed on the left ear and transferred to the fattening cages (8-9 rabbits per cage)
135 until marketing at 63 days. Both breeding animals and progeny were fed *ad libitum* on
136 pelleted commercial rations. The animals were kept under controlled 16-h light: 8-h
137 dark photoperiods.

138 Mating males and females in the maternal lines always belonged to the same
139 generation, i.e. non-overlapping generations mating. In these maternal lines does for
140 the next generations were selected from 25 – 30 % of the best evaluated matings, with
141 a limit of 4 does per mating. Each sire contributed a son to the next generation, and
142 was selected from the best mating of the sire.

143 Management of animals in line R is somewhat different compared to other lines as, in
144 the latter generations, the does were artificially inseminated and the candidates for
145 selection were genetically evaluated exclusively from their phenotypic values (average
146 growth of the previous four weeks), i.e. mass selection. Similarly to the maternal lines,
147 in the R line each sire contributes a son to the next generation and does are selected
148 at a rate of around 20%. Mating was conducted in separated generations until the 25th
149 generation. The generation interval is about 6 months and the estimated response to
150 selection was about 0.5 g/day per generation (Estany et al. 1992). In maternal lines the
151 generation interval is about 9 months and the response to selection ranged from 0.076
152 (Tudela et al., 2003) to 0.085 (García and Baselga, 2002) kit weaned per parturition by
153 generation.

154 For a suitable genetic evaluation of animals in the nucleus, some common culling
155 criteria in commercial farms were not considered, i.e. does with low levels of production
156 or fertility issues were not culled.

157 **Data and Statistical Models**

158 The analysed trait was the length of the productive life (LPL). This trait was measured
159 as the difference in days between the date of the first positive palpation test and the
160 date of death or culling for involuntary causes (Sánchez et al., 2008). Once again, does
161 were never culled based on production results, therefore, LPL reflected a direct
162 measurement of functional longevity. Date and reason for culling or death were
163 systematically recorded, as well as all the information regarding mating and parturition
164 dates, pregnancy status after the abdominal palpation and prolificacy. Does removed
165 to free space for females of the next generation or eliminated because of accidents or
166 other technical reasons not related to health status were treated as censored (Piles et
167 al., 2006b). Thus, the record of each animal included the denoted censoring code,
168 representing (0 = censored; 1 = uncensored) and all the information related to
169 physiological status of the female during its entire life (reproductive and lactation
170 status), as well as all the prolificacy records and the line to which the animal belonged.
171 Functional longevity was analysed using Cox models. A Weibull model was rejected
172 because it did not fit well the data due to the high proportion of does dying in the first
173 parturition (Sánchez et al., 2004; Piles et al., 2006b). The number of does with records
174 was 15,670 and the pedigree involved 19,405 animals. Among the total number of
175 females with records, 5,775 were censored (Table 1). Most of these does were
176 removed before the end of their productive life because space limitations in the nucleus
177 prevented keeping them for longer as the next generation of animals had to enter
178 reproduction.

179 In order to perform the comparison of the LPL between the lines, this data set was
180 used either completely, for the comparison at the lines' foundation, or in different
181 subsets for the comparisons of lines at given periods of the selection process. The

182 number of does for the comparisons at foundation and at fixed times are shown in
 183 Table 1.

184 In a first analysis, the complete data set from the foundation of each line until March
 185 2013 was considered, including the full pedigree. In this analysis a complete genetic
 186 model (CM) was used fitting the systematic effects of line-year-season combination
 187 (LYS), positive palpation order (OPP), number born alive at each kindling (NBA) as
 188 time-dependent factors and the additive genetic value of the animal as a random effect.
 189 In detail, the CM model was:

$$190 \quad \lambda_i(t|\mathbf{x}'_i(t)) = \lambda_0(t) \exp\{\mathbf{x}'_i(t)_{\text{LYS}}\boldsymbol{\beta}_{\text{LYS}} + \mathbf{x}'_i(t)_{\text{OPP}}\boldsymbol{\beta}_{\text{OPP}} + \mathbf{x}'_i(t)_{\text{NBA}}\boldsymbol{\beta}_{\text{NBA}} + \mathbf{z}'_i\mathbf{u}\}$$

