

SMARTER

SMALL RuminanTs breeding for Efficiency and Resilience

Research and Innovation action: H2020 – 772787

Call: H2020-SFS-2017-2

Type of action: Research and Innovation Action (RIA)

Work programme topic: SFS-15-2016-2017

Duration of the project: 01 November 2018 – 30 June 2023

Report on trajectory characteristics of resilient animals, and strategies to manipulate these

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DELIVERABLE D3.5

Workpackage N°3

Due date: M56 (30/06/2023)

Actual date: 31/05/2023

Dissemination level: Public

About the SMARTER research project

SMARTER will develop and deploy innovative strategies to improve Resilience and Efficiency (R&E) related traits in sheep and goats. SMARTER will find these strategies by: i) generating and validating novel R&E related traits at a phenotypic and genetic level ii) improving and developing new genome-based solutions and tools relevant for the data structure and size of small ruminant populations, iii) establishing new breeding and selection strategies for various breeds and environments that consider R&E traits.

SMARTER with help from stakeholders chose several key R&E traits including feed efficiency, health (resistance to disease, survival) and welfare. Experimental populations will be used to identify and dissect new predictors of these R&E traits and the trade-off between animal ability to overcome external challenges. SMARTER will estimate the underlying genetic and genomic variability governing these R&E related traits. This variability will be related to performance in different environments including genotype-by-environment interactions (conventional, agro-ecological and organic systems) in commercial populations. The outcome will be accurate genomic predictions for R&E traits in different environments across different breeds and populations. SMARTER will also create a new cooperative European and international initiative that will use genomic selection across countries. This initiative will make selection for R&E traits faster and more efficient. SMARTER will also characterize the phenotype and genome of traditional and underutilized breeds. Finally, SMARTER will propose new breeding strategies that utilise R&E traits and trade-offs and balance economic, social and environmental challenges.

The overall impact of the multi-actor SMARTER project will be ready-to-use effective and efficient tools to make small ruminant production resilient through improved profitability and efficiency.

Table of contents

About the SMARTER research project.....	1
1 Summary.....	3
2 Introduction.....	4
3 Modelling studies to characterize trajectory characteristics of resilient animals and predict the response to selection on these.....	5
3.1 Materials and Methods.....	6
3.1.1 <i>Data simulation for the validation of resilience indicators</i>	6
3.1.2 <i>Calculating resilience indicators</i>	10
3.1.3 <i>Evaluation of resilience indicators using simulated data</i>	11
3.1.4 <i>Predicting response to selection</i>	13
3.2 Results.....	13
3.2.1 <i>Classification of response types</i>	13
3.2.2 <i>Sensitivity to host response characteristics</i>	16
3.2.3 <i>Sensitivity to data recording frequency and duration</i>	17
3.2.4 <i>Predicting response to selection for resilience</i>	19
3.3 Discussion.....	20
3.4 References.....	21
4 Resilience trajectory analyses of Smarter data: response to nutritional challenge in two Alpine goat lines selected on divergent longevity.....	25
5 Resilience trajectory analyses of Smarter data: response to inflammatory challenge in two Alpine goat lines selected on divergent longevity.....	48
5.1 Introduction.....	48
5.2 Material and methods.....	48
5.2.1 <i>Dataset</i>	48
5.2.2 <i>Estimation of target trajectories</i>	48
5.2.3 <i>Calculation of individuals' resilience indicators</i>	49
5.2.4 <i>Statistical model</i>	49
5.2.5 <i>Validation</i>	49
5.3 Results.....	49
5.4 Discussion.....	51
5.5 Conclusions.....	52
6 General conclusions and recommendations.....	52
7 Deviations or delays.....	53

1 Summary

Resilience refers to the capacity of an animal to be minimally affected by disturbances or to rapidly return to its state in the absence of challenge. In line with this definition, resilience trajectories were inferred, modelled, and characterized using both simulated data (Tasks 3.3) and Smarter experimental data (Task 3.2). Specifically, simulation studies were carried out to validate various novel statistical resilience indicators that are increasingly proposed in the animal breeding literature as breeding goal traits to improve animals' resilience to short-term disturbances through genetic selection. These statistical resilience indicators include the skewness, autocorrelation, area under the curve, mean of squares and log of variance of the observed deviations from an animal's estimated target trajectory (i.e., performance in ideal condition). The aim of the simulation study was to obtain a better understanding of these resilience indicators in their ability to discriminate between different response types and their dependence on diverse data and response characteristics. To this purpose, three broad response types to short-term challenges were simulated: *Fully Resilient* animals whose performance is not affected by the challenge, *Non-Resilient* animals whose performance is permanently affected by the challenge and *Partially Resilient* animals that are affected but recover after a period. A within response type variation was included in the simulations. A statistical comparison of animals from different response types was carried out using different indicators, and different statistical methods for estimating unknown target trajectories were assessed. It was found that all resilience indicators can reliably distinguish between the *Fully Resilient* group and either of the other two groups in all scenarios. However, when the comparison was between *Partially Resilient* and *Non-Resilient*, only log of variance, area under the curve and mean of squares could correctly identify *Partially Resilient* group as the more resilient, provided that the ratio of observation/perturbation period was large enough. Skewness was in general the least reliable indicator, but all the indicators had correct dependency on the magnitude of perturbation. In addition, all resilience indicators except for autocorrelation were robust in terms of frequency of measurements and the statistical method used to infer target trajectories. In conclusion, validation of the resilience indicators using simulated data showed that three of the five proposed resilience indicators can correctly discriminate between fully resilient, partially and non-resilient animals if sufficient data in the absence and during perturbations are available. The manuscript for publishing the results of this work in a scientific journal will be submitted in July 2023.

Real-time resilience trajectories were inferred and characterized from Smarter's experimental data, using the above and other statistical approaches. The data included longitudinal performance and fertility records of two Alpine goat lines divergently selected for low and high function longevity (low_LGV/ high_LGV) prior, post and during short term nutritional and inflammatory challenges generated in Task 3.2. Similar response and recovery profiles of milk yield and milk fat content were observed during both types of short-term challenges for both lines. However, the lines differed significantly in their milk protein resilience trajectories. Analyses of lifetime trajectories of body weight and lactation suggested that the low_LGV goats were more adapted to allocate resources to meet an expected physiological change such as gestation and lactation. However, high_LGV goats allocate more for structural mass and may better cope with an unexpected short-term environmental change such as nutritional deficit, or infection. Altogether, the results of the Smarter data-analyses demonstrate that analyses of short-and long-term resilience trajectory characteristics from genetically divergent lines experimentally exposed to nutritional and infection challenges is useful to observe the wide range

of realized resilience trajectories in animals and thus to identify animals' diverse adaptive strategies under challenging environments. Furthermore, the results for the divergent longevity goat lines also suggest that genetic selection of functional longevity may improve animals' resilience to short-term environmental challenges, although this may only be apparent for specific traits (e.g. milk composition). A manuscript describing the results from the nutritional challenge experiment has been submitted to the journal *Animal*.

In connection to WP5, and to assess the scope of genetic strategies for improving animals' resilience to short-term challenges, a previously published mechanistic model of parasite infections in sheep was used to predict the response to selection on the validated statistical resilience indicators in terms of resilience, performance and health. The model predictions demonstrate that it is possible to improve individuals' resilience to infections through genetic selection on statistical resilience indicators. However, in the context of infectious disease, selection for resilience may not always be the best method to improve individuals health and performance. Selection for disease resistance may be more effective, if it is possible to collect appropriate resistance phenotypes. The results of this study will be presented at the American Dairy Science Association annual meeting in June 2023.

2 Introduction

Resilience, as defined by the Smarter consortium and others, refers to the capacity of an animal to be minimally affected by disturbances or to rapidly return to its state in the absence of challenge (Colditz and Hine, 2016; Berghof, Poppe and Mulder, 2019; Garcia-Baccino *et al.*, 2021). Based on this definition, resilience is described by an animal's health or performance trajectory that captures the deviation from, and recovery to, the unchallenged state. Characterizing an animal's resilience trajectory thus requires longitudinal data before, during and after a perturbation period. Thanks to the increasing abundance of automated on-farm monitoring systems, such data become more routinely available for each individual (Knap and Doeschl-Wilson, 2020; Neethirajan and Kemp, 2021; Poppe *et al.*, 2021). The potential to provide new resilience phenotypes from such longitudinal data for genetic improvement has been well recognized within Smarter (e.g., (Ithurbide *et al.*, 2022)) and by others (e.g. Berghof *et al.* 2019; Knap and Doeschl-Wilson, 2020; Neethirajan and Kemp, 2021; Abdelkrim *et al.*, 2021).

In particular, several statistical measures capturing individuals' deviations from target trajectories under non-challenge conditions have been proposed as useful resilience indicator traits of individuals for quantitative studies and genetic selection. These include autocorrelation, skewness, area under the curve, log of variance and the mean square of deviations (e.g. Berghof *et al.* 2019; Poppe *et al.*, 2020 & 2021, Chen *et al.* 2023). However, most studies to date focused on genetic analyses of these resilience indicators. It is however not known to what extent these indicators can discriminate between different resilience response types, and in particular between individuals that experience no perturbation, temporary perturbation or never recover from a challenge. Calculation of the diverse statistical resilience indicators requires specification of individuals' target trajectory in the absence of challenge. Since an animal cannot be simultaneously challenged or not challenged, this target trajectory usually needs to be estimated. Various methods have been proposed in the literature among which repeated regression and quantile regression have been proposed as the most reliable (Adriaens *et al.*, 2020; Poppe *et al.*, 2020). However, it is not known how these different approaches affect the value of the resilience indicators. Furthermore, it is not known how individuals' resilience features, such as those related to the magnitude of perturbation and time to recovery affect the values of these

resilience indicators, and what the data requirements on the length of window of observation and the frequency of measurements are for obtaining reliable resilience indicator values.

This report is structured as follows: In section 3 extensive validation of the previously proposed statistical resilience indicators was carried out using simulation studies to assess the ability of these indicators to discriminate between different response types and to assess how the values of these resilience indicators depend on diverse data and response characteristics. A mechanistic model of sheep that genetically differ in their response to gastro-intestinal parasite infections was then used to predict the impact of genetic selection on the diverse resilience indicators on resilience, performance, and health. These modelling studies were led by UEDIN.

The subsequent sections 4&5 refer to the inference and characterization of real-time resilience trajectories using Smarter data generated in Task 3.2. The data consisted of longitudinal performance records of the two Alpine goat lines divergently selected for low and high function longevity (low_LGV/high_LGV) prior, post and during short-term under-feeding challenges and subsequent inflammatory challenges, as described in the deliverable report D.3.2. Specifically, section 4 focuses on the characterization of life-time resilience trajectories and on the response to the nutritional challenges that was carried out by INRAE. The study complements previous analyses of milk metabolite response curves for these datasets that have demonstrated that milk metabolite profiles provide promising non-invasive resilience measures of individuals (see deliverable report D3.2 and (Ithurbide *et al.*, 2022)). Section 5, led by UEDIN, focuses on the response of goat from the two divergent LGV lines to the inflammatory challenge that mimics mastitis infections. Specifically, differences in the resilience to this challenge between the two goat lines were examined using the statistical resilience indicators introduced above and validated in section 3. Section 6 provides a general conclusion that summarizes the key findings obtained from the diverse modelling and data analyses of this deliverables and their potential implications for future research and practice.

3 Modelling studies to characterize trajectory characteristics of resilient animals and predict the response to selection on these

In this simulation study we assumed that all animals are subjected to the same one-off or short-term challenge, such as an infection, food shortage, extreme temperature, or any other challenge that may cause a temporary or long-term perturbation in animals' performance from that corresponding to non-challenge conditions. It was assumed that animals vary in their performance or health response to this challenge. In particular, three distinct response types were simulated depending on whether animals deviate from their target performance or health trajectory and eventually return to it as a result of the challenge. Furthermore, within each response types, animals were assumed to vary in the time or amplitude of perturbation, the speed of recovery, or the route to recovery as outlined below. Five different statistical resilience indicators were evaluated with respect to their ability to correctly distinguish the more resilient from the less resilient response type in pairwise comparison. In addition, the resilience indicators were also evaluated with regards to their sensitivity to variation in the timing and amplitude of perturbation, the speed of and route to individuals' recovery, as well as to the frequency of measurement and observation period. Finally, the effect of unknown linear and non-linear target trajectories and different methods to estimate these on the performance of the resilience indicators was assessed.

Further, response to selection based on these resilience indicators on health and performance profiles on sheep was assessed using a previously developed mechanistic model for gastro-intestinal parasite infection in sheep that differ genetically (polygenic variation) in their response to parasites.

3.1 Materials and Methods

3.1.1 Data simulation for the validation of resilience indicators

3.1.1.1 Modelling response types – known target trajectory

For simplicity, we first assume that the target performance, health or feed intake trajectory of each animal throughout the challenge period, i.e., in the absence of challenge, is known or can be reliably estimated, using e.g. the method proposed by (Nguyen-Ba, van Milgen and Taghipoor, 2020) based on pre- and post-challenge data. Therefore, the residual deviations have a mean value of zero in the absence of challenge. In addition, we assume that pre-challenge data exists, and that all individuals' perturbation starts at the same time. Lastly, we assume a fixed observation period, which exceeds the duration of the perturbation period, i.e., the performance measures of each individual converge to their original or a new performance trajectory. In the base scenario, the observation period starts at 1 day-old (days in milk, etc.) up-to 360 days with perturbation period being 90 days in the middle. However, the effect of variation in observation period and onset of perturbation on the value of resilience indicators are also studied later.

Individuals' responses to the challenge are classed into three distinct response types depending on whether they deviate from their target trajectory and eventually return to it as a result of the challenge. The deviations for the three main response types described above assuming known target trajectories are shown in Figure 1. The first type corresponds to *Fully Resilient* animals whose performance is not systematically affected by the challenge. Hence, their deviation for their target trajectory is the line coinciding with the horizontal axis, and individual performance records may fluctuate around this line (Figure 1A). The second response type refers to *Non-Resilient* individuals that suffer a long-term or even permanent effect from the challenge (Figure 1B). Finally, the third response type, the *Partially Resilient* type, corresponds to animals that experience a temporary reduction in performance following the challenge, but eventually fully recover to resume their original challenge-free performance trajectory (Figure 1C).

Resilience indicators may not only be affected by whether animals experience or recover from a perturbation, but also by how they recover. Therefore, three within-response-type variations of the *Partially Resilient* animals are considered based on their route to recovery (Figure 1C). These are the *Steady Recovery* type, who experiences a gradual recovery in performance over time until they reach their target trajectory, the *Compensatory recovery* individuals, who overcompensate in performance for a period (e.g., by eating more), and the *Relapsed Recovery* individuals who experience some relapse over the course of recovery, and hence their performance oscillates mostly below the target trajectory.

The health, food intake or performance deviations for the above response types can be represented by a series of sinusoidal waves. More specifically, the average deviation of a response type (baseline) is represented by a series of waves (or modes, M_k), each having their support for half a period, i.e., from one periodic maximum to the next periodic minimum or vice versa. The modes are concatenated at their extremums. This way, mode k with performance value M_k for $k \geq 1$, is active from time t_{k-1} to t_k and is defined as follows:

$$M_k(t) = \begin{cases} A_k \sin^2 \left(\frac{\pi(t - t_{k-1})}{2(t_k - t_{k-1})} \right) + M_{k-1}(t_{k-1}), & t_{k-1} \leq t < t_k, \\ 0, & \text{otherwise,} \end{cases} \quad 1$$

where A_k is the signed amplitude (i.e., negative when animal's performance is reducing and positive when the animal is recovering) and $M_0 = t_0 = 0$. The values for the average amplitudes and periods are given in Figure 1 for each response type. For ease of comparison, we first assumed that the deviation for all response types have the same average amplitude A_1 for the first reduction of performance (except for the *Fully Resilient* group that does not have reduced performance by definition). Similarly, all response types were assumed to reach their post-challenge equilibrium performance on average at the same time. Any oscillation after the equilibrium time is thus white noise. For *Non-Resilient* animals, the equilibrium time is defined as when the simulated deviation reaches a constant value.

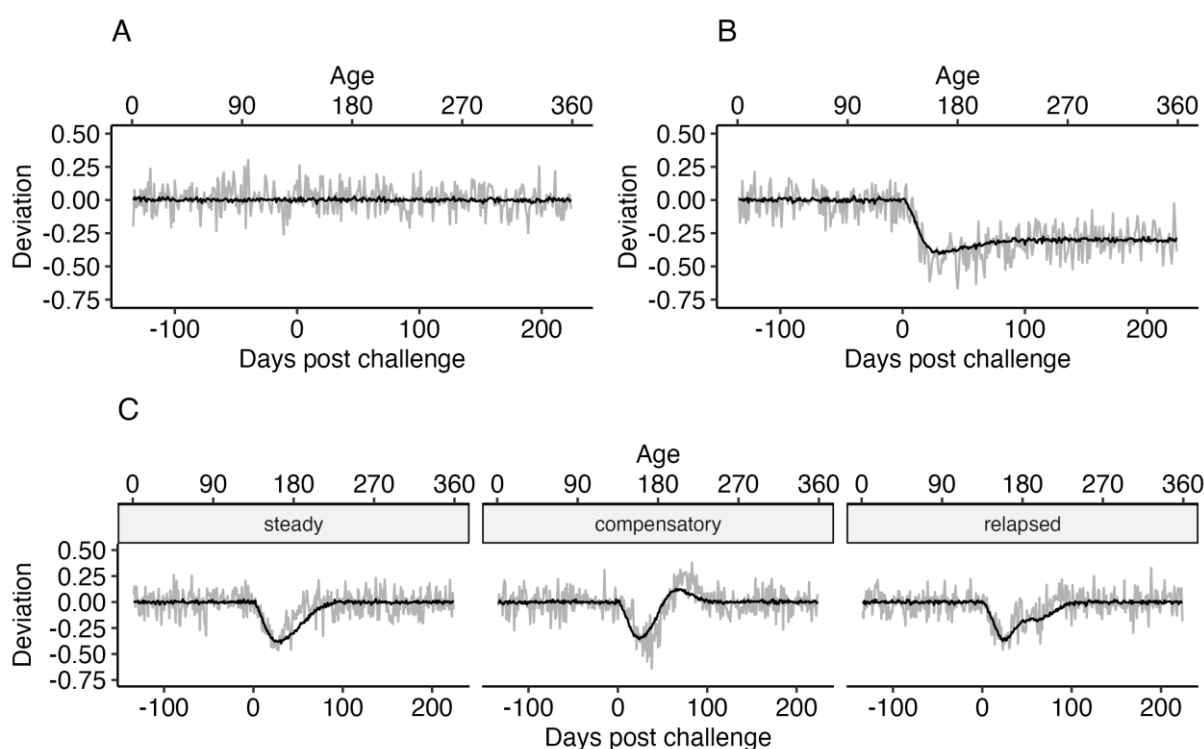


Figure 1. Simulated deviations from target performance or health trajectories for three response types: A) Fully-Resilient, B) Non-Resilient and C) Partially-Resilient for a period of 360 days. At age 135 days (equivalent to 0 for days post challenge) all individuals experience a perturbation. The solid line represents the average for each response type. One individual for each group is also shown with grey line. Group B individuals have two modes of amplitudes (-0.4, 0.1) and phases (25, 65) respectively. Similarly, there are 2 modes for the steady (amplitudes (-0.4, 0.4), phases (25, 65)), 3 modes for compensatory (amplitudes (-0.4, 0.5, 0.1), phases (25, 42, 23)) and 4 modes for relapsed sub-group (amplitudes (-0.4, 0.3, -0.1, 0.2), phases (25, 22, 20, 23)) of the Partially-Resilient group

3.1.1.2 Adding within response type variation

Individual variation in performance response to the challenge (i.e., deviation) was simulated for each response type by sampling the amplitude and phase of each mode for each individual from independent normal distributions with corresponding means A_k and t_k as specified in Figure 1 for each response type, and coefficients of variation of 2 and 0.01 (small enough to obtain visually distinct

response types) for phase and amplitude, respectively, across all modes. Hence, the amplitude and phase for mode k of individual j is sampled from

$$\begin{pmatrix} A_{k,j} \\ t_{k,j} \end{pmatrix} \in \mathcal{N} \left(\begin{pmatrix} A_k \\ t_k \end{pmatrix}, \begin{pmatrix} 0.01^2 \cdot A_k^2 & 0 \\ 0 & 2^2 \cdot t_k^2 \end{pmatrix} \right) \quad 2$$

Finally, white noise was added ($e_{i,j}$) from a normal distribution with variance 0.1. Hence, the deviation in performance for animal j at time t_i , $x_{i,j}$, from its target trajectory is defined as

$$x_{i,j} = \sum_{k=1}^K M_{jk}(t_i) + e_{i,j}, \quad 3$$

where $M_{jk}(t_i)$ is calculated using Equation 1 with amplitudes and phases drawn from normal distributions as described above.

For each simulation run, performance trajectories for 100 individuals per response (sub-)type were generated. The simulation was replicated 100 times.

3.1.1.3 Unknown target trajectories and their estimation

The target performance trajectory of an animal in the absence of challenge is often unknown or difficult to estimate in the absence of pre- and post-challenge data. To accommodate this situation, we superimposed the above deviations (equation 3) on simulated, supposedly unknown target trajectories. Two types of unknown target trajectories were simulated: a linear trajectory, corresponding e.g. to body weight measures during a linear growth phase (Doeschl-Wilson *et al.*, 2004), and a non-linear trajectory, corresponding, e.g., to milk yield records of dairy cows using Wood lactation curve (Wood, 1967)

$$MY = c_1 t^{c_2} e^{c_3 t}, \quad 4$$

where MY is the milk yield, t is days in lactation and c_1 , c_2 and c_3 are constants. Different response types for these traits are shown in Figure 2-3. Without loss of generality (as target trajectories were estimated for each individual separately, see below), individuals were assumed to have identical target trajectories but vary in their response to challenge (i.e., only different in deviation from their identical target trajectory). The individual deviations for the different response types defined in equation (3) above were then scaled and added to these linear or non-linear target trajectories,

$$y_{i,j} = Y_i + x_{i,j} Y_i, \quad 5$$

where $y_{i,j}$ is the performance of animal j at time t_i , $x_{i,j}$ is the residual and is simulated from Equation 3 and Y_j is the value of the corresponding target trajectory evaluated at time t_t .

Two methods were used to estimate target trajectories: quantile regression and repeated regression. In quantile regression with threshold τ , the coefficients of the objective function are calculated such that τ -quantile of the residuals is minimum (Fahrmeir *et al.*, 2013). For this study we used quantile 0.7 to reduce the effect of negative deviation on the fitted function as suggested by (Poppe *et al.*, 2021). In a repeated regression approach, large negative residuals are removed after a least square method and the remaining data are used for the next step. The process is repeated until all residuals lie within a threshold of predictions. We used a threshold of 0.8 as suggested by (Adriaens *et al.*, 2020). The final residuals from either of the fitting methods were then used as the deviations to calculate the resilience indicators. The packages `quantreg` (Koenker, 2021) and `stats` of R (R Core Team, 2021) were used for estimation of target trajectories using quantile or repeated regression, respectively.

More specifically, target trajectories were estimated by fitting a linear function or a Wood lactation curve to the data y of each individual separately, i.e., for each animal j ,

$$y_{i,j} \sim \widetilde{Y}_{i,j} + \widetilde{x}_{i,j}, \quad 6$$

where $\widetilde{x}_{i,j}$ is the estimated residual and $\widetilde{Y}_{i,j}$ takes the form of linear or Wood lactation curve and is fitted using either a quantile regression method or a repeated regression method. Finally, since the noise was scaled in the simulation (Equation 4), the estimated deviations at time i for animal j , $\widetilde{x}_{i,j}$, were also scaled by the estimated target trajectory for animal j at time i , $\widetilde{Y}_{i,j}$. The resulting scaled residuals from these fitting procedures were then used as the deviations from which the diverse resilience indicators outlined below were calculated.

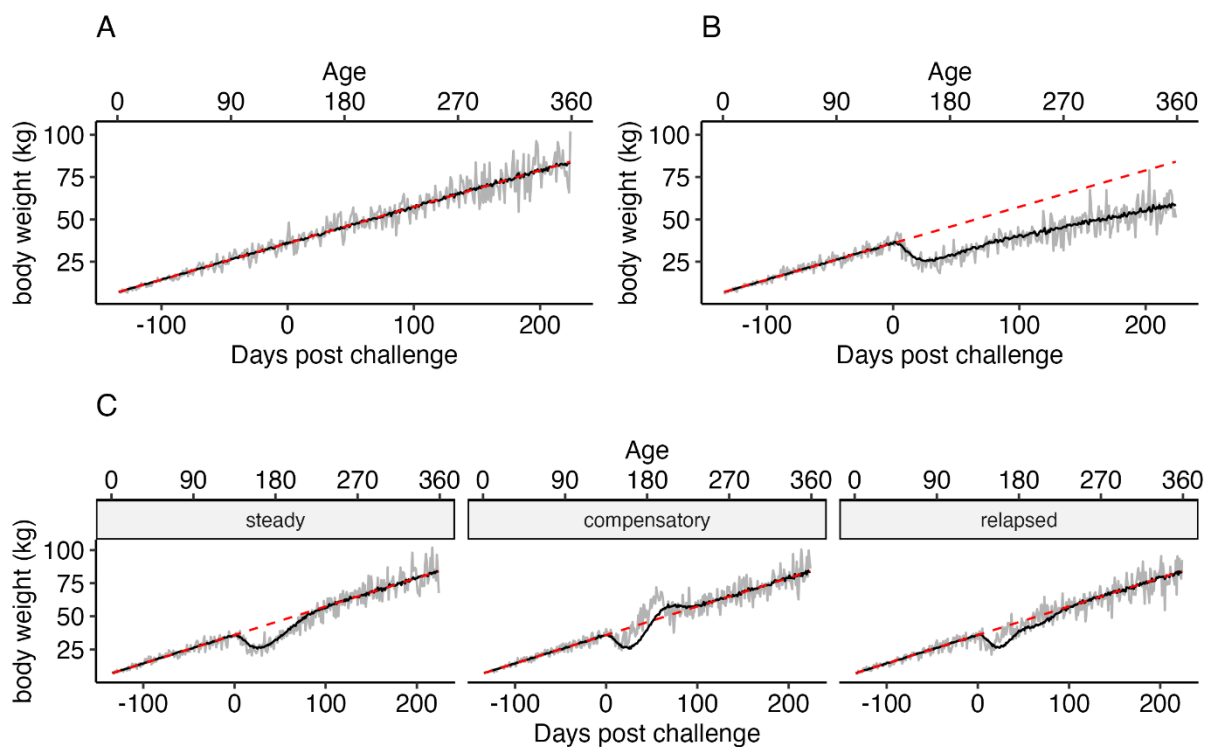


Figure 2. Simulated linear trends for three response types: A) Fully-Resilient, B) Non-Resilient and C) Partially-Resilient for a period of 360 days. The solid black shows mean trend in each group and grey shows one example individual. At age of 135 days, individual experience a challenge. Response types simulated in Figure 1 are superposed on the linear target trajectory with intercept 6.9 and slope 0.215 (see Equation 5) that is shown by the dashed red line. The data may represent the linear part of sheep growth (D3.2). To keep data consistent with other nonlinear simulation (Figure 3), 360 days is assumed for linear trend, however, the effect of smaller window of observation is studied in section 3.2.3.3.

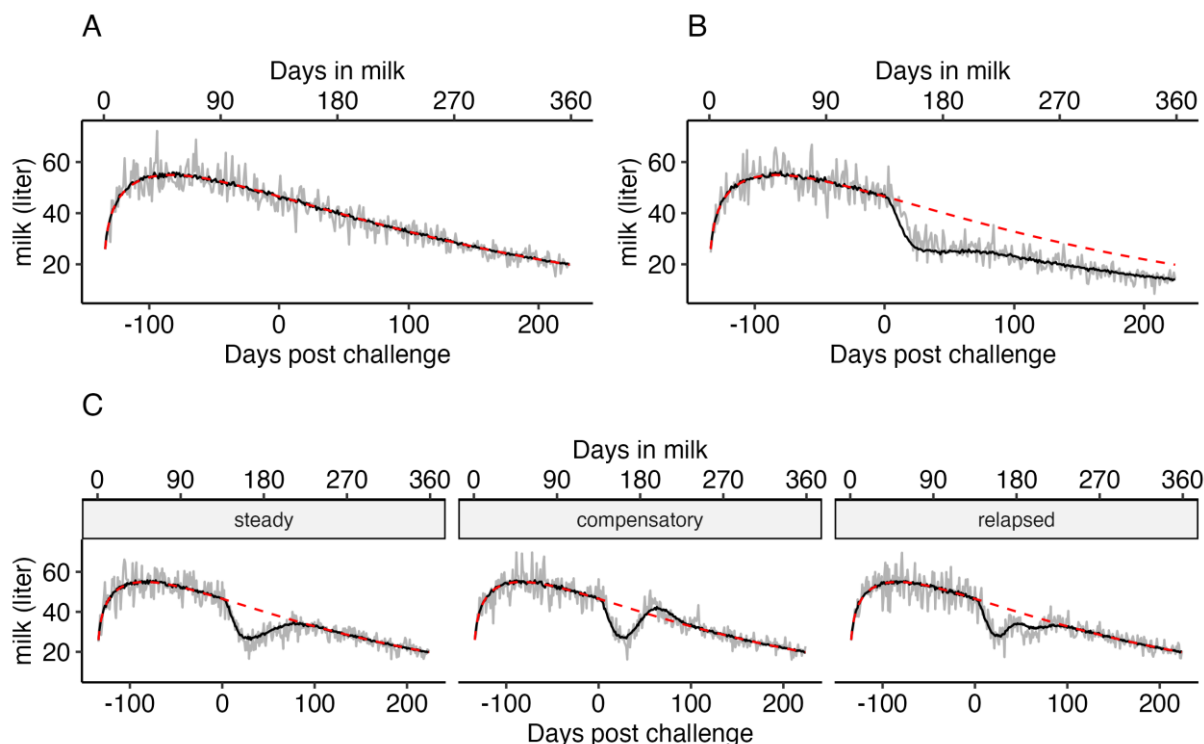


Figure 3. Simulated nonlinear trends (e.g., milk yield) for three response types: A) Fully-Resilient, B) Non-Resilient and C) Partially-Resilient for a period of 360 days. The solid black shows mean trend in each group and grey shows one example individual. At 135 of days in milk, individual experience a challenge. Response types simulated in Figure 1 are superposed (see Equation 5) on the target trajectory modelled as a Wood lactation curve ($c_1=26.057$, $c_2=0.253$ and $c_3=-0.0049$ in Equation 4) that is shown with dashed red line.

3.1.2 Calculating resilience indicators

Five statistical resilience indicators derived from deviations from target trajectories were evaluated in the study, of which four had been previously proposed (Scheffer *et al.*, 2015; Berghof, Poppe and Mulder, 2019; Putz *et al.*, 2019; Poppe *et al.*, 2020): the natural logarithm of the variance (LV), the natural logarithm of mean of squares (LMS), the lag-1 autocorrelation (AC1) and skewness (S). The fifth resilience indicator considered in this study was the area under the curve (AUC) of the deviations from the target trajectory, representing cumulative deviations over the perturbation period.

The LV for animal j is defined as the natural logarithm of the variance of the deviations for animal j evaluated at n_j time points.

$$LV_j = \ln \left(\frac{\sum_{i=1}^{n_j} (x_{ij} - \bar{x}_j)^2}{n_j - 1} \right), \quad 7$$

where x_{ij} may be the true (for known target trajectories) or the estimated deviation of animal j at time t_i , and \bar{x}_j is the mean of deviations for animal j . High values of LV correspond to lower resilience because less resilient animals are expected to deviate more from their target trajectory. Log-transformation is done to normalize the distribution of the variance (Hill and Mulder, 2010; Berghof, Bovenhuis and Mulder, 2019).

The LMS is defined as

$$LMS_j = \ln \left(\frac{1}{n_j} \sum_{i=1}^{n_j} x_{i,j}^2 \right). \quad 8$$

where, $x_{i,j}$ is the i^{th} deviation of animal j with n_j records.

The LMS of a *Fully Resilient* individual is small, whereas higher LMS indicate lower resilience.