191 where $\lambda_i(t|\mathbf{x}'_i(t))$ is the hazard of animal i at time t , for time-dependent factors, treated
 192 as covariates where $\mathbf{x}'_i(t) = \{\mathbf{x}'_i(t)_{\text{LYS}}, \mathbf{x}'_i(t)_{\text{OPP}}, \mathbf{x}'_i(t)_{\text{NBA}}, \mathbf{z}'_i\}$; $\lambda_0(t)$ is the baseline
 193 hazard function at time t , approximated by a step-wise function given by $\lambda_0(t) = \lambda_{0m}$
 194 for $t \in [\tau_{m-1}, \tau_m]$; $m = 1, \dots, M + 1$, where τ_1, \dots, τ_M are the M different ordered survival
 195 times, $\tau_0 < \tau_1 < \dots < \tau_M < \tau_{M+1}$; $\tau_0 = 0$ and $\tau_{M+1} = \infty$. $\boldsymbol{\beta}_{\text{LYS}}$, is the vector of
 196 regression coefficients for the line-year-season (LYS) combinations with 212 levels,
 197 where the year-season was defined by 6 months' time intervals. The number of levels
 198 were 63, 63, 17, 20 and 49 for the subsets of A, V, H, LP and R lines, respectively.
 199 $\boldsymbol{\beta}_{\text{OPP}}$, is the vector including the effect of the three levels of the positive palpation order
 200 (OPP) (1, 2 and 3 or more positive palpation orders), the changes of level in this factor
 201 occurred after every pregnancy test. $\boldsymbol{\beta}_{\text{NBA}}$ is the 5 classes vector of number born alive
 202 in each kindling (NBA). The first level corresponded to does that had 0 NBA, the
 203 second level to parturitions with 1 to 4 born alive, the third to parturitions with 5 to 8
 204 NBA, the fourth to parturitions with 9 to 12 NBA and the fifth level which corresponded
 205 to parturition with at least 13 NBA. The changes of levels in this time-dependent factor
 206 occurred at parturition. Finally, u_i is the additive genetic effect of the animal i , this factor

207 was assumed to follow *a priori* a multivariate normal distribution with mean 0 and
 208 (co)variance \mathbf{G} . In order to account for the genetic heterogeneity between the five lines,
 209 \mathbf{G} was defined as a block-diagonal matrix formed by elements $\mathbf{A}_i \sigma_{a,i}^2$, where \mathbf{A}_i is the
 210 numerator relationship matrix of the line i , and $\sigma_{a,i}^2$ is the additive genetic variance for
 211 that particular line. The additive genetic variances ($\sigma_{a,i}^2$) were assumed to be known
 212 and equal to 0.17, 0.05, 0.29, 0.29 and 0.07 for A, V, H, LP and R lines, respectively
 213 (EL Nagar et al., 2020). The prior distributions for the remaining model parameters
 214 were defined in the same way as in Sánchez et al. (2006b). Baseline hazard step-wise
 215 function elements β_{om} for $m = 1, \dots, M + 1$ were assumed to be independent and
 216 identically distributed (i.i.d.): $p(\beta_{om}) \sim \frac{1}{h_{om}}$, where $0 < \beta_{om} < \infty$. This is a long-uniform
 217 prior which supposes a uniform distribution for the logarithm of β_{om} . The elements of
 218 all $\boldsymbol{\beta}$ were assumed to be i.i.d. following a uniform distribution.

219 In the analysis of the complete data set using CM, additive genetic effects account for
 220 the genetic responses in the different lines. Thus, the contrast of the differences
 221 between each pair of lines based on the year-season levels shared by both lines reflect
 222 the difference between the lines at their foundation, reflecting genetic differences
 223 between the lines when the respective populations were created. The periods in which
 224 each pair of lines were sharing the same environmental and management conditions
 225 were from March 1983 to September 2003 and from March 2006 to March 2013 for
 226 lines A and V; from March 1997 to September 1998 for lines A and H; from March 2006
 227 to March 2013 for lines A and LP; from March 1990 to March 2013 for lines A and R;
 228 from March 1997 to September 1998 for lines V and H; from September 2004 to March
 229 2013 for lines V and LP; from March 1990 to September 2003 and from March 2006
 230 to March 2013 for lines V and R; from March 1997 to September 1998 for lines H and
 231 R; and from March 2006 to September 2013 for lines LP and R. The lines H and LP

232 only shared one year-season, for this reason the contrast between them was not
233 estimated.

234 It is possible to compute actual differences between lines at different periods of time
235 shared by some of them, without relying on the genetic model and by using only the
236 records from those given periods. For the computation of this actual difference
237 between the lines, the model should be the same as that previously described but
238 removing the additive genetic effect. We name this as incomplete model (IM). In this
239 case, the line effects refer to the real genetic merit of the lines at the time of comparison
240 as a consequence of selection and genetic drift, but not being dependent on the genetic
241 model. The difference between two lines at a defined period was computed as the
242 difference between the averages of the year-season effects within line for that period.
243 The periods chosen for comparison were arbitrarily defined by the last three year-
244 seasons shared by at least four of the lines under the same management conditions.
245 These periods were from March 1997 to September 1998 for comparisons between
246 the lines A, V, H and R, and from March 2011 to September 2012 for comparisons
247 between the lines A, V, LP and R. It is also possible to predict the actual differences
248 between the lines (those calculated with the IM) at the defined periods using the results
249 of the analysis with the CM model and the complete data set. The predicted differences
250 between the lines at fixed times can be computed as the contrast between line effects
251 during the shared year-seasons, plus the difference between the averages of the
252 additive genetic values of the animals of each line which lived in that period. These
253 predicted estimates depend on the genetic model and the complete data (Ragab and
254 Baselga, 2011). The estimated differences between lines, calculated with IM model,
255 can be compared with the predicted differences obtained using CM model and the