The skewness (S) of the deviations for animal j with n_j records is defined as (Joanes and Gill, 1998)

$$S_j = \frac{n_j}{s_j^3(n_j - 1)(n_j - 2)} \left| \sum_{i=1}^{n_j} (x_{i,j} - \bar{x}_j)^3 \right|, \quad 9$$

where, $x_{i,j}$ is the deviation at recording time t_i of the j^{th} animal and \bar{x}_j and s_j are the mean and the standard deviation of these measures, respectively. A skewness value close to zero is expected to indicate high resilience, as more resilient animals are expected to have similar number of positive and negative deviations. In contrast less resilient animals have more negative deviations and thus are expected to have negative skewness (Berghof, Poppe and Mulder, 2019). We have used absolute value as animals with positive skewness are deviating from their target trajectory and therefore may not be resilient.

The lag-1 autocorrelation AC1 is defined as the correlation between the deviations corresponding to two consecutive time points,

$$AC1_j = \frac{1}{s_j^2(n_j - 1)} \sum_{i=1}^{n_j-1} ((x_{i,j} - \bar{x}_j)(x_{i+1,j} - \bar{x}_j)). \quad 10$$

The AC1 of *Fully Resilient* animals is expected to be zero as the deviations are white noise. Less resilient animals are expected to have longer stretches of negative deviations, manifested in higher AC1.

Finally, the AUC for the deviations is defined as

$$AUC = \frac{1}{t_{\text{end}} - t_0} \left| \int_{t_0}^{t_{\text{end}}} x_j(t) dt \right|, \quad 11$$

where $x_0 = t_0 = 0$. *Fully Resilient* individuals have a zero or very small value of AUC, whereas less resilient animals have generally negative deviations (therefore, higher AUC). As individuals are not expected to have predominant positive deviations, the absolute value function is used to associate high AUC with lower resilience. Therefore, positive deviations do contribute to lower the value of AUC.

3.1.3 Evaluation of resilience indicators using simulated data

3.1.3.1 Correct classification of response types

To determine to what extent the diverse resilience indicators are able to distinguish between the different response types, a pair-wise comparison between any two response types was carried out using the area under the curve for the receiver operating characteristics (AUROC) as a quantitative measure (Fawcett, 2006). The receiver operating characteristic curve (ROC) is commonly used to evaluate the performance or accuracy of diagnostic tests (here resilience indicator) and plots the true test positive rate versus the false positive rate. The AUROC represents the probability of correctly assigning individuals into their response types based on a particular resilience indicator, with $0 \leq$

$AUROC \leq 1$. When $AUROC = 0.5$, the resilience indicator is not able to distinguish between the two response types, whereas the closer the AUROC to either 0 or 1, the better the resilience indicator is at distinguishing between the two response types. Response types were ordered such that an AUROC below 0.5 implies that the resilience indicator wrongly tends to classify the more resilient animal as less resilient. Figure 4 shows an example of ROC for comparison of *Partially Resilient* (compensatory) with *Non-Resilient* group. The `pROC` package in R (Robin *et al.*, 2011) was used to calculate the AUROC values.

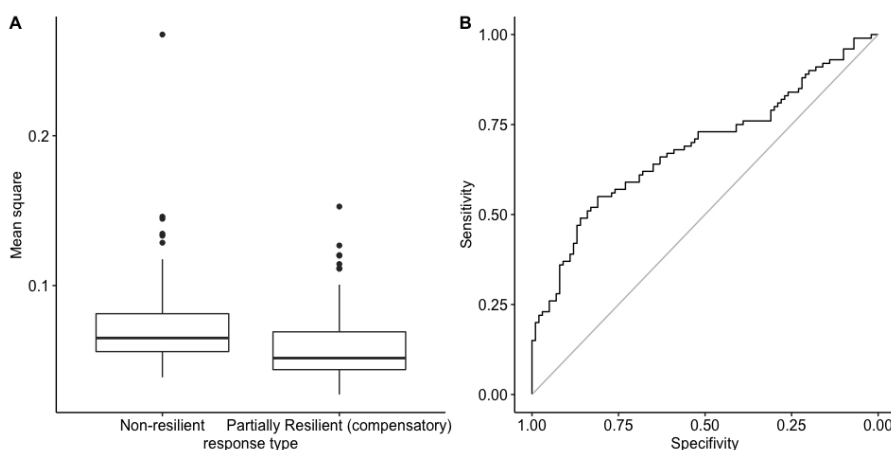


Figure 4. Example of ROC. A) MS values of *Non-Resilient* group and *Partially Resilient* (compensatory) group estimated from an unknown linear target trajectory. B) Specificity vs. sensitivity for various threshold values (from $-\infty$ to $+\infty$) such that controls $>$ threshold \geq cases. Here, *Non-Resilient* is the control group and the *Partially Resilient* are the cases. The area bounded by the sensitivity vs specificity and the x-axis (0.69) is AUROC.

3.1.3.2 Sensitivity analysis of resilience indicators to host response characteristics and to features of data

To systematically assess the impact of response characteristics on the resilience indicators, the value of the resilience indicators was calculated with respect to the following changes in the simulated deviations and model parameters: early/late response, magnitude of perturbation, recovery speed, data frequency and window of observation. To implement early or delayed response for individual, simulated deviations were shifted left/right up-to 120 days while keeping the observation windows fixed to 360 days. To investigate the effect of the magnitude of the perturbation on the resilience indicators, the amplitudes of the first and second modes in Eq. 1 were changed by an equal amount. The recovery speed was changed by increasing the period of the second mode. The frequency of measurement was changed by pruning the dataset at equidistant interval. Finally, the window of observation was changed by trimming the number of days pre- and post-challenge simultaneously but ensuring all individuals reach their new equilibrium. The values for the base case of these parameters as well their alternate values are given in Table 1.

Table 1. Parameters for simulation of data

Parameter	Base value	Alternative values
Pre-perturbation (days) ¹	135	15, 25, ..., 255
Days between measurements ²	1	2, 3, 4, 5, 6, 9, 10, 12, 15
Observation window (days)	360	330, 300, 270, ..., 180
Perturbation magnitude	0.4	0.41, 0.42, ..., 0.5
Recovery period (days)	65	75, 85, ..., 135

¹Pre-perturbation days is changed while the observation window is fixed.

²The value 1 corresponds to daily measurements, 2 to every other day, etc.

3.1.4 Predicting response to selection

To assess the impact of genetic resilience control strategies, response to selection on the statistical resilience indicators on resilience, performance and health were assessed using a mechanistic model for gastro-intestinal parasite infections in sheep. Specifically, data were simulated based on the mechanistic model sheep by (Vagenas, Bishop and Kyriazakis, 2007b, 2007a; Doeschl-Wilson *et al.*, 2008) that mimics the response of sheep that differ genetically in their response to short-term challenge with gastro-intestinal parasites. The model is similar to the mechanistic model created in Task 3.3 (see deliverable report D3.3) but generates a wider variety of response types as it had not been adapted to a specific data set. The genomes of 10,000 sheep and genomic selection was simulated following the approaches developed in Smarter WP5 (Ghaderi Zefreh *et al.*, 2023) with population structure, values for the genetic parameters, and parameters specifying the challenge dose and diet specifications from (Doeschl-Wilson *et al.*, 2008). In particular, the model represents a population of growing sheep (each generation consisting of 8100 offspring from 270 males and 2700 females) from a breed with high average susceptibility to gastro-intestinal parasites that were trickle challenged after weaning daily with 3000 L3s of *Teladorsagia circumcincta* for a period of 4 months. Sheep differed in their genetic growth potential and in their genetic resistance to the parasites, assuming zero correlations between the resistance and growth traits. To calculate the values of the statistical resilience indicators, two trajectories were simulated for each individual from the mechanistic model, one modelling the response trajectories of sheep under challenge (realised trajectory) and one without the challenge (i.e., the true target trajectory). The deviations were calculated simply as difference between the two simulated trajectories. The deviations were used to calculate the diverse statistical resilience indicators as defined in equations 7-11. In each of the 5 generations of selection, the best males and females were selected based on the estimated breeding value for the resilience indicators. To compare the response to selection for resilience with the predicted response to resistance or production potential, the simulations were repeated with maximum faecal egg count and protein mass at maturity as the breeding goal traits for resistance and production potential, respectively.

3.2 Results

3.2.1 Classification of response types

Table 2 shows the AUROC values obtained from the pair-wise comparison of two response types in terms of their simulated deviations i.e., under various scenarios. When the target trajectory is known, all 5 resilience indicators can correctly distinguish the *Fully Resilient* type from the other less resilient types with AUROC values generally above 0.88. Hence, in these scenarios, all resilience indicators considered can correctly rank a *Fully Resilient* individual above another individual that is affected by a perturbation in 88% of times. The only exception was skewness that had a reduced value of 0.72. The same is true when comparing *Partially Resilient* and *Non-Resilient* types. The corresponding AUROC values for skewness are less than 0.5 (between 0.0 to 0.1), indicating that individuals that do not recover would be identified as more resilient than those that do recover (between 90% to 100% of times). Other resilience indicators had values above 0.96.

When the target trajectory is an unknown linear function (similar to the known target trajectory scenario), all resilience indicators (except skewness) can correctly rank *Fully Resilient* individuals above

the other response types irrespective of the estimation method for target trajectories (i.e., quantile regression and repeated regression). When comparing the *Partially Resilient* types with the *Non-Resilient* types LV, LMS and AUC could still correctly classify the majority of individuals into their correct response types, with average AUROC generally above 0.9. However, skewness and AC1 had average AUROC values of 0.06 and 0.56, respectively. Estimation method had little effect on the AUROC values. In general, skewness had highest dependence on the estimation method.

The scenario of unknown non-linear target trajectory was similar to the linear case. However, the values of AUROC were improved for skewness in comparison of *Fully-Resilient* and *Non-Resilient*. In the comparison of *Partially Resilient* and *Non-Resilient*, only LV, LMS and AUC had AUROC values above 0.5.

In all simulated scenarios, the route to recovery had relatively minor effect on the ability of the resilience indicators to distinguish the *Partially Resilient* types from the other two response types, although the distinction between the *Partially Resilient* and *Non-Resilient* types was generally poorest for individuals with a *Steady* recovery route. Hence, for the remaining part of this report, the three sub-categories are *Partially Resilient* are combined and reported as one category. Similarly, as there was little difference between estimation method for target trajectory, only the result of quantile regression is shown in the remainder of this report.

Table 2. AUCROC values and (standard deviation) for different resilient indicators in pair-wise comparison of different response types. The first and second row of header indicate the two response types compared. For unknown target trajectories first row (normal) values are quantile regression method and second row values (italic) show the result of repeated regression method. Values close to 1 indicate that the resilience indicator can distinguish between two lines and would correctly classify the more resilient response type. Values close to 0 indicates that resilience indicator distinguishes between response types but would wrongly classify the groups. Finally, values close to 0.5 mean the resilience indicator cannot distinguish between the two response types.

Target trajectory	RI	Fully resilient vs				Non-Resilient vs				Non-Resilient Fully resilient
		Partially resilient				Partially resilient				
		steady	comp.	relapsed	pooled	steady	comp.	relapsed	pooled	
Known	LV	1.00 (7.1e-5)	1.00 (0.00)	1.00 (8.4e-4)	1.00 (3.1e-4)	0.98 (9.6e-3)	0.99 (3.9e-3)	0.99 (8.5e-3)	0.99 (7.3e-3)	1.00 (0.00)
	LMS	1.00 (3.0e-5)	1.00 (0.00)	1.00 (7.0e-4)	1.00 (2.4e-4)	1.00 (0.00)	1.00 (0.00)	1.00 (1.6e-4)	1.00 (5.4e-5)	1.00 (0.00)
	S	1.00 (2.3e-3)	0.94 (1.8e-2)	1.00 (4.7e-3)	0.98 (8.2e-3)	0.00 (3.6e-3)	0.09 (2.2e-2)	0.01 (7.2e-3)	0.04 (1.1e-2)	0.72 (3.6e-2)
	AC1	1.00 (1.0e-5)	1.00 (0.00)	1.00 (6.7e-4)	1.00 (2.3e-4)	0.96 (1.2e-2)	0.99 (6.8e-3)	0.98 (1.0e-2)	0.98 (9.6e-3)	1.00 (0.00)
	AUC	1.00 (1.0e-4)	0.88 (2.9e-2)	1.00 (3.1e-3)	0.96 (1.1e-2)	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)
Unknown linear	LV	1.00 (2.7e-4) <i>1.00 (0.00)</i>	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (6.5e-4) <i>1.00 (4.5e-4)</i>	1.00 (3.1e-4) <i>1.00 (1.5e-4)</i>	0.93 (1.8e-2) <i>0.95 (2.6e-2)</i>	0.98 (9.0e-3) <i>0.99 (1.1e-2)</i>	0.96 (1.4e-2) <i>0.98 (1.8e-2)</i>	0.96 (1.3e-2) <i>0.97 (1.8e-2)</i>	1.00 (0.00) <i>1.00 (0.00)</i>
	LMS	1.00 (3.4e-4) <i>1.00 (0.00)</i>	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (7.3e-4) <i>1.00 (1.9e-4)</i>	1.00 (3.6e-4) <i>1.00 (6.4e-5)</i>	0.92 (2.0e-2) <i>0.97 (2.0e-2)</i>	0.98 (8.0e-3) <i>0.99 (7.6e-3)</i>	0.95 (1.6e-2) <i>0.98 (1.4e-2)</i>	0.95 (1.4e-2) <i>0.98 (1.4e-2)</i>	1.00 (0.00) <i>1.00 (0.00)</i>
	S	1.00 (2.0e-3) <i>1.00 (4.0e-3)</i>	0.94 (2.0e-2) <i>0.95 (2.8e-2)</i>	1.00 (4.1e-3) <i>0.99 (8.9e-3)</i>	0.98 (8.7e-3) <i>0.98 (1.4e-2)</i>	0.01 (6.6e-3) <i>0.02 (1.4e-2)</i>	0.07 (2.1e-2) <i>0.12 (4.0e-2)</i>	0.02 (9.6e-3) <i>0.04 (1.3e-2)</i>	0.03 (1.3e-2) <i>0.06 (2.3e-2)</i>	0.53 (4.0e-2) <i>0.74 (4.5e-2)</i>
	AC1	1.00 (3.3e-4) <i>1.00 (0.00)</i>	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (9.8e-4) <i>1.00 (7.4e-4)</i>	1.00 (4.3e-4) <i>1.00 (2.5e-4)</i>	0.40 (4.3e-2) <i>0.48 (8.0e-2)</i>	0.43 (4.3e-2) <i>0.52 (6.3e-2)</i>	0.64 (4.0e-2) <i>0.69 (6.8e-2)</i>	0.49 (4.2e-2) <i>0.56 (7.0e-2)</i>	1.00 (0.00) <i>1.00 (0.00)</i>
	AUC	1.00 (7.5e-4) <i>1.00 (2.6e-3)</i>	0.98 (1.1e-2) <i>1.00 (0.00)</i>	0.99 (4.6e-3) <i>0.99 (8.6e-3)</i>	0.99 (5.4e-3) <i>1.00 (3.7e-3)</i>	0.82 (3.0e-2) <i>0.99 (9.8e-3)</i>	0.96 (1.2e-2) <i>1.00 (2.7e-3)</i>	0.89 (2.5e-2) <i>0.98 (1.1e-2)</i>	0.89 (2.3e-2) <i>0.99 (7.7e-3)</i>	1.00 (1.0e-5) <i>1.00 (0.00)</i>
Unknown Nonlinear	LV	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (5.6e-4) <i>1.00 (7.7e-4)</i>	1.00 (1.9e-4) <i>1.00 (2.6e-4)</i>	0.54 (8.5e-2) <i>0.74 (8.6e-2)</i>	0.63 (9.9e-2) <i>0.85 (6.1e-2)</i>	0.69 (9.4e-2) <i>0.88 (5.1e-2)</i>	0.62 (9.3e-2) <i>0.82 (6.6e-2)</i>	1.00 (0.00) <i>1.00 (0.00)</i>
	LMS	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (5.6e-4) <i>1.00 (7.7e-4)</i>	1.00 (1.9e-4) <i>1.00 (2.6e-4)</i>	0.57 (8.5e-2) <i>0.72 (8.5e-2)</i>	0.69 (9.9e-2) <i>0.86 (5.7e-2)</i>	0.72 (9.3e-2) <i>0.87 (5.1e-2)</i>	0.66 (9.3e-2) <i>0.82 (6.4e-2)</i>	1.00 (0.00) <i>1.00 (0.00)</i>
	S	1.00 (2.3e-3) <i>1.00 (7.8e-3)</i>	0.99 (1.4e-2) <i>0.94 (4.2e-2)</i>	1.00 (1.8e-3) <i>1.00 (9.1e-3)</i>	1.00 (5.9e-3) <i>0.98 (2.0e-2)</i>	0.23 (6.6e-2) <i>0.04 (3.3e-2)</i>	0.22 (9.4e-2) <i>0.20 (7.3e-2)</i>	0.25 (8.7e-2) <i>0.09 (4.5e-2)</i>	0.24 (8.2e-2) <i>0.11 (5.0e-2)</i>	0.98 (1.8e-2) <i>0.84 (5.3e-2)</i>
	AC1	1.00 (0.00) <i>1.00 (1.1e-3)</i>	1.00 (0.00) <i>1.00 (0.00)</i>	1.00 (0.00) <i>1.00 (7.8e-3)</i>	1.00 (0.00) <i>1.00 (3.0e-3)</i>	0.15 (6.2e-2) <i>0.22 (4.6e-2)</i>	0.14 (5.2e-2) <i>0.19 (6.4e-2)</i>	0.27 (9.1e-2) <i>0.45 (6.8e-2)</i>	0.18 (6.8e-2) <i>0.28 (5.9e-2)</i>	0.99 (1.8e-2) <i>1.00 (0.00)</i>
	AUC	1.00 (5.6e-4) <i>1.00 (1.1e-3)</i>	1.00 (1.0e-2) <i>1.00 (0.00)</i>	1.00 (5.4e-3) <i>1.00 (7.7e-4)</i>	1.00 (5.4e-3) <i>1.00 (6.3e-4)</i>	0.70 (8.4e-2) <i>0.66 (7.9e-2)</i>	0.87 (6.1e-2) <i>0.87 (6.2e-2)</i>	0.80 (8.4e-2) <i>0.82 (6.1e-2)</i>	0.79 (7.6e-2) <i>0.78 (6.7e-2)</i>	1.00 (0.00) <i>1.00 (0.00)</i>

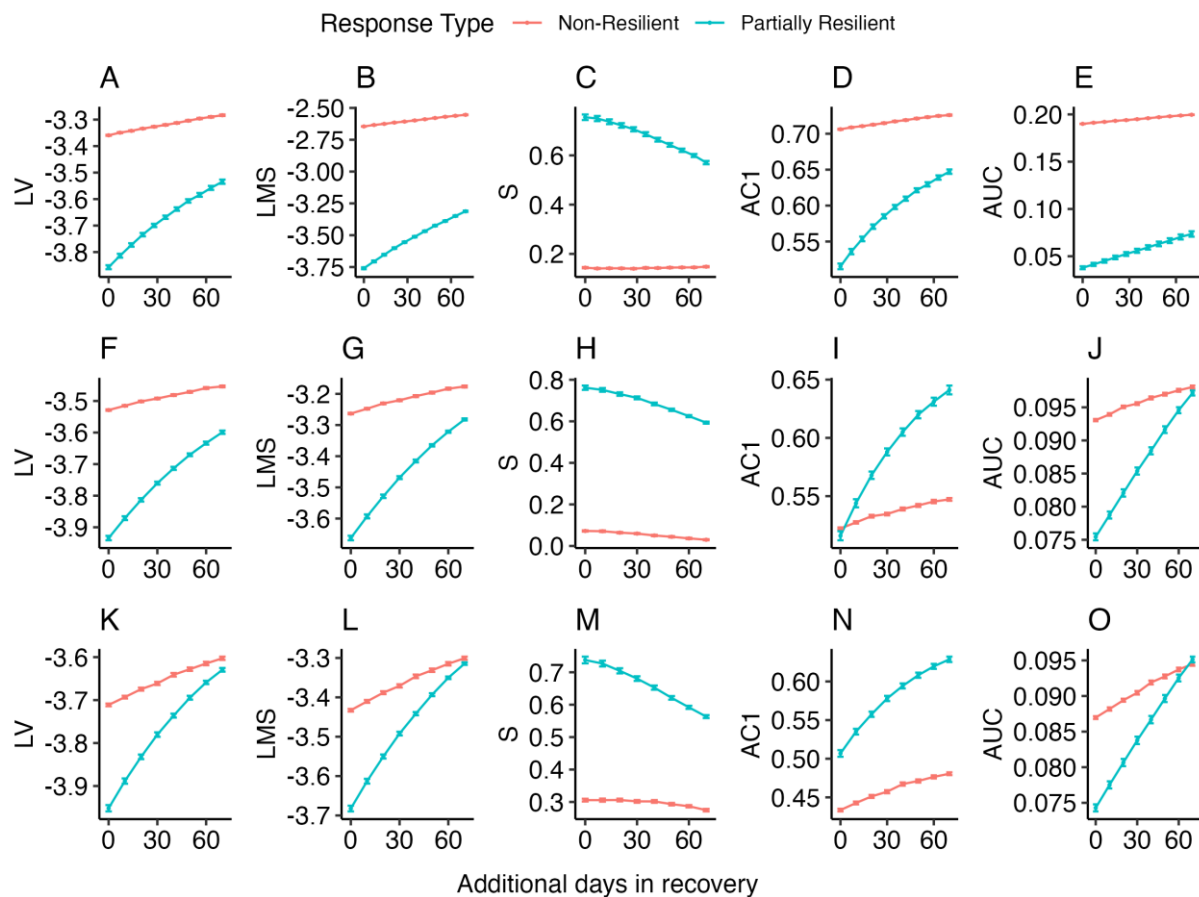
1 3.2.2 Sensitivity to host response characteristics

2 3.2.2.1 Variation in amplitude of perturbation

3 The value of all resilience indicators was found to increase linearly with increasing amplitude, regardless
 4 of whether the target trajectory was known or estimated (results not shown). This confirms that these
 5 indicators correctly identify animals experiencing more severe perturbations in terms of reduced
 6 performance as less resilient. In the addition, the rankings of the groups remained constant as the
 7 perturbation amplitude changed.

8 3.2.2.2 Variation in time to recovery

9 Longer recovery period is associated with higher values of resilience indicators when the target trajectory
 10 is known (see Figure 5), except for skewness, which shows the opposite. However, an increase in the
 11 recovery period affects the AC1 of *Partially Resilient* individuals more than that of the *Non-Resilient*
 12 individuals when the target trajectory is an unknown linear function Figure 5I. This results in a re-ranking
 13 of Partial and Non-Resilient group for longer recovery times. Note that for base case the value of AUROC
 14 is slightly above 0.5. Therefore, for smaller recovery periods (i.e., total recovery period less than 60 days),
 15 AC1 may be able to correctly rank these two groups.



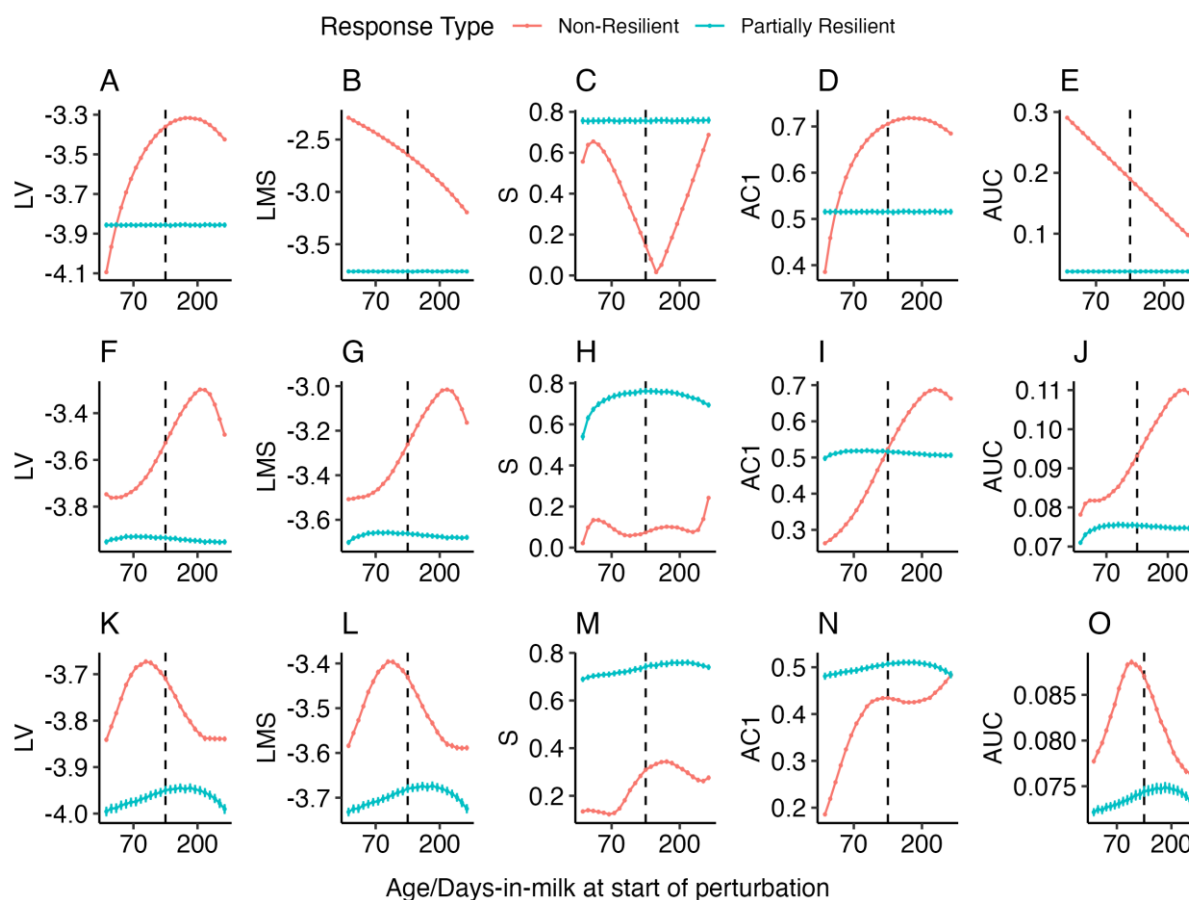
16

17 Figure 5. Effect of the recovery period on the value of different resilience indicators when the target trajectory is known (A-E),
 18 unknown linear (F-J) and unknown nonlinear(K-O). Additional days in recovery is added to the second mode in the simulation of
 19 deviations. The value 0 corresponds to the base simulation. Error bars indicate 95% confidence intervals.

20 3.2.3 Sensitivity to data recording frequency and duration

21 3.2.3.1 Variation in pre-perturbation recording period

22 Figure 6 shows the impact of pre-perturbation data on the value of different resilience indicators for
23 different response types. Here, the observation window is fixed to 0-360 (age or days in milk), therefore,
24 lower age/days-in-milk is associated with fewer pre-perturbation data. As the period between the day an
25 animal experiences challenge and reaches a stable condition is 90 days, the simulated data comprises the
26 full perturbation period (see Table 1). In the case of known target trajectory (Figure 6A-E), a change in the
27 length of pre-perturbation data is a mere shift in the response. Hence, for the *Partial-Resilient* response
28 type, the resilience indicators are not affected by changes in the onset of perturbation. For the *Non-*
29 *resilient* type, however, shorter pre-perturbation implies shorter zero deviation (i.e., before the animal is
30 challenged) and longer negative deviation (because the observation period contains more post-
31 perturbation data for this group). Therefore, as expected, the value of resilience indicators is strongly
32 affected by length of pre-perturbation data: AUC and LMS show a steady increase in the resilience
33 indicators value indicating decreasing resilience as the length of pre-perturbation data decreases. AC1 and
34 LV, on the other hand, show that individuals with more pre-perturbation data are less resilient followed
35 by a reverse trend after 200 days of pre-perturbation data. In particular, AC1 and LV show a re-ranking of
36 groups at circa. 40 days of pre-perturbation. When the pre-perturbation data is less than 40 days, the
37 negative deviations in the data are more frequent than the zero deviation. Hence, zero deviations are
38 considered as the outliers. Similarly, the value of the skewness has an inflection at this point. However,
39 skewness shows another irregularity (at day 100) and starts to increase with an increase in the pre-
40 perturbation period.



41

42 *Figure 6. Effect of pre-perturbation data on the value of different resilience indicators when target trajectory is known (A-E),*
 43 *unknown linear function (F-J) and unknown nonlinear (K-O). The x-axis denotes the onset of perturbation at the age (A-J)*
 44 *in milk (K-O) for the animal that experiences challenge. The dashed vertical line is the base case scenario. Error bars indicate the*
 45 *95% confidence intervals.*

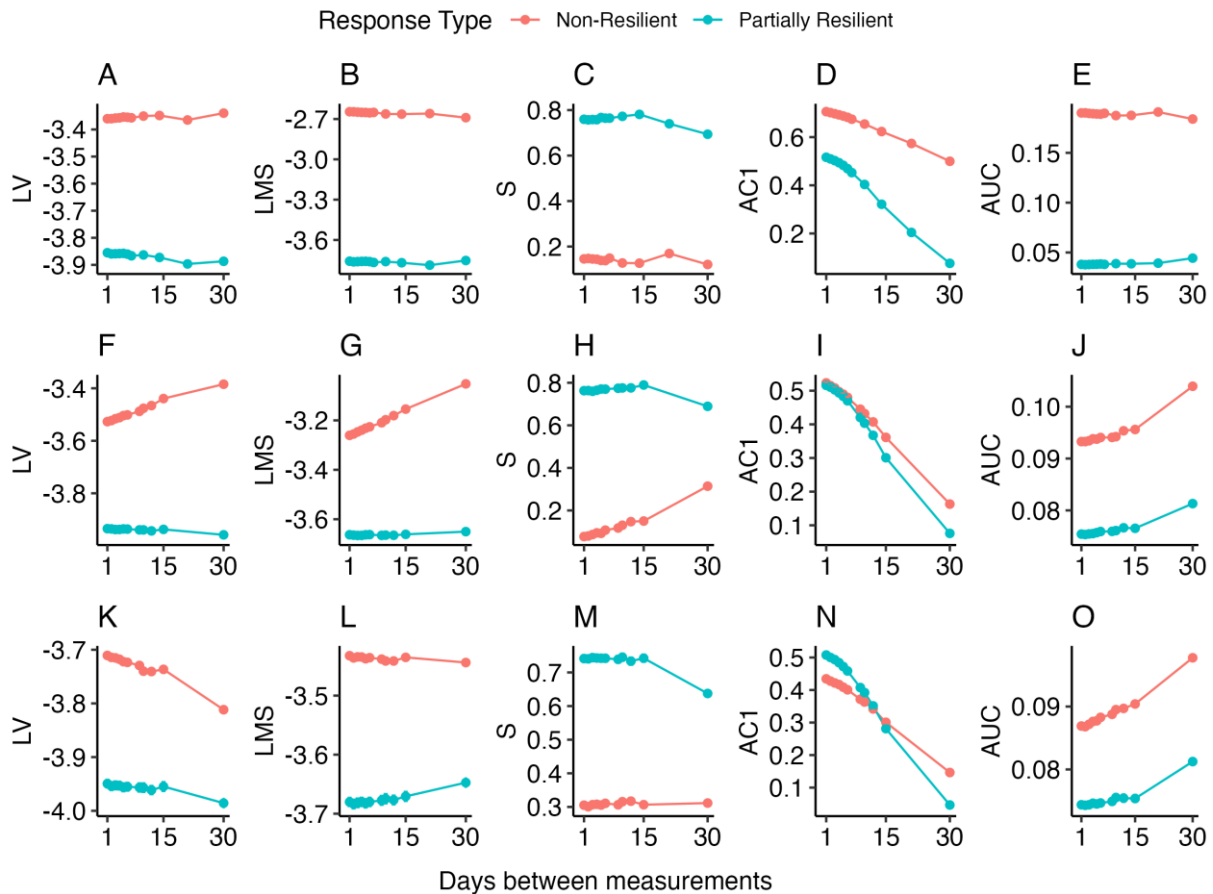
46 When the target trajectory is an unknown linear function, longer pre-perturbation does not affect the
 47 value of the resilience indicators for *Partially Resilient* groups, except skewness (Figure 6F-J). For the *Non-*
 48 *Resilient* group, the value of all resilience indicators, except for skewness, generally increased as the length
 49 of pre-perturbation increased. In particular, individuals that had less than 30 days of pre-perturbation
 50 records had reduced values for all resilience indicators. Therefore, based on these indicators, individuals
 51 with shorter pre-perturbation data show higher resilience.