256 whole data set. This comparison could be considered as a way to check the adequacy
257 of the CM model to explain the complete longevity data set.
258 For both CM and IM, parameter estimation was performed by a Bayesian approach,
259 based on statistics computed from samples of the marginal posterior distributions
260 obtained using a Gibbs sampling algorithm. The Gibbs sampler algorithm comprised
261 200,000 iterations, discarding the first 20,000 in order to allow the algorithm to reach
262 convergence to the marginal posterior distributions. Afterwards, one sample in each
263 20 was saved to avoid high correlations between consecutive samples. The post-Gibbs
264 analysis used to calculate the parameters of interest of the marginal posterior
265 distributions was implemented with the coda package of the R program (Plummer et
266 al., 2006). Convergence of the chains for the parameters and contrasts of interest was
267 assessed using the Z-criterion of Geweke (Geweke, 1992).

268

269 **RESULTS AND DISCUSSION**

270 **Comparison between lines at foundation**

271 Monte Carlo standard errors were very small in all cases (ranging from 0.019 to 0.087)
272 and they are not presented in the tables. Geweke test did not detect lack of
273 convergence in any case. The comparison among lines at their foundation is shown in
274 Table 2. The contrasts are estimable functions between each pairs of lines through the
275 years-season in which both lines were submitted to the same environmental and
276 management conditions. Using all data and the full pedigree, the additive effects of the
277 animals were considered in the model, the selection response was accounted for by
278 this effect, and consequently, the effects of the lines (included in the line-year-season
279 combination) expressed the values at their foundation. The lines V, H and LP showed
280 a substantial superiority in functional longevity over line A. The R line had a higher risk

281 of death or culling with relevant differences when compared to V, H and LP lines. The
282 maximum relative risks were observed between LP and R, and between LP and A
283 lines. The relative risk describes how much more likely it is that culling or death occurs
284 within one level of a given factor relative to another level of the same factor. For
285 instance, at foundation it was 3.152 times more likely for an A doe to die/be culled than
286 for a LP doe (Table 2). Line LP was created from does that had at least 25 parities
287 (Sánchez et al., 2008). The results presented in Table 2 seem to show inconsistencies.
288 For example, the difference between lines A and V at their foundation was 0.495 and
289 was 1.148 between lines A and LP. The difference ($1.148 - 0.495 = 0.653$) is not (exactly)
290 0.436, the contrast between lines V and LP. This deviation between the two values is
291 due to the different sets of year-seasons involved in each particular contrast and also
292 to the fact that the model included the interaction line-year-season. The interaction
293 terms involved in the contrasts A-V and A-LP are, obviously, different to those involved
294 in that estimated between V and LP lines, thus the last one cannot be exactly
295 reconstructed from the previous.

296 The longer productive life of LP does could be considered as an indicator of the
297 successful foundation procedure of this line. Line A was created by mating does and
298 bucks of the New Zealand White breed belonging to populations selected for the
299 standard morphological characteristics of the breed. This line was shown to have a
300 high susceptibility to enterocolitis disease, which occurred during some periods shared
301 with the other lines (Ragab and Baselga, 2011). Piles et al. (2006a) also found, in a
302 diallel cross experiment, relevant differences in the genetic effects for functional
303 longevity between maternal rabbit lines A, V, Prat and the crossbred females Prat \times A.
304 They stated that an A doe was twice as likely to be replaced than a crossbred Prat \times
305 A doe and, in general, the genetic groups with the highest relative risks were those

306 involving the A line. All these results, particularly those presented in the current study
307 that refer to the situation at the foundation, support the hypothesis that founding the
308 line A based only on morphological aspects of the animals, without considering any
309 productive criteria, created a genetic load, related to susceptibility to diseases or lack
310 of longevity. We could speculate that if the founder animals were selected for any
311 performance criteria, this genetic load would be minimized, since those animals with
312 the putative deleterious alleles would not be selected since their performance
313 phenotypes would be deteriorated.