52 For the nonlinear unknown target trajectory, both early and late response to perturbation changes the
 53 value of the resilience indicators for most response types (Figure 6K-O). The changes in length of pre-
 54 perturbation data had nonlinear and complex effect on the value of the resilience indicators. However,
 55 similar to the linear case, individuals with small pre-perturbation data (less than 30 days) have generally
 56 lowest resilience indicators values and therefore are more resilient.

57 3.2.3.2 Effect of data recording frequency

58 Figure 7 shows the impact of the frequency of recordings on the value of resilience indicators. AC1 is the
 59 most sensitive resilience indicators with respect to frequency; its value consistently reduced on average
 60 by 16% when frequency changed from daily to weekly and 50% for daily to biweekly. However, LV, LMS
 61 and AUC had a maximum change of 4% when frequency decreased from daily to biweekly. In the case of
 62 unknown target trajectory (Figure 7F-O), all resilience indicators significantly changed when the frequency

63 of measurement reduced to monthly. In general, the minimum number of records in order to obtain
 64 reliable AC1 values is one every four days, although the Partially Resilient group are identified as less
 65 resilient than the Non-Resilient group.



66
 67 *Figure 7. Effect of frequency of measurements (in terms of number of days between measurements) on the value of different*
 68 *resilience indicators when the target trajectory is known (A-E), unknown linear (F-J) and unknown nonlinear(K-O). The value 1*
 69 *corresponds to the base simulation, i.e., everyday recording. Error bars indicate 95% confidence intervals*

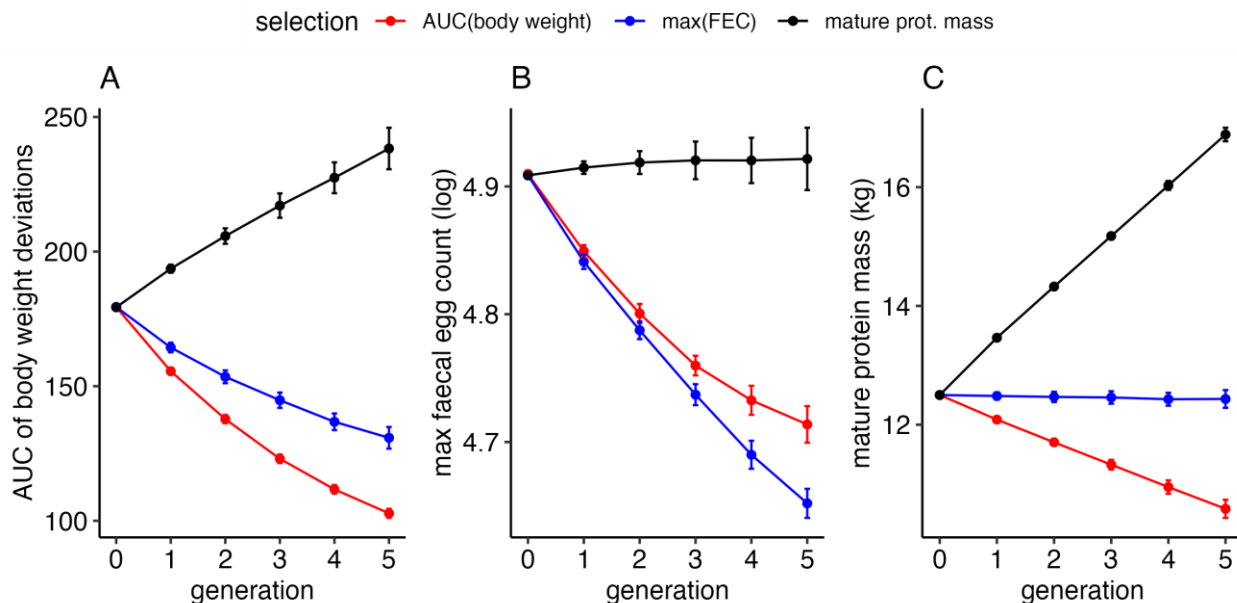
70 3.2.3.3 Window of observation

71 Except for skewness, a shorter period of recording was associated with a reranking of the Partially Resilient
 72 and Non-Resilient group for all resilience indicators (results not shown).

73 3.2.4 Predicting response to selection for resilience

74 Figure 8 shows the response to selection for resilience (represented by AUC of body weight deviations),
 75 resistance (represented by maximum Faecal Egg Counts (FEC) during the challenge period) and growth
 76 potential (represented by mature protein mass in the absence of challenge) for five generations of
 77 selection as predicted by the mechanistic model. Predicted genetic gains are shown for all three breeding
 78 goal traits. Selection for resilience improves resilience (i.e. lower AUC of body weight, Figure 8A) and
 79 resistance (Figure 8B) but has negative impact on the production potential of individuals in good
 80 environments (Figure 8C). Selecting animals with lower FEC results in the healthiest animals (in terms of
 81 FEC) compared to the other two methods and it also increases the resilience of animals. The response to
 82 selection against FEC on the production potential, however, was close to zero. Selection based on
 83 performance results in poorer animals in terms of both resistance and resilience but it was the only method
 84 that results in animals with higher production potential.

85



86

87 *Figure 8. Genetic gain in (A) resilience, (B) resistance and (C) production after 5 generations of selection for resilience (red),*
 88 *resistance (blue) and production potential (black). Lower values of AUC in figure A indicate higher resilience and lower value of*
 89 *maximum of faecal egg count are associated with higher resistance in figure B. Error bars are standard deviation.*

90

91 3.3 Discussion

92 In this study, different summary statistics proposed in the literature (variance, integral, lag-1
 93 autocorrelation, mean of squares and skewness of deviations) were applied as resilience indicators for
 94 different simulated response types to a short time challenge. The aim of the first simulation study was to
 95 investigate to what extent each indicator can identify the diverse response types and correctly discriminate
 96 animals that differ in their resilience. In addition, the sensitivity of these resilience indicators to diverse
 97 response features were tested. It was found that all indicators can identify the most resilient type, i.e.,
 98 individuals that are not perturbed by challenge, compared to other response types. However, the
 99 existence of individuals that do not recover is an issue for some of these indicators, particularly when the
 100 target trajectory is unknown. The danger is that individuals that do not recover from the challenge may be
 101 ranked as more resilient than those who are perturbed but eventually recover. While changes in the length
 102 and amplitude of the perturbation had linear and predictable effect on the value of resilience indicators,
 103 the length of pre-perturbation period and the observation window changed the value of resilience
 104 indicators in a less predictable, non-linear way.

105 Our results show that LV, LMS and AUC are the best resilience indicator that are less likely to rank Non-
 106 Resilient individuals above Partially Resilient and are robust to changes in frequency or measurement. We
 107 found skewness the least reliable resilience indicator in terms of ranking groups and an appropriate
 108 relationship with features of recovery, i.e., the perturbation period. Previous studies have postulated that
 109 a value of zero for skewness refers to high resilience, because resilient animals have as many positive
 110 deviations as it has negative ones with almost same magnitude (Berghof, Poppe and Mulder, 2019). It
 111 should be noted that skewness, is not a measure of asymmetry of a distribution. The set $\{-8, -7, 1, 5, 9\}$
 112 has an asymmetric distribution but zero skewness, using the definition from (Joanes and Gill, 1998).
 113 Therefore, it is important that these measurements are assessed in different scenarios.

114 The resilience indicators considered in this study have been applied to real data (Berghof, Poppe and
115 Mulder, 2019; Putz *et al.*, 2019; Poppe *et al.*, 2021; Bedere *et al.*, 2022) and have been tested for
116 heritability and genetic correlation with health and production traits. In our study, we found a positive
117 correlation between all resilience indicator values and the perturbation amplitude. The correlation
118 between the perturbation magnitude and variance of deviation has been confirmed at genetic level in
119 dairy cows (Poppe, Mulder and Veerkamp, 2021).

120 The base assumption in this, and most previously published studies using these resilience indicators is that
121 all animals in a contemporary group experience the same challenge. However, in reality, different animals
122 in a farm may experience different exposures or micro-environmental disturbances affecting their
123 performance (Le, Rohmer and David, 2022). In addition, animals are affected differently at various stage
124 of their lifetime by a challenge. For example, decrease in fertility and fat content in dairy cattle is more
125 pronounced in early lactation than in late lactation (de Vries and Veerkamp, 2000). Hence, it is important
126 to incorporate the level and time of challenge each individual experiences in the statistical models for a
127 better inference of resilience. Estimation of challenge at animal level, however, can be very complex and
128 labor intensive (Knap and Doeschl-Wilson, 2020). To our knowledge, this is the first study that assesses the
129 effect of features of recovery and data on the value of resilience indicators.

130 The results of this simulation study show that the duration of pre-perturbation data can have various
131 effects on the resilience indicators. The length of pre-perturbation data can be the result of different onset
132 of perturbation and may be due to variations in delay to response to challenge. Given a constant window
133 of observation, a delay did not affect the value of resilience indicators if the deviations were simulated.
134 This is because when the actual target trajectory is available, all deviations will have the same weight.
135 However, when the deviations are estimated, different onsets of perturbation provide different values for
136 the resilience indicators. Therefore, in the case of unknown target trajectory, the onset of perturbation
137 needs to be appropriately adjusted for in the calculation of the resilience indicators. This may be
138 complicated in field conditions when the onset of the perturbation is not known. However, in this case,
139 the onset of perturbation may be estimated following the method in (Nguyen-Ba, van Milgen and
140 Taghipoor, 2020; Le, Rohmer and David, 2022).

141 The simulations of different response types provided valuable insights regarding the ability of the diverse
142 statistical resilience indicators to discriminate between individuals with full, partial and low resilience
143 depending on the data available. However, it provided little insight how animals' resilience could be
144 improved through e.g. genetic selection. For this purpose, a previously published mechanistic model for
145 gastro-intestinal parasite infections in a growing population of sheep with genetic variation in resistance
146 and growth potential was used. The model demonstrated that in the context of an infectious disease,
147 genetic selection for disease resilience may not always be the best option for improving animal health and
148 production. Instead, selection for disease resistance may be more effective as animals with high resistance
149 are by definition also more resilient (Knap and Doeschl-Wilson, 2020). This study highlights the importance
150 of modelling studies for evidence-based decision making. Future modelling studies should investigate
151 diverse strategies for improving resilience, considering also the effect of nutritional control strategies on
152 resilience as well as other economically important traits.

153 3.4 References

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241 4 Resilience trajectory analyses of Smarter data: response to nutritional 242 challenge in two Alpine goat lines selected on divergent longevity

243

244 This study was carried out by INRAE, and is described in detail by the manuscript below, which is currently
245 under review in the journal “Animal”.

246

247 **Analysis of reproduction success, growth and milk trajectories and response to nutritional challenge in** 248 **two Alpine goat lines selected on divergent longevity**

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255

256 **Abstract**

257 This study aims to investigate whether the variation in reproduction success, growth, and milk trajectories
258 is associated with different adaptive strategies in the short term (response to an acute nutritional
259 challenge), using two Alpine goat lines. A total of 382 Alpine goats (179 low_LGV and 203 high_LGV),
260 selected for divergent functional longevity from a commercial population were monitored for 4 years and
261 recorded for body weight, reproduction and milk performance. Every year, an average of fifty primiparous
262 goats were exposed to a 2-d nutritional challenge in early lactation. A polynomial model was used to
263 analyse the lifetime trajectory of lactation and body weight. A piecewise model was used to analyse the
264 individual milk yield and milk components responses to the nutritional challenges. The statistical analysis
265 revealed that the both lines had quite similar performance for the total milk yield in the first lactation,
266 body weight at birth and at first kidding, litter size and weight, kidding-interval and interval from the first
267 insemination to conception. Body weight trajectories revealed that low_LGV goats had a greater body
268 weight in pregnancy but then lost more weight in early lactation compared to high_LGV goats, which
269 showed a greater body weight after kidding. Milk trajectories showed that the high_LGV goats had a higher
270 initial milk yield, an earlier but less marked lactation peak and more persistency in milk production in late
271 lactation than low_LGV goats. Except for milk protein content, quite similar response and recovery profiles
272 of milk yield and milk fat content were observed during the challenge for both lines. The response to the
273 challenge was positively correlated to the initial level of milk production in early lactation but negatively
274 correlated with milk production decline after the peak. This finding suggests that the low_LGV goats were
275 more adapted to allocate resources to meet an expected physiological change such as gestation and
276 lactation. However, high_LGV goats allocate more for structural mass and may better cope with an
277 unexpected environmental change such as nutritional deficit.

278

279 **Keywords:** dairy goat, functional longevity, allocation, challenge

280

281 **Implications**

282 Selection to improve the functional longevity in goats is becoming highly relevant and of great economic importance. In this work, we have evaluated reproduction, milk and body weight performance
283 in two Alpine goat lines selected on divergent longevity. The variation in their performance trajectories
284 at lifetime level and to a short-term nutritional challenge were explored. This approach combining
285 genetically divergent lines and nutritional experiments is useful to identify animal adaptative strategies
286 under challenging environments.
287

288 **Introduction**

289 Driven by climate change and demand for animal products, livestock production is facing increasing
290 challenges that compromise productivity, welfare and longevity of animals (Cheng et al., 2022;
291 Chaidanya et al., 2015). To address such challenges, genetic improvement is a potential component of
292 climate change adaptation strategies to improve animal adaptive capacity, and thereby secure animal
293 production. Having animals with good potential for both productivity and longevity in the changing
294 climate scenario is a priority to sustain small ruminant production (Joy et al., 2020). This implies developing
295 balanced breeding schemes that account for trade-offs and synergies between production, reproduction
296 and health traits. In other words, we need breeding strategies that find a more sustainable
297 balance between animal efficiency and resilience (Ramón et al., 2021).

298 Longevity, or productive lifespan, of an animal in the herd is a trait that reflects the performance of
299 the animal and its efficiency to overcoming various challenges throughout its career. True longevity
300 takes into account all the reasons for an animal being removed from the herd. When true longevity is
301 adjusted for production, it gives an approximation of functional longevity (Castañeda-Bustos et al.,
302 2014). Functional longevity refers to an animals ability to delay involuntary culling, which can be
303 assumed to reflect its adaptive capacity (Rostellato et al., 2021).

304 Longevity has not been included in dairy goat breeding programs but several approaches have been
305 proposed to integrate it into the selection index for goats (Palhière et al., 2018; Ithurbide et al., 2022).
306 Further, direct or indirect evaluation of longevity was always expected to increase the overall economic
307 efficiency of the dairy goat industry (Scholtens et al., 2018). Different criteria calculated at the scale of
308 the female career, such as productive lifespan, survival rate, milk persistency and somatic cell score
309 (Rupp et al., 2019; Astruc et al., 2021) have been studied to reveal their correlations with longevity in
310 goats. However, to date the link between productive lifespan and adaptive capacity has rarely been
311 studied in small ruminants. Adaptive capacity can be estimated from natural occurring environmental
312 perturbations (Poppe et al., 2021) or, as in the present study, using planned perturbations. In this context,
313 the impact of environmental challenge on animal performance has been shown to be proportional
314 to the deviations in performance trajectories over time (Garcia-Baccino et al., 2021).

315 Accordingly, the aim of the current study was firstly to investigate whether variation in reproduction
316 success, growth, and milk trajectories is associated with different adaptive strategies in the short term
317 (response to an acute nutritional challenge), using two Alpine goat lines. These lines, selected for divergent
318 functional longevity (Ithurbide et al., 2022), were expected to increase the diversity of adaptive
319 strategies. Accordingly, the second aim of the study was to quantify the differences between the
320 two lines in long- and short-term performance trajectories, as this information is important for design
321 of future selection strategies and simulation of the impact of changing environments thereon.

322 **Materials and methods**

323 Guided by the desire to enhance and integrate the functional longevity into goat selection programs,
324 INRAE has been committed since 2016 to produce two lines of goats selected on divergent functional
325 longevity. The experiment was carried out in accordance with the French legislation on animal experi-
326 mentation and European Convention for the Protection of Vertebrates Used for Experimental and
327 Other Scientific Purposes with experimental approval number APAFIS#8613-2017012013585646. Ani-
328 mals were raised at the experimental INRAE research unit P3R of Bourges (La Sapinière, Osmoy, France,
329 Unit approval C18-174-01).