314 In another study comparing lines LP and V, Sánchez et al. (2008) indicated higher
315 survival ability of the line LP over the V line, especially at later cycles. They attributed
316 this result to the foundation procedure of the LP line which was focused on late life
317 survival. In spite of this result being the same as the one we have reported in this study,
318 this comparison between LP and V lines was not a comparison at foundation time,
319 because for V line only the closest relationships sibs were considered in the study. In
320 contrast, in the present study all the available pedigree information was used.

321 Line R showed higher risk at foundation compared to the other lines, and the
322 differences between line R and both LP and V lines were relevant. Considering that
323 line R was created by mating animals maintaining the standard morphological
324 characteristics of the Californian breed with animals from another synthetic line created
325 by mating animals from three commercial paternal lines (Estany et al., 1992), the
326 argument considered with regard to A line about the genetic load that was created
327 during the foundation of the line only applies partially. For the case of the R line, part
328 of the founders came from populations selected for growth performances. Thus, the
329 lower survival ability of the R line with respect to the other lines could be also linked to
330 a certain genetic antagonism between early growth and length of the reproductive life.

331 **Comparison between lines at fixed periods**

332 The estimated differences between the lines A, V, H and R from March 1997 to
333 September 1998 and between the lines A, V, LP and R from March 2011 to September
334 2012 are presented in Table 3. These contrasts reflect differences at the foundation of
335 the lines plus the differences generated as a consequence of the selection process.
336 Lines A and R had a greater risk of death or culling than lines V and H. These overall
337 trends were the same as those observed in the comparison at the foundation time of
338 these lines. The contrasts show the inferiority of the line A for longevity over the other
339 maternal lines during the two periods of comparison. This result is in agreement with
340 those of Ragab et al. (2011) who found that line A was more sensitive to the risk factors
341 compared to V and LP lines. The LP does had a lower risk of death or culling compared
342 to A, V and R lines, this result could be explained, again, as a direct consequence of
343 the foundation process of the LP line. The same result was found by Sánchez et al.
344 (2008) who reported that the LP line had a longer reproductive life than the V line.
345 In general, as the selection process evolves, the differences between the lines were
346 systematically reduced. This may be a consequence of a natural selection (unintended
347 artificial selection process), which is more intense for the lines of lower longevity. For
348 animals with lower longevity, the probability of dying before leaving progeny selected
349 for litter size is higher than for animals having higher longevity. Moreover, the selected
350 progeny of parents with low longevity would have a higher probability of dying before
351 reaching maturity, thus not leaving offspring for the next generation. In other words,
352 the rabbit does which had more parities during their productive lives (long-lived) had
353 the chance to leave more daughters for the next generation, and those which had not
354 more parities (short-lived) did not leave offspring for selection. This improves the global
355 longevity of the rabbit does as the selection generations pass and the differences

356 between the selected lines tend to decrease. This phenomenon can be clearly
357 observed in line A, which had low longevity at its foundation, but it has greatly improved
358 its longevity along many selection generations, thus in the comparisons at fixed times
359 the magnitude of the differences with the other lines are clearly lower than at
360 foundation. Other evidence of these natural selection processes in the A line can be
361 seen in the differences between the breeding values of animals of each line involved
362 in the comparison, which seem to favour the line A (Table 4). This progress of line A is
363 consistent with the genetic trend drawn by its relatively higher additive genetic variance
364 (0.17; EL Nagar et al., 2020). Considering that all the differences between lines go in
365 one direction (reduced by selection), this means there has been a systematic factor
366 similarly affecting the lines; this factor could be an unintended artificial selection.

367 The case of the R line is different to that of the A line. In the comparisons made
368 between March 1997 and September 1998, a certain improvement with respect to the
369 situation at the foundation was observed, but this improvement was less evident than
370 that for the A line, this being compatible with the low additive variance estimated for
371 this line (0.07) (EL Nagar et al., 2020). In the second period of comparison (March
372 2011 – September 2012) an opposite pattern was observed; for example, with respect
373 to the V line, R line log-hazard was slightly worse than that at foundation, -0.697 and -
374 0.620, respectively. The comparisons involving R line should be considered with
375 caution, since, as we previously stated, the reproduction of this line has been organized
376 in a different way to that of the other populations: in the last generations artificial
377 insemination has been used and mating between animals from different generations
378 has been allowed. The change from natural mating to artificial insemination was a
379 management decision adopted to overcome the low fertility observed in the population,
380 this has been a serious handicap to properly generate candidates for the selection.

381 Even after the change to reproduction by artificial insemination these fertility problems
382 remained, probably associated to an excess of body fat in the females. These low
383 fertility issues have had strong consequences in the correct implementation of the
384 selection process for post-weaning growth and they are probably also the reason why
385 in the last generations the LPL of the R line seems to have deteriorated. Nonetheless,
386 the genetic trend seems to be favourable, as reported by EL Nagar et al. (2020) and it
387 is also observed when comparing contrasts between breeding value prediction
388 averages in Table 4. Thus, the observed deterioration of the LPL in the R line, during
389 the last generations, must be explained by the involvement of the interaction between
390 lines and year-seasons effects. As we stated before, for R line, the environmental
391 factors could be said to be particularly unfavourable, associated with the low fertility of
392 the line in the last year-seasons considered in the comparison.

393 The reported responses for LPL in the studied maternal lines are most likely
394 associated, as previously indicated, directly to an unintended selection for longevity
395 and not to a correlated response associated to the selection for criteria considered in
396 each line. We proposed this idea because EL Nagar (2015) reported that, in the
397 maternal lines under study, the genetic correlation between longevity and prolificacy
398 traits (the selection criteria) were nearly null. In that study, the genetic correlation
399 estimates between LPL and NBA were 0.01(0.01), 0.01(0.01), 0.16(0.20), 0.09(0.02)
400 and -0.12(0.33) for A, V, H, LP and R lines, respectively. Moreover, Sánchez et al.
401 (2006a) showed that in V line rabbits, longevity and litter size were not antagonistic
402 traits and the genetic correlations between longevity and number of born alive and
403 number at weaning were 0.16 ± 0.09 and -0.17 ± 0.11 , respectively. For the case of the
404 R line, the hypothesis of the observed response on LPL to be a correlated response

405 cannot be discarded, since for this population the correlation between longevity and
406 post-weaning growth has not been estimated.

407 Beyond the selection process itself, other force that might be argued to explain the
408 trend in the differences between lines along the generations could be genetic drift,
409 since our populations are of limited size. Nonetheless, as we observe a clear common
410 trend for all the lines, i.e. the differences in longevity are reduced as the selection
411 advances; it is hard to propose the drift as a major factor to explain this. Genetic drift
412 is a completely random process, thus different patterns would be expected for the
413 different pairs of lines. In any case, it has to be indicated that the available material
414 does not allow a proper assessment of the role of genetic drift in our selection
415 processes. Another factor that might have played its role in the trend observed with
416 regard to the differences between the lines along the selection process is the
417 inbreeding increase and the depression associated with it. The foundation procedures,
418 effective population sizes and genetic loads are different for the different lines. Thus,
419 both the inbreeding increase and the trends in the genetic loads (Varona et al., 2019)
420 between the different lines could be different across lines. These differences in the
421 putative trends of the genetic load, expected to be reduced as a consequence of the
422 genetic purge, could also be involved in the trend we observed, i.e. an improved
423 longevity within the lines and a systematic reduction of the differences in longevity
424 between the lines. It has to be remarked, however, for this purging process to exist a
425 certain degree of selection must be needed. On this regard, the aforementioned
426 unintended selection process for longevity, i.e. only females reaching to its third or
427 fourth parturition leave offspring to the next generation, could be the driven force of
428 this deleterious alleles purging.

429 Other aspects associated with the inbreeding depression are less likely to be relevant
430 because the inbreeding depression is expected to have a negative effect (Casellas et
431 al., 2008; Fernández et al., 2017; EL Nagar et al., 2020). Thus, a reduction of the
432 longevity along the selection process in the different lines would be expected while we
433 have observed a certain improvement.

434 The differences between lines at fixed times, obtained using the dataset limited to
435 these times with the CM are presented in Table 4. Comparing these differences with
436 those estimated using the IM, we can see that, for the case of the maternal lines (A, V,
437 H and LP) they are relatively similar. This can be interpreted as evidence about the
438 suitability of the genetic model to describe this longevity data in order to predict the
439 breeding values and to estimate differences between the lines at their origins. Similar
440 conclusions were obtained by Ragab and Baselga (2011) regarding reproductive traits
441 and by Mínguez et al. (2016) for growth traits for the same four lines. For the paternal
442 line R, the differences predicted using CM did not match well with those estimated
443 using IM. Thus, according to our previous reasoning for this line it should be concluded
444 that the model is not suitable for fitting the available LPL data. As we previously stated,
445 this line presents physiological characteristics very different to those of the other lines
446 considered in this study. Moreover, for line R the management of breeding animals
447 and the selection criteria (post-weaning growth) were different compared to other lines.
448 These peculiar characteristics are reflected in the statistical model, for example by
449 making the year-season effect have a completely different meaning than that in the
450 maternal lines, and as these interaction terms are also included in the contrasts, we
451 have reported that they completely alter the results. In any case, the output of our study
452 in this regard is that it seems that for the R line the model for fitting LPL should be
453 reviewed.