330 **Animals**

331 Alpine AI bucks (35) were selected from commercial populations based on the length of functional
332 life of their daughters and used to breed two lines of Alpine goat: a high longevity (high_LGV) and a
333 low longevity (low_LGV) lines at the INRAE experimental facility of Bourges Farm (Ithurbide et al.,
334 2022). Sires of the two lines had a reliable (reliability ≥ 0.80) and extremely unfavorable or favorable
335 EBV for functional longevity and were also required to show similar and favorable EBV for milk produc-
336 tion traits to avoid confounding effects from an indirect response to selection for production traits
337 (Table 1). The experiment was conducted from 2017 until 2021, with all females born from the two
338 lines between 2017 and 2020 raised in the same facility and fed with a ration based on lucerne hay,
339 supplemented with concentrates.

340 Reproduction was seasonal and goats were inseminated at an average age of 8 months. The artificial
341 inseminations (AI) were grouped in August until early September then followed by three natural mat-
342 ings to maximise herd fertility. Kidding ranged from January to early March. The kidding date, the
343 difficulty of the birth, the size and the weight of the litter were recorded. During lactation, goats were
344 milked twice a day until late October to then be dried-off for three months. Morning and evening
345 milkings were combined to obtain the individual daily milk production. Monthly milk records were
346 taken and milk components analysis were performed for protein and fat content (FC, PC).

347 ***Lifetime growth, milk production and reproductive data***

348 The complete dataset collected from 382 goats born from 2017 to 2020 was used to study growth
349 performance trajectories throughout lifetime. Goats were weighed three to four times per month from
350 birth to the first breeding, after that, they were weighed one time per month. A total of 7314 body
351 weight (BW) records from 382 goats (179 low_LGV and 203 high_LGV) were included for the growth
352 and BW trajectories analysis.

353 Out of these 382 goats born, 135 low_LGV and 137 high_LGV goats were considered for the
354 insemination program. Further, a dataset of 547 records related to reproduction events was used to
355 assess the variation between lines in performance and reproduction success. Reproductive success
356 was measured by the length of the interval between the first AI and the date of parturition (Freret et
357 al., 2018). The first AI is considered fertile if the interval is between 140 and 160 days. It is considered
358 to have failed if the interval is between 161 and 300 days. In the latter case, the second insemination
359 is considered fertile. In the case when the interval is less than 140 days, the female is considered to
360 have aborted. The kidding interval was measured for all the herd. The interval between the first IA and
361 the fertilizing mating was also calculated for goats that had an interval between the first AI and the
362 date of parturition greater than 160 days. After parturition, only 106 low_LGV and 109 high_LGV goats
363 started their first lactation. A final data set consisting of 2646 test-day milk yield records collected from

364 351 lactations was used to investigate the diversity of milk production and lactation curves in Alpine
365 lines goats during the first 3 lactations. The duration of lactation is 300 days and goats were required
366 to have at least 8 test-day records for production to be assessed. The Fleishmann method (Tekel et al.,
367 2019) was used to calculate total milk production during 280 days of the first lactation. Another dataset
368 consisting of 2271 milk yield records, collected from 2018 to 2021 during a short-term nutritional
369 challenge from the 96 low_LGV, and 97 high_LGV primiparous dairy goats that underwent the
370 challenge, was used to study responses of milk production and contents of fat and protein to the
371 nutritional challenge.

372 **Nutritional Challenge**

373 Every year, from 2018 to 2021, almost fifty primiparous dairy goats from both lines underwent a 2-d
374 underfeeding challenge during early lactation (mean DIM = 41, SD =12.6). The design of the animal trial
375 followed the protocol described in detail in Friggens et al. (2016). The experiment consisted of a 7-day
376 pre-challenge period, followed by a 2-day challenge period, and a 7-day post-challenge period. During
377 the pre- and post-challenge periods the goats received a standard ration based on lucerne hay,
378 supplemented with concentrate. During the challenge, goats received chopped straw only. The goats
379 had ad libitum access to feed and water throughout the experiment and were milked twice per day,
380 milk samples were collected only from the morning milking and milk composition analysis were
381 performed.

382 **Analysis**

383 All statistical analyses were performed using R software (RCore Team, R Foundation for Statistical
384 Computing, 2020). Generalized linear models with random regression (lme package) were used to
385 generate comparative descriptive statistics of repeated growth (model 1) and milk production (model
386 2) between the two lines. Logistic regression with animal as a random effect was performed (glmer
387 function) to compare reproductive success between lines (model 3). The fixed effects of line, year of
388 birth, parity, and age of the first insemination were included in the regression model.

389 Milk and BW trajectories throughout lifetime were fitted using a polynomial model that makes no
390 assumptions about the shape of the curve and combines flexibility of fitting with mathematical
391 simplicity. The flexibility in the model fitting depends on the degree of the polynomial used, but high-
392 degree polynomials will tend to overfit the data because the decline of the estimator's bias and the
393 increases of the variance. The choice of degree of the polynomial model should appropriately consider
394 the balance between bias and variance (Gajewicz-Skretna et al., 2021). Milk production and BW data
395 were fitted using polynomials of 3 to 6 degrees and Bayesian Information Criterion (BIC) were used to
396 choose the most appropriate models, with the lower BIC values indicating a better model fit. (Schwarz,
397 1978). Finally, in this study, a 5-degree polynomial was used to fit milk production and a 3-degree
398 polynomial was used to fit BW. The random effect of animal was modelled using a quadratic model
399 that describes individual deviations in milk and BW performance. An additional analysis of variance on
400 BW during the first pregnancy was performed to look at the difference in growth performance
401 between the two lines in pregnancy.

402 **Model1:**

$$403 Y_{it} = (\beta_0 + \beta_1 t + \beta_2 t^2 + \beta_3 t^3) * (\text{line} + \text{reproduction} + \text{Age_IA1} + \text{year}) + e_{it}$$

404 **Model2:**

405 $Y_{it} = (\beta_0 + \beta_1 t + \beta_2 t^2 + \beta_3 t^3 + \beta_4 t^4 + \beta_5 t^5) * (\text{line} * \text{reproduction} + \text{Age_IA1} + \text{year} + \text{lactation} + \text{litter_size}) +$
 406 e_{it}
 407

408 **Model3:**

409 $Y_i = \mu + \text{line} + \text{year} + \text{age-IA1} + \text{parity} + e_i$

410 Where y is the growth, milk production, or reproduction performance of goat i on day t (models 1 and
 411 2), β represents the polynomial model parameter, t is the age or days in milk (models 1 and 2), μ is the
 412 population mean and e_{it} the residual. Line (high_LGV, low_LGV), reproduction (success, failure), age-
 413 IA1 (<8 months, >8months), year (2017-2020), lactation (1:3), litter_size (1, 2+) and parity (for the ith
 414 parity) are the fixed effects of line, reproductive success, age at first insemination, year of birth,
 415 lactation rank, litter size and parity.

416 Milk persistency in the decreasing phase of the lactation is most often defined as the measure of the
 417 decrease in production over a time interval (Cobuci et al., 2004). The persistency of milk production
 418 during late lactation was measured by the decrease in production between the 200 and 300 lactation
 419 days. The peak milk yield was measured as the maximum of individual milk production throughout
 420 lactation, the time of peak lactation was thus defined as the time when peak yield occurred. Analysis
 421 of variance with animal as a random effect, and line and lactation rank as fixed effects, was then used
 422 to establish the difference between the two lines in terms of lactation peak and persistence.

423 For the milk yield and milk component responses to the nutritional challenges in the first lactation,
 424 the statistical analyses were performed using a piecewise model (see detailed description in Friggens
 425 et al., 2016). The piecewise model parameters characterize individual profile of response and recovery
 426 to the challenge as follows:

427 $Y_i = V_1 + V_2 + V_3 + V_4 + V_5 + e_i$

428 Where Y_i is the milk yield of goat i, V_1 is the prechallenge level, V_2 is the linear slope of the response
 429 during the 2-d challenge, V_3 is the linear component of the recovery, V_4 is the quadratic component
 430 of the recovery, V_5 is the postchallenge level and e_i is the residual error.

431 Animal was fitted as a random effect, and line and year of challenge as fixed effects were included
 432 in the piecewise model to explore inter- and intra-line variation of response to the challenge. The
 433 animal specific set of parameters V_1 to V_5 was then used to assess the correlations between parame-
 434 ters of the piecewise model for milk yield and milk fat and protein contents and those of polynomial
 435 lactation curves. The random coefficients of the polynomial model could be used to describe the shape
 436 of the lactation curve: β_0 is the intercept of the curve corresponding to the initial milk yield, β_1 corre-
 437 sponds to the descendant linear phase, while β_2 corresponds mainly to ascendant quadratic phase of
 438 the lactation curve.

439 Results

440 *Milk production, growth, and reproductive averages performance*

441 As shown in Table 2, there were no significant effects of longevity line on the cumulative milk yield
 442 in the first lactation, or on BW at birth (average BW at birth was 4 kg for both lines). The average age
 443 at the first parturition was estimated at 14.5 months and BW at this age was identical for the two lines

444 (46kg). There was no significant effect of line on litter weight or litter size for any parity; the maximum
445 litter size was 5 for high_LGV and 4 for low_LGV. There was no significant interaction between line and
446 the litter size on the litter weight. The odds of being pregnant were 0.87 smaller for High_LGV goats
447 than for low_LGV goats, but the difference was not significant (0.59). The kidding interval and the
448 interval between the first insemination and the fertilizing mating were identical for both lines in goats
449 that have a failure at the first IA.

450 ***Body weight trajectories***

451 The results of fitting the polynomial model to the overall test-day data of the BW, as affected by the
452 different levels of explanatory factors are reported in table 3. The parameters of the polynomial
453 models do not have a real biological explanation but could be used to describe the different parts of
454 the BW curve: β_0 is the Intercept of the curve which corresponds to birth weight, β_1 refers to the linear
455 part of the curve, and β_2 corresponds to the quadratic part of the curve.

456 There were no significant effects of line on the intercept (β_0) and the linear components (β_1) of the
457 polynomial function. Fitted BW curves did not show significant differences between the two lines in
458 birth body weight and during the growth period (Figure 1). However, line had a significant effect on
459 the quadratic and third-order components (β_2 , β_3) of the polynomial function. These results were
460 complemented by the analysis of variance of BW during gestation. These revealed a significant effect
461 of line in gestation and after kidding. Low_LGV goats had a significantly ($p < 0.05$) higher BW than
462 high_LGV goats at early gestation. Moreover, low_LGV goats had a significantly greater BW decrease
463 from the end of gestation until early lactation compared to goats high_LGV (Figure 1). The interactions
464 between the line, age at the first mating, and reproduction success had no significant effect on the
465 shape of the BW curves. The variance components of the polynomial model attributed to the random
466 intercept was on average 0.743, while the residual variance was on average 2.257.
467 Individual BW curves showed a high variability relative to the average fitted curve during adult age in
468 both lines ($sd = 16.1$, Figure 2). Fitted BW curves for the two lines are shown in Figures 1 and 2.

469 ***Milk trajectories***

470 Parameters of lactation curve are useful to understand the underlying pattern of milk production of
471 the two lines and to assess the effect of genetic and non-genetic factors on this pattern. The fitting of
472 the lactation curve using the polynomial function resulted in a mean lactation curve with an initial milk
473 yield of 2.9L and a peak yield of 3.2L occurring at day 43 (Figure 3). The random intercept variance was
474 0.272, while the residual variance was 0.224. Individual lactation curves showed a high variability
475 relative to the average fitted curve ($sd = 0.8$) (Figure 4). The cumulative milk of the total lactation yield
476 was estimated to be 650L (± 20) at 280 days in the first lactation.

477 Estimated lactation curve parameters obtained by fitting the polynomial function to the overall test-
478 day data of the milk production with the different levels of factors of variation considered in this study
479 are summarized in Table 4. Differences between lines of Alpine dairy goats were found to significantly
480 ($p < 0.05$) affect the parameters β_0 , β_1 , β_2 , and β_3 of the fitted lactation curve. The parameter β_0
481 corresponds to the intercept of the lactation curve, high_LGV goats had a higher initial milk yield than
482 low_LGV goats. An additional analysis of variance on milk peak and persistency showed a significant
483 difference between the two lines. The time of the lactation peak was different for both lines, low_LGV
484 goats showed a later peak time than high_LGV goats (46 vs 38 days). The decline in milk yield after the
485 peak was also different between the two lines, high_LGV goats were significantly ($p < 0.01$) more

486 persistent in later lactation than low_LGV goats. The persistency coefficient measured by the decrease
487 in milk production between the 200 and 300 lactation days, showed a decrease in daily milk yield of
488 0.01L/day for the low_LGV goats and a decrease of 0.007L/day for high_LGV goats.

489 The polynomial function was fitted for the lactation rank effect, the shape of the lactation curve was
490 similar for the three first lactations, even though the initial level and the peak of milk production
491 differed markedly between lactations (Figure 5). When compared with multiparous goats, first parity
492 goats had a significant ($P < 0.01$) lower initial level of production, by about 0.6L when compared with
493 the third parity and about 1L when compared with the second parity. First parity goats had also a later
494 and lower peak yield when compared with later parities, the second parity goats had the highest peak
495 yield, about 3.5L. Differences in the shape of the lactation curve were also found for different years of
496 birth, however, age at the first insemination and litter size had no significant effect. The interaction
497 between line and reproductive success had a significant effect on initial milk yield. The high_LGV
498 pregnant goats had a significantly ($p < 0.05$) lower initial milk yield than non-pregnant low_LGV goats.

499 ***Milk trajectories and responses to nutrition challenge***

500 *Line effect on variation in challenge response and recovery profiles*

501 The trajectories of the individual profiles and the average milk yield, milk fat, and milk protein
502 contents through the different periods of the challenge in early lactation are shown in Figure 6.
503 Average pre-challenge values of milk yield, milk protein, and milk fat content were 1.99 (± 0.47) L/d,
504 33.1g/L, and 35.64 g/L. As shown in Table 5, there were no significant effects of line on the model
505 parameters that characterize individual profiles to the challenge. The two lines showed similar
506 response and recovery slopes in milk yield to the challenge (Figure 6). The effect of the year on the
507 model parameters was significant, milk response and recovery profiles vary with the year of the
508 challenge (Figure 6). Line and year of challenge were found to significantly ($p < 0.05$) affect milk protein
509 content response and recovery to the challenge (V2, V3), milk protein content increased more in
510 low_LGV goats than high_LGV goats in response to the challenge. There were no significant effects of
511 line and year of challenge on milk fat content, the challenge response and recovery slopes for milk fat
512 content were similar for the two lines in different challenge years (Figure 6).

513 *Challenge responses and individual variability in milk trajectories*

514 The correlation between the challenge response coefficients (Table 6) for milk yield and milk
515 contents, and the full lactation curve coefficients sheds light on the relationship between the response
516 of the animal to the challenge relative to the variation in overall milk production and the lactation
517 curve. As expected, the results confirmed the high correlation (0,82) between the initial milk levels
518 from the lactation curve (β_0) and the milk level before the challenge (V1). It is noteworthy that there
519 is a high negative correlation between the response to the challenge (parameter V2) and the intercept
520 (β_0) of the lactation curve ($R = -0.81$), animal responses to the challenge seem to be negatively
521 correlated to their initial milk production. The correlations of the response to the challenge parameter
522 (V2) with the descendant linear phase (β_1) were highly negative ($R = -0.37$). However, they were highly
523 positive ($R = 0.60$) with the ascendant quadratic phase (β_2). Correlations with milk fat and protein
524 contents are not so high (Table 6).

525 **Discussion**

526 The purpose of this study was to identify the differences in performance trajectories between two
527 lines of Alpine goats from a commercial population that have been selected for divergent functional
528 longevity. The main idea was to look at the link between the variation in individual performance
529 trajectories and the responses to short-term nutritional perturbation, to improve our understanding
530 of the adaptive capacity of the two lines. Environmental conditions are likely to affect resource
531 availability and compromise the form and extent of the trade-offs that develop in animal populations.
532 Thus, the adaptive capability of the animal, in terms of production and reproduction to overcome the
533 direct and indirect impact of adverse environmental conditions throughout lifetime, may be affected
534 by the selection environment (Joy et al., 2020). Consequently, the trajectories of productive traits are
535 of particular interest, providing an integrated picture of the animal's adaptive capacity and the
536 adaptive responses to environmental change.