CONCLUSIONS

454

455 By studying functional longevity data from five populations raised partially under the
456 same management and environmental conditions, we have observed that the
457 differences between the lines at their foundation clearly respond to the selection criteria
458 used for recruiting the animals for the base population. In this regard, two clear extreme
459 examples have been reported: i) LP line, selected for LPL at its foundation, which
460 clearly favoured the trait. ii) A line, not selected for any performance criteria, but for the
461 morphological characteristics of a breed, which seems to have created a genetic load
462 in the population that still segregates and penalizes performance and fitness. Along
463 the generations, at least for the maternal lines under study, a natural selection seems
464 to exist or an unintended artificial selection process that have improved the survival
465 ability of the females and systematically reduce the differences between lines with
466 regard to their LPL or risk of being culled. This phenomenon may be attributed to the
467 purging of unfavorable genes during the artificial selection. The R line, selected for
468 post-weaning growth, shows a clearly different pattern probably associated with the
469 unsuitability of the used model to properly fit the peculiar physiological characteristics
470 of this line that alter its management.

471

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481

482 **CONFLICT OF INTERESTS**

483 The authors declare that they have no competing interests.

484

485 **DATA AVAILABILITY STATEMENT**

486 The datasets used and analysed during the current study are available from the
487 corresponding author on reasonable request.

488

489 **REFERENCES**

490 Cartuche, L., Pascual, M., Gómez, E. A., & Blasco, A. (2014). Economic weights in
491 rabbit meat production. *World Rabbit Science*, 22,165-
492 177. <https://doi.org/10.4995/wrs.2014.1747>

493 Casellas, J., Varona, L., Ibáñez-Escriche, N., Quintanilla, R., & Noguera, J. L. (2008).
494 Skew distribution of founder-specific inbreeding depression effects on the
495 longevity of Landrace sows. *Genetics Research*, 90(6), 499-508.
496 [doi:10.1017/S0016672308009907](https://doi.org/10.1017/S0016672308009907).

497 Cifre, P., Baselga, M., Gacia-Ximenez, F., & Vicente, J. (1998). Performance of
498 hyperprolific rabbit line. I. Litter size traits. *Journal of Animal Breeding and*
499 *Genetics*, 115, 131-138. <https://doi.org/10.1111/j.1439-0388.1998.tb00336.x>

500 García-Ximénez, F., Vicente, J. S., Cifre, P., & Baselga, M. (1996). Foundation of a
501 maternal rabbit line using hysterectomy and embryo cryopreservation. Proceeding
502 of the 6th World Rabbit Congress, Toulouse, France, 2, 285-288.

503 García, M. L., & Baselga, M. (2002). Estimation of genetic response to selection in

504 litter size of rabbits using a cryopreserved control population. *Livestock Production*
505 *Science*, 74, 45-53.

506 EL Nagar, A. G. (2015). Genetic analysis of longevity in specialized lines of rabbits.
507 *Ph.D. Thesis. Universidad Politécnica de Valencia, Valencia, Spain.*

508 EL Nagar, A. G., Sánchez, J. P., Mínguez, C., Ragab, M., & Baselga, M. (2020).
509 Genetic variability of functional longevity in five rabbit lines. *Animal*, 1-9.
510 doi:10.1017/S1751731119003434.

511 Estany, J., Baselga, M., Blasco, A., & Camacho, J. (1989). Mixed model methodology
512 for the estimation of genetic response to selection in litter size of rabbits. *Livestock*
513 *Production Science*, 21,67–75.

514 Estany, J., Camacho, J., Baselga, M., & Blasco, A. (1992). Selection response of
515 growth rate in rabbits for meat production. *Genetics Selection Evolution*, 24, 527-
516 537.

517 Fernández, E. N., Sánchez, J. P., Martínez, R., Legarra, A., & Baselga, M. (2017).
518 Role of inbreeding depression, non-inbred dominance deviations and random
519 year-season effect in genetic trends for prolificacy in closed rabbit lines. *Journal*
520 *of Animal Breeding and Genetics*, 134, 441–452.
521 <https://doi.org/10.1111/jbg.12284>.

522 Geweke, (1992). Evaluating the accuracy of sampling-based approaches to the
523 calculation of posterior moments in: Bernardo Jm, Berger Jo, Dawid Ap and Smith
524 Afm Editors, Bayesian Statistics 4. *Oxford University Press, Oxford, Uk*, 169-193.

525 Larzul, C., Ducrocq, V., Tudela, F., Juin, H., & Garreau, H. (2014). The length of
526 productive life can be modified through selection: an experimental demonstration
527 in the rabbit. *Journal of Animal Science*, 92, 2395-2401.
528 <https://doi.org/10.2527/jas.2013-7216>.

529 Mínguez, C., Sánchez, J. P., EL Nagar, A. G., Ragab, M., & Baselga, M. (2016).
530 Growth traits of four maternal lines of rabbits founded on different criteria.
531 Comparisons at foundation and at last periods after selection. *Journal of Animal*
532 *Breeding and Genetics*, 133, 303–315. <https://doi.org/10.1111/jbg.12197>.

533 Piles, M., Sánchez, J. P., Orengo, J., Rafel, O., Ramon, J., & Baselga, M. (2006a).
534 Crossbreeding parameter estimation for functional longevity in rabbits using
535 survival analysis methodology. *Journal of Animal Science*, 84, 58-62.
536 <https://doi.org/10.2527/2006.84158x>

537 Piles, M., Garreau, H., Rafel, O., Larzul, C., Ramon, J., & Ducrocq, V. (2006b). Survival
538 analysis in two lines of rabbits selected for reproductive traits. *Journal of Animal*
539 *Science*, 84, 1658-1665. <https://doi.org/10.2527/jas.2005-678>

540 Plummer, M., Best, N., Cowles, K., & Vines, K. (2006). CODA: Convergence diagnosis
541 and output analysis for MCMC. *R News* 6, 7-11.

542 Ragab, M., & Baselga, M. (2011). A comparison of reproductive traits of four maternal
543 lines of rabbits selected for litter size at weaning and founded on different criteria.
544 *Livestock Science*, 136, 201-206. <https://doi.org/10.1016/j.livsci.2010.09.009>

545 Ragab, M., Sánchez, J. P., Mínguez, C., EL Nagar, A. G., & Baselga, M. (2011).
546 Longevidad funcional en un cruce dialélico entre cuatro líneas maternas de
547 conejo. Aida (2011), XIV *Jornadas sobre Producción Animal*, Tomo II, 473-475.
548 Zaragoza. Spain.

549 Ramon, J., & Rafel, O. (2002). Diez años de gestión global en España. In Proceedings
550 of the 2th *Congreso Internacional de Producción y Sanidad Animal*, 5-8 November
551 2002, Expoaviga, Barcelona, Spain, pp. 113-117.

552 Rosell, J. M. 2003. Health status of commercial rabbitries in the Iberian Peninsula. A
553 practitioners study. *World Rabbit Science*, 11,157-

554 169. <https://doi.org/10.4995/wrs.2003.505>

555 Sánchez, J. P., Baselga, M., Peiró, R., & Silvestre, M. A. (2004). Analysis of factors
556 influencing longevity of rabbit does. *Livestock Production Science*, 90, 227-234.
557 <https://doi.org/10.1016/j.livprodsci.2004.06.002>.

558 Sánchez, J. P., Baselga, M., & Ducrocq, V. (2006a). Genetic and environmental
559 correlations between longevity and litter size in rabbits. *Journal of Animal Breeding
560 and Genetics*, 123, 180-185. <https://doi.org/10.1111/j.1439-0388.2006.00590.x>.

561 Sánchez, J. P., Korsgaard, I. R., Damgaard, L. H., & Baselga, M. (2006b). Analysis of
562 rabbit doe longevity using a semiparametric log-normal animal frailty model with
563 time-dependent covariates. *Genetics Selection Evolution*, 38, 281-295.
564 <https://doi.org/10.1186/1297-9686-38-3-281>.

565 Sánchez, J. P., Theilgaard, P., Mínguez, C., & Baselga, M. (2008). Constitution and
566 evaluation of a long-lived productive rabbit line. *Journal of Animal Science*, 86,
567 515-525. <https://doi.org/10.2527/jas.2007-0217>.

568 Tudela, F., Hurtaud, J., Garreau, H., & De Rochambeau, H. (2003). Comparaison Des
569 Performances Zootechniques De Femelles Parentales Issues d'une Souche
570 Temoin Et d'une Souche Selectionnee Sur La Productivite Numerique.
571 Proceeding of *The 10^{emes} Journees de la Recherche Cunicole*, Paris, France Pp.
572 53–56.

573 Varona, L., Altarriba, J., Moreno, C., Martínez-Castillero, M., & Casellas, J. (2019). A
574 multivariate analysis with direct additive and inbreeding depression load
575 effects. *Genetics, selection, evolution: GSE*, 51(1), 78.
576 <https://doi.org/10.1186/s12711-019-0521-3>.

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TABLES

580 **Table 1** Number of rabbit does involved in the study

Line	Foundation[†]	First period[‡]	Second period[§]
A	4986	348	320
V	5275	350	362
H	1156	317	-
LP	1224	-	333
R	3029	243	266
All lines	15670	1258	1281

581 [†]Total number of does. [‡]Number of does at first period comparison. [§]Number of does
582 at second period comparison.