537 In this context, a number of studies of Alpine goat performance have been reported that highlight
538 the potential of the breed. The mean birth weights in this study (4Kg) were higher than those reported
539 by Đuričić et al. (2021) and Gaddour et al. (2012) for Alpine goats (3.46±0.48 kg, 3.66 Kg). Birth weight
540 of kids is an important indicator of its potential for growth and survival, it had a positive correlation
541 with subsequent weight gain and has been deemed a principal risk factor for kids' viability and survival
542 that is crucial for the profitability of goat farms (Ceyhan et al., 2022). However, no difference in birth
543 weight and litter weight was found between high_LGV and low_LGV kids in this study. Indeed,
544 Ithurbide et al. (2022) found no effect of birth and litter weights on the survival of these animals. Body
545 weight at the first insemination and kidding were also identical in the different lines.

546 The estimate of the BW curve parameters of the goats did not show any significant difference
547 between the lines from birth to the first insemination. The mean weight at the first insemination was
548 32.6±0.4Kg. However, the effect of the line on BW was significant from the first insemination until early
549 lactation. Low_LGV goats had a greater BW during early gestation but then lost more weight from later
550 gestation into early lactation, compared to high_LGV goats which showed a greater BW after the kidding.
551 It seems that low_LGV goats allocate more to body reserves during the gestation followed by a greater
552 mobilization of body reserves peripartum. Therefore, safeguarding reproductive function (Friggens,
553 2003) seems to be a priority for the low_LGV goats, although this did not translate into significant
554 differences in reproductive performance. Despite increased gestation and lactation requirements
555 around the parturition, high_LGV goats maintained an increased growth rate during gestation and
556 lactation. This increase in BW may suggest that high_LGV goats allocate more resources to growth,
557 which may be a factor in them having a greater longevity. Low energy intake in late pregnancy combined
558 with high energy outflow via parturition requirements and milk production is associated with a negative
559 energy balance (Kinoshita et al., 2018). Consequently, more body reserves gain in pregnancy may explain
560 animal strategies to support the nutritional demands peripartum and in early lactation. It seems that
561 low_LGV goats prioritise body reserves mobilization in late gestation to safeguard reproduction which
562 may suggest that low_LGV goats were more adapted to cope with the expected physiological change.
563 However, more resource allocation to growth during gestation could suggest that high_LGV use their
564 structural mass to better respond to other life functions under unexpected perturbations.

565 Several models of lactation curves have been developed as one of the available tools for analyzing
566 the performance of dairy animals, mainly because milk production is the most important factor
567 affecting nutritional requirements (Pulina et al., 2005). In the same way, the pattern of milk production
568 is a reference tool that can be used to identify animals with steady production throughout the lactation
569 and those with a substantial decline after a high level of production until the peak (Takma et al., 2009).
570 Thus, better quantification of the lactation curve can be used as a tool for better management and
571 selection. A simple polynomial model was used in this study to characterize the variability in the

572 performance trajectories throughout lifetime of two lines of Alpine goats that have been selected for
573 divergent functional longevity. This model makes no assumptions about the shape of the lactation
574 curve. Thus, it does not introduce bias into the quantification of the relationship between milk
575 production performance and response to short-term nutritional perturbations.

576 In the present study, lactations lasted 280d on average, for a cumulate total production of 650L (± 20)
577 of milk. Thomas et al. (2021) reported an average milk yield of 719 kg over 250 days for the first
578 lactation in Alpine goats. An average total production of 964.1 kg of milk was also reported (Arnal,
579 2018). First parity goats had a lower initial level of production, later and lower peak yield, when
580 compared with multiparous goats. However, Arnal (2018) and León et al. (2012), reported that
581 primiparous goats have higher persistency, earlier peak, and lower total milk production, compared to
582 multiparous goats.

583 Our Results found that age at the first insemination and the litter size had no effect on the lactation
584 shape and milk production. Rojo-Rubio et al. (2016) demonstrated in their study that litter size had a
585 significant effect on all the parameters of the lactation curve, this effect was attributed to the
586 hormonal effect during pregnancy and to the greater stimuli that more kids exert compared to only
587 one when suckling maternal milk (Salvador and Martínez, 2007). The non-significant effect of litter size
588 shown in our study could be explained by the uniform intensity of udder stimulation when milking
589 goats, which is not the case when more kids suckle the udder. Goats that kidded youngest (9–10
590 months) were reported to have a lower milk production level but higher persistency (Arnal, 2018). In
591 our study, the age of the first insemination ranged from 7 to 10 months which corresponds to the
592 youngest age in Arnal (2018) study, and that could explain the non-significant effect of the age of the
593 insemination on the lactation curve coefficients. The shape of the lactation curve was not significantly
594 affected by the reproductive status except for the initial milk yield, which was significantly ($p < 0.05$)
595 lower for concomitantly pregnant high_LGV goats than non-pregnant low_LGV goats. Given that
596 persistency is the degree of maintenance of the milk yield after reaching the maximum daily milk yield
597 (Cobuci et al., 2004), animals with low persistency presented a higher peak of lactation and a steeper
598 curve. High persistency animals that presented a slow rate of decline could be better suited to future
599 efficient production systems (Cole and Null, 2009; Siqueira et al., 2017). Thus, the high_LGV goats
600 showed better milk persistency profiles than low_LGV goats with similar total milk quantities over the
601 lactation. In fact, better milk production in early lactation reflects a good metabolic balance around
602 parturition and suggests that high_LGV goats had a better capacity to acquire resources in early
603 lactation.

604 Body weight and milk trajectories taken together tend to suggest a different allocation profile for
605 the two goats' lines. The decline on BW in later gestation and early lactation combined with lower
606 initial milk production and the later lactation peak may suggest that low_LGV goats gain more body
607 reserve in pregnancy to safeguard future reproduction. It seems that low_LGV goats were more
608 adapted to allocate resources to anticipate their expected physiological change after the conception.
609 The increase in growth rate which suggests a greater allocation of resources to more structural mass,
610 with better persistency at the end of lactation could be considered as an indicator of greater longevity
611 of high_LGV goats and maybe a better response to unexpected environmental change. Furthermore,
612 the high_LGV line was found to have better survival after the first kidding, whereas both lines had the
613 same survival during the first 15 months (Ithurbide et al., 2022).

614 Friggens (2003) reported that mammals evolved the strategy of the priority to safeguarding
615 reproductive investment by the accumulation of body lipid reserves in pregnancy. Acquisition capacity
616 and allocation pattern, reflecting the females priorities throughout life, are expected to be modified
617 by their genetic potential (Arnau-Bonachera et al., 2018). Thus, animals that anticipate their

618 physiological change after conception and allocate more to safeguard reproduction may decrease their
619 ability to safeguard life functions such as growth, which gives them a better structural mass for reacting
620 to unforeseen perturbations.

621 The differences observed between the two lines in milk and BW trajectories lead to the hypothesis
622 of a difference in acquisition and allocation strategy between high and low longevity goats. In the sense
623 of determining the difference between the two lines in terms of resources allocation, the study of the
624 response of the two lines to a nutritional challenge was an asset. The piecewise mixed model was
625 performed to characterize individual profiles during pre-challenge, the challenge, and post-challenge
626 periods.

627 Relative to the pre-challenge period, the nutritional challenge resulted in a reduction in milk yield
628 and an increase in the milk fat and protein content. The recovery from the challenge was proportional
629 to the response slope from the challenge. The nutritional challenge occurred in early lactation, and
630 the average response and the recovery profiles of milk yield and milk fat content were quite similar for
631 both lines during the different challenge years but line was found to significantly ($p < 0.05$) affect milk
632 protein content response and recovery to the challenge. In a similar study, Huau et al. (2020) reported
633 significant differences in beta-hydroxybutyrate response profiles following a nutritional challenge in
634 early lactation between the two lines suggesting a greater dependence on body reserves and metabolic
635 stress in low_LGV goats at the end of gestation and a strong mobilization of body reserves for high_LGV
636 goats following the nutritional challenge. Although no significant line differences were found in milk
637 yield response and recovery slopes, the correlation between the indicator parameters of the lactation
638 curve and those of the challenge showed a positive correlation between the response to the challenge
639 and the ascending phase (β_2) of the lactation curve. The level of milk production in early lactation (β_0)
640 was negatively correlated to the slope of the response to the challenge. Hence, the response to the
641 challenge was negatively correlated with the decline of milk level after the lactation peak (β_1).
642 Accordingly, milk persistency and initial yield were strongly correlated with the slope of the response
643 to the challenge. This finding indicates that milk yield and milk components responses to the challenge
644 could be in part predictable from pre-challenge levels. Friggens et al. (2016) also found that the size of
645 the response to an externally applied challenge is related to the initial level of animal performance.
646 Individual performance patterns through lifetime and in the short term were relevant to show the
647 variability in the population in allocation during normal conditions and in response to perturbation.
648 This has been found in other studies, in cattle, pigs, and poultry (Nguyen-Ba et al., 2020; Poppe et al.,
649 2021).

650 If it seems necessary to select lines to improve the functional longevity it should also be important to
651 preserve the diversity of the population where each animal has its particular strategy for allocation
652 and survival. Individual heterogeneity in adaptive capacity and trade-offs has been shown to be
653 important for system or population level resilience (Nussey et al., 2007), and this will be increasingly
654 important in agro-ecological livestock systems (Ducos et al., 2021). The findings of the present study,
655 taken together, suggest that there are differences in adaptive capacity between the high longevity and
656 low longevity goats. However, measures of feed intake would be needed to confirm this difference
657 between acquisition and allocation mechanisms.

658 Conclusion

659 This study showed that goats divergently selected for low longevity allocate more resources for
660 body reserve in pregnancy to safeguard reproduction whereas high longevity goats allocate more
661 resources to structural mass and had better milk production persistency in late lactation which

662 supports the idea that high functional longevity goats were more adapted to respond to unexpected
663 perturbations. Although, there were no significant differences between the lines in response to short-
664 term nutritional challenge in early lactation, response-recovery profiles were correlated to some
665 aspects of the goats lifetime performance trajectories.

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Table1: Estimated breeding values [mean (SD)] for functional longevity and milk production traits for 35 bucks that sired the high- and low-LGV lines

<i>Traits</i>	<i>High_LGV bucks</i>	<i>line</i>	<i>Low_LGV bucks</i>	<i>line</i>	<i>Contemporary bucks</i>
<i>EBV for functional longevity (days)</i>	85.1 (89.3) a		-108.7 (121.0) b		-12.5 (122.3) a, b
<i>Length of productive life(days)</i>	1071 (722) a		909 (651) b		1006 (697) c
<i>EBV for milk yield (kg)</i>	2.4 (58.3) a		8.5 (66.5) a		-39.2 (73.8) a
<i>EBV for fat content (g/kg)</i>	0.86 (2.87) a		-0.37 (2.12) a		0.37 (2.22) a
<i>EBV for protein content (g/kg)</i>	0.13 (1.29) a		0.08 (1.09) a		0.14 (1.40) a
<i>Total days in milk (days)</i>	865 (539) a		752 (496) b		824 (529) c
<i>Number of lactations</i>	3.39 (1.96) a		2.95 (1.76) b		3.22 (1.90) c

Table 2: Descriptive statistics of the difference in performance between high_LGV and low_LGV Alpines goat lines.

<i>Performance</i>	<i>High_LGV</i>		<i>Low_LGV</i>		<i>P-value</i>
	No. of observation	lsmean (SE)	No. of observation	lsmean (SE)	
Body weight at birth (kg)	203	3.97 (0.06)	179	3.96 (0.06)	0.74
Body weight at 1st kidding (kg)	124	46.2 (0.76)	113	46.7 (0.79)	0.87
Total milk yield in 1st lactation (L,280 days)¹	101	648 (20.1)	101	651 (19.9)	0.91
Litter size	172	1.72 (0.06)	158	1.63 (0.07)	0.70
Litter weight(kg)	172	6.73 (0.11)	158	6.81 (0.11)	0.56
Reproduction success, (Odds Ratio)	254	0.87 [0.52-1.46]	241	1.31 [0.68 - 2.52]	0.59
kidding_interval	87	367 (3.39)	70	365 (3.78)	0.61
Interval from AI1_I Af ²	87	30.9 (3.96)	60	29.1(4.48)	0.74

1. Total cumulate milk for the first lactation, goats that hadn't records in early and late lactation are not considered.
2. Interval from the first insemination to conception for animals that failed to conceive at the first IA.

Table 3: Additive effects of line, reproductive success, age at first AI, and year on body weight curve parameters of the high_LGV and low_LGV Alpines goat lines, using a polynomial model of degree three

	β_0	β_1	β_2	β_3
<i>Intercept</i>	3.403*	6.656*	-0.374*	7.23 x10 ⁻⁰³ *
<i>Line (high_LGV)</i>	-0.020	0.291	-0.058*	3.08 x10 ⁻⁰³ *
<i>Reproductive success</i>	0.549*	-0.860*	0.023*	-9.64 x10 ⁻⁰³ *
<i>Age-IA1(>8 mo)</i>	-0.244	0.119	-0.041	2.69 x10 ⁻⁰³ *
<i>Year_2018</i>	-0.401	0.434*	-0.093*	4.01 x10 ⁻⁰³ *
<i>Year_2019</i>	-0.243	-0.465*	-0.004	2.93x10 ⁻⁰³ *
<i>Year_2020</i>	-0.032	-1.025*	0.217*	-9.84 x10 ⁻⁰³ *

-- Intercept: Line (low_LGV), Reproductive failure, Age-IA1(<8 months), Year_2017.

-- * Signify significant effects of a factor, i.e. a polynomial coefficient significantly different from 0 (p<0.05).

-- β_0 , β_1 , β_2 and β_3 : coefficient of the polynomial model degree three.

Table 4: Additive effects of line, reproductive success, age at first AI, lactation rank, litter size, and year on lactation curve parameters of the high_LGV and low_LGV Alpines goats' lines, using a polynomial model of degree five.

	β_0	β_1	β_2	β_3	β_4	β_5
<i>Intercept</i>	2.221*	4.08x10 ⁻⁰² *	-6.82x10 ⁻⁰⁴	4.39x10 ⁻⁰⁶	-1.28x10 ⁻⁰⁸	1.30x10 ⁻¹¹
<i>Line (high_LGV)</i>	1.36*	-6.33x10 ⁻⁰² *	1.13x10 ⁻⁰³ *	-8.74x10 ⁻⁰⁶ *	3.05x10 ⁻⁰⁸	-3.93x10 ⁻¹¹
<i>Age-IA1(>8mo)</i>	-1.63x10 ⁻⁰¹	8.09x10 ⁻⁰³	-1.43x10 ⁻⁰⁴	1.18x10 ⁻⁰⁶	-4.33x10 ⁻⁰⁹	5.77x10 ⁻¹²
<i>Reproductive success</i>	2.05x10 ⁻⁰¹	-6.14x10 ⁻⁰³	1.01x10 ⁻⁰⁴	-5.86x10 ⁻⁰⁷	1.44x10 ⁻⁰⁹	-9.30x10 ⁻¹³
<i>Litter size (simple)</i>	-2.07x10 ⁻⁰¹	1.13x10 ⁻⁰²	-1.85x10 ⁻⁰⁴	1.21x10 ⁻⁰⁶	-3.49x10 ⁻⁰⁹	3.74x10 ⁻¹²
<i>Lactation2</i>	1.104*	-2.68x10 ⁻⁰² *	4.05x10 ⁻⁰⁴	-3.16x10 ⁻⁰⁶	-4.33x10 ⁻⁰⁸	-1.53x10 ⁻¹¹
<i>Lactation3</i>	6.07x10 ⁻⁰¹ *	-3.27x10 ⁻⁰² *	4.74x10 ⁻⁰⁴	-2.89x10 ⁻⁰⁶	7.66x10 ⁻⁰⁹	-6.96x10 ⁻¹²
<i>Year_2018</i>	-6.29x10 ⁻⁰¹ *	2.91x10 ⁻⁰² *	-4.35x10 ⁻⁰⁴	2.87x10 ⁻⁰⁶	-8.60x10 ⁻⁰⁹	9.75x10 ⁻¹²
<i>Year_2019</i>	-1.99x10 ⁻⁰¹	4.56x10 ⁻⁰⁴	-5.09x10 ⁻⁰⁵	6.15x10 ⁻⁰⁷	-2.51x10 ⁻⁰⁹	3.71x10 ⁻¹²
<i>Year_2020</i>	1.032*	-8.16x10 ⁻⁰² *	1.52x10 ⁻⁰³ *	-1.18x10 ⁻⁰⁵ *	4.15x10 ⁻⁰⁸ *	-5.36x10 ⁻¹¹ *
<i>Line (LGV+): Reproductive success</i>	-1.292*	5.98x10 ⁻⁰² *	-1.09x10 ⁻⁰³ *	8.47x10 ⁻⁰⁶	-2.97x10 ⁻⁰⁸	3.86x10 ⁻¹¹

-- Intercept: Line (low_LGV), Age-IA1(<8months), Reproductive failure, Litter size (double), Lactation1, Year_2017.

-- * Signify significant effects of a factor, i.e. a polynomial coefficient significantly different from 0 (p<0.05).

-- β_0 , β_1 , β_2 , β_3 , β_4 and β_5 : coefficient of the polynomial model degree five.

Table 5 : Additive effects of line and year on the piecewise model estimated parameters of the high_LGV and low_LGV Alpine goats milk yield.

	V1 (pre-challenge level, kg)	V2 (linear slope of response during challenge, kg/d)	V3 (linear slope of recovery post-challenge, kg/d)	V4 (quadratic slope of recovery post-challenge, kg/d/d)
Intercept	1.725*	-0.523*	0.704*	-0.115*
Line (high_LGV)	-0.026	0.291	-0.065	-0.065
Year_2019	0.253*	-0.106*	0.106	-0.011
Year_2020	0.480*	-0.199 *	0.171*	-0.029 *
Year_2021	0.198*	0.050	-0.015	0.007

-- Intercept: Line (low_LGV), Year_2018.

-- * Signify significant effects of a factor on that piecewise model parameter ($p < 0.05$).

-- V1, V2, V3 and V4 are coefficients of the piecewise model describing response to a short-term nutritional challenge.

Table 6: Correlations between the lactation curve coefficients and the challenge parameters.

Milk traits	Milk yield			Milk fat content			Milk protein content		
	β_0	β_1	β_2	β_0	β_1	β_2	β_0	β_1	β_2
V1	0.82	0.37	-0.61	-0.11	-0.35	0.35	-0.27	-0.28	0.33
V2	-0.81	-0.37	0.60	-0.02	0.25	-0.22	0.03	-0.01	0.03
V3	0.79	0.40	-0.64	0.14	-0.03	-0.02	0.21	0.26	-0.33
V4	-0.79	-0.40	0.64	0.15	0.01	0.04	-0.22	-0.27	0.33

-- β_0 , β_1 , and β_2 : random coefficients of the polynomial model for lactation curves.

-- V1, V2, V3 and V4: random coefficients of the piecewise model describing response to a short-term nutritional challenge.

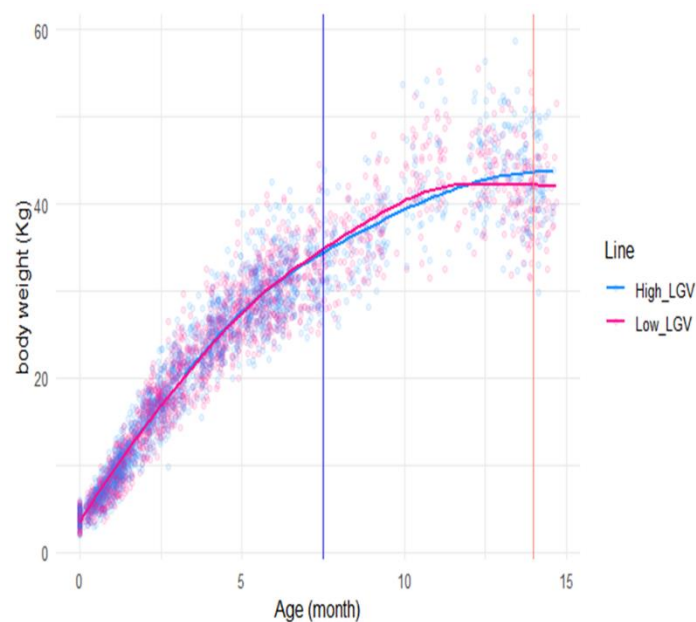
Figures


Fig. 1. Average trajectories of body weight described by the fixed effects of a 3rd order polynomial model: high_LGV (blue) and low_LGV (pink). Vertical lines refer to the average first insemination age (blue) and the average first kidding age (red).

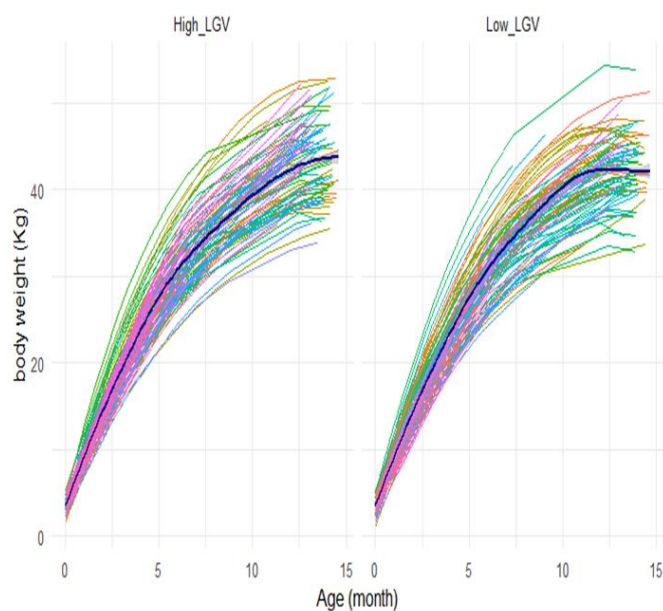


Fig. 2. Individual trajectories of body weight described by the random effects of the polynomial model for the high_LGV and low_LGV line. Black curves refer to the average body weight trajectories.

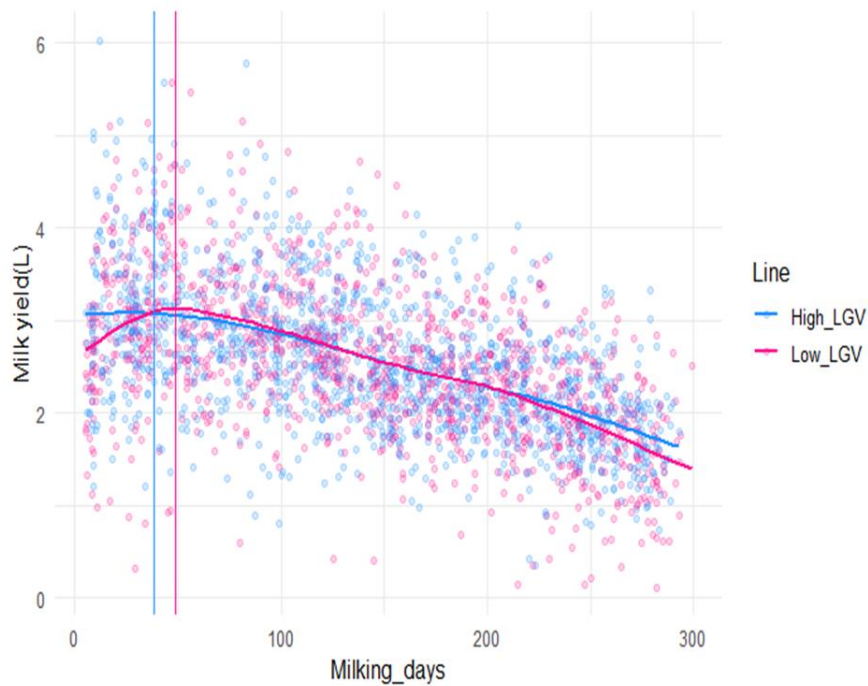


Fig. 3. Average milk yield trajectories in first lactation described by the fixed effects of a fifth order polynomial model. Vertical lines refer to the lactation peak: high_LGV (blue) and low_LGV (pink).

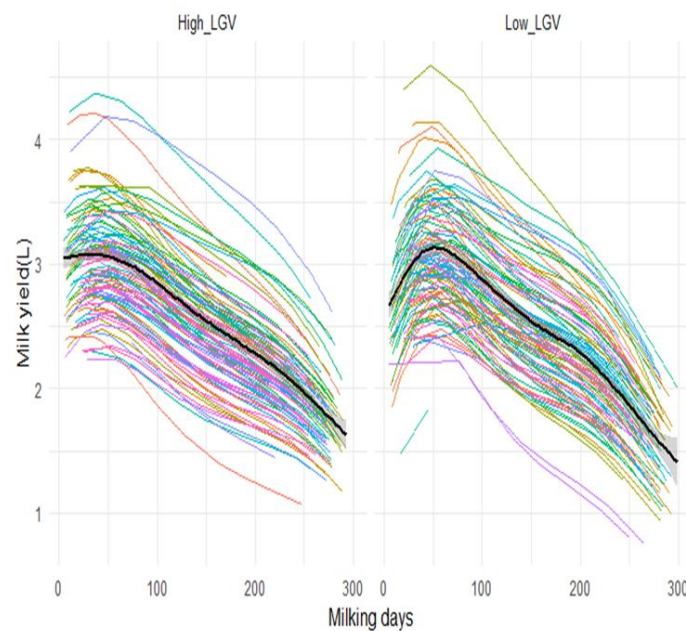


Fig. 4. Individual milk yield trajectories in first lactation described by the random effects of the polynomial model for the high_LGV and low_LGV line. Black curves refer to the average milk yield trajectories.

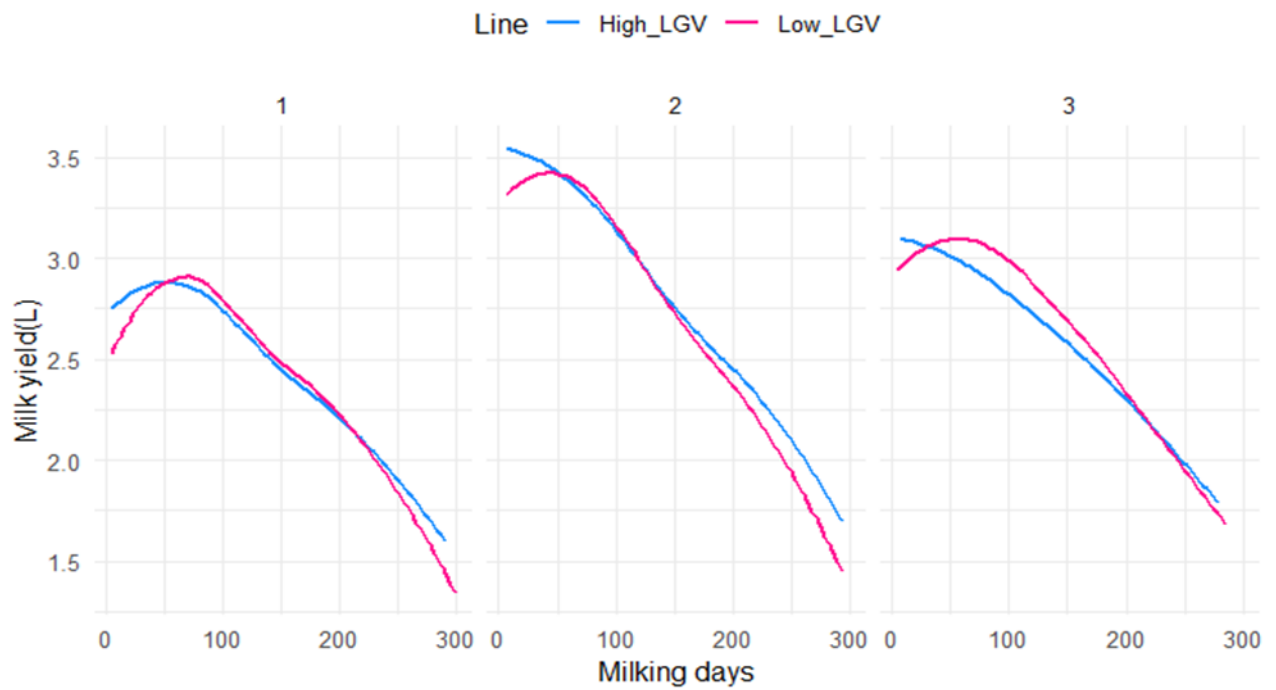


Fig. 5. Average lactation curve described by the fixed effects of a fifth order polynomial model (within lactation) for the first three lactation: high_LGV (blue) and low_LGV (pink).

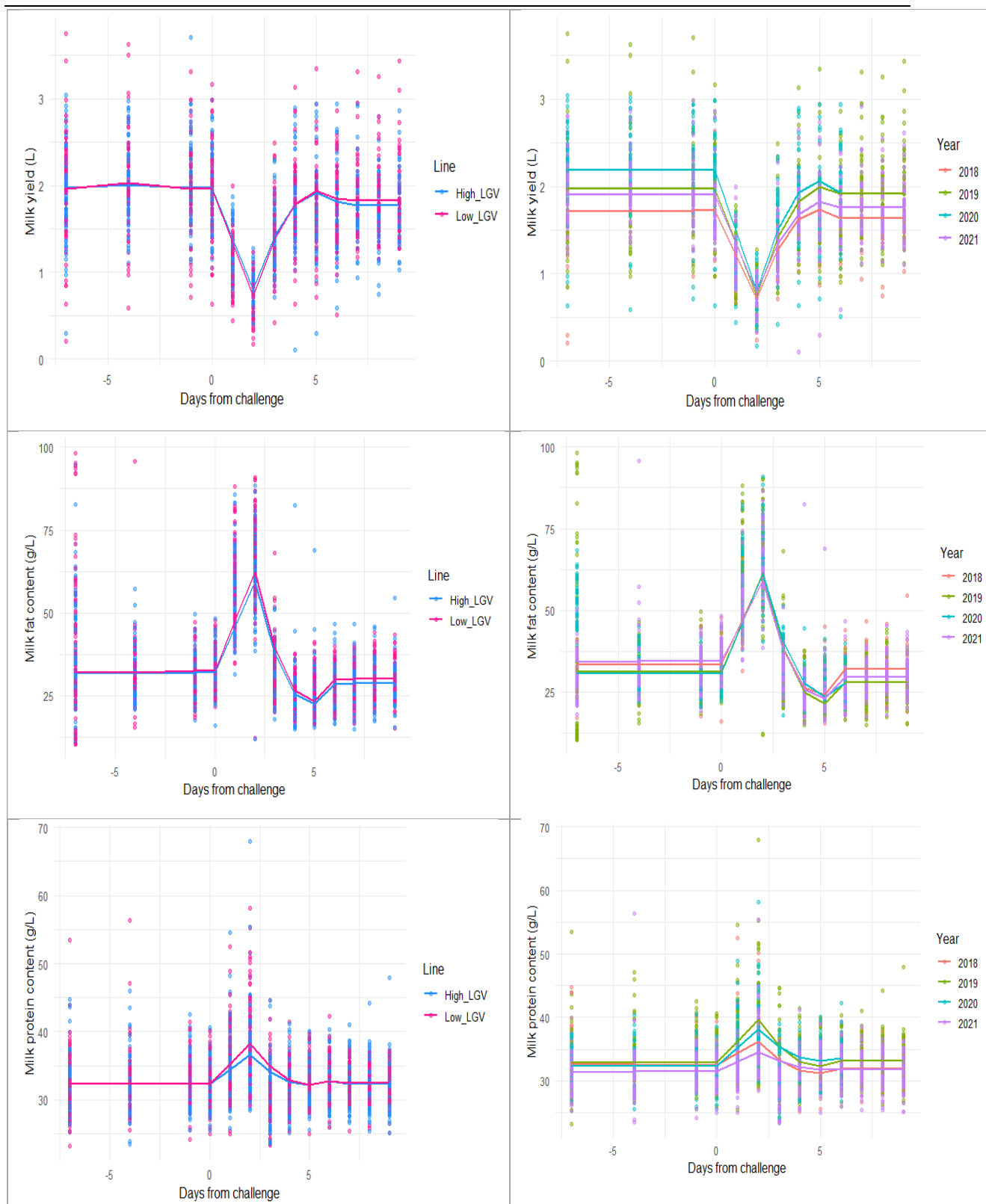


Fig. 6. Response and recovery profiles for milk yield, milk protein and fat content estimated by a piecewise model for (left) high_LGV (blue) and low_LGV (pink) lines and for (right) different challenge years.

5 Resilience trajectory analyses of Smarter data: response to inflammatory challenge in two Alpine goat lines selected on divergent longevity

5.1 Introduction

In section 3, novel statistical resilience indicators based in deviations of individuals' performance from an estimated