583 **Table 2** Differences between the lines at foundation for longevity (log-hazard) estimated with the complete genetic model and all
 584 data set

Contrast	PM*	PSD**	RR***	HPD95%†	P(%)‡
A-V	0.495	0.230	1.640	0.029 , 0.936	99
A-H	0.699	0.280	2.012	0.162 , 1.270	99
A-LP	1.148	0.321	3.152	0.510 , 1.753	100
A-R	-0.125	0.240	0.882	-0.611 , 0.345	77
V-H	0.050	0.192	1.051	-0.333 , 0.418	60
V-LP	0.436	0.192	1.547	0.072 , 0.819	99
V-R	-0.620	0.158	0.538	-0.935 , -0.321	100
H-R	-0.344	0.185	0.709	-0.734 , -0.003	97
LP-R	-1.432	0.156	0.239	-1.725 , -1.119	100

585 *Marginal posterior mean. ** Marginal posterior standard deviation. ***Relative risk = exp(contrast). †Marginal posterior highest
 586 density region covering 95% of the density.

587 ‡Probability of the difference being >0 when the contrast >0 and probability of the difference being <0 when the contrast <0.

588

589 **Table 3** Differences between the lines for longevity (log-hazard) at fixed times estimated with the incomplete model and data set of
 590 the fixed times

Contrast	PM*	PSD**	RR***	HPD95%†	P(%)‡
<i>March 1997 - September 1998 (First period)</i>					
A-V	0.395	0.111	1.484	0.177 , 0.611	99
A-H	0.295	0.119	1.343	0.052 , 0.515	99
V-H	-0.099	0.121	0.906	-0.347 , 0.129	79
A-R	0.148	0.115	1.160	-0.078 , 0.374	90
V-R	-0.247	0.121	0.781	-0.488 , -0.012	98
H-R	-0.147	0.128	0.863	-0.400 , 0.102	88
<i>March 2011 - September 2012 (Second period)</i>					
A-V	0.122	0.120	1.130	-0.121 , 0.365	83
A-LP	0.564	0.156	1.758	0.270 , 0.881	99
V-LP	0.442	0.150	1.556	0.145 , 0.735	99
A-R	0.015	0.134	1.015	-0.248 , 0.271	54
V-R	-0.107	0.132	0.899	-0.364 , 0.149	79
LP-R	-0.550	0.163	0.577	-0.852 , -0.227	100

591 *Marginal posterior mean. ** Marginal posterior standard deviation. ***Relative risk = exp(contrast). †Marginal posterior highest
 592 density region covering 95% of the density.

593 ‡Probability of the difference being >0 when the contrast >0 and probability of the difference being <0 when the contrast <0.

594

595

596 **Table 4** Differences between the lines for longevity (log-hazard) at fixed times estimated with the complete genetic model and data
 597 set of the fixed times

Contrast	PM*	PSD**	RR***	HPD95%†	P(%)‡	D1§	D2¶
<i>March 1997 - September 1998 (First period)</i>							
A-V	0.314	0.113	1.369	0.087 , 0.532	99	0.648	-0.334
A-H	0.251	0.120	1.285	0.008 , 0.479	98	0.699	-0.448
V-H	-0.063	0.125	0.939	-0.302 , 0.181	69	0.050	-0.113
A-R	-0.073	0.111	0.930	-0.285 , 0.143	74	0.355	-0.428
V-R	-0.387	0.114	0.679	-0.622 , -0.179	100	-0.293	-0.094
H-R	-0.324	0.122	0.723	-0.570 , -0.089	100	-0.344	0.020
<i>March 2011 - September 2012 (Second period)</i>							
A-V	0.104	0.127	1.110	-0.152 , 0.345	80	0.655	-0.551
A-LP	0.710	0.157	2.034	0.412 , 1.029	100	1.332	-0.623
V-LP	0.605	0.153	1.831	0.298 , 0.896	100	0.677	-0.072
A-R	-0.592	0.127	0.553	-0.835 , -0.341	100	-0.251	-0.342
V-R	-0.697	0.121	0.498	-0.930 , -0.456	100	-0.906	0.209
LP-R	-1.302	0.154	0.272	-1.614 , -1.010	100	-1.583	0.281

598 *Marginal posterior mean. **Marginal posterior standard deviation. ***Relative risk = exp(contrast). †Marginal posterior highest
 599 density region covering 95% of the density. ‡Probability of the difference being >0 when the contrast >0 and probability of the
 600 difference being <0 when the contrast <0. §Part of PM due to differences between lines at foundation. ¶Part of PM due to
 601 differences in the additive genetic values of the animals belonged to each line involved in the comparison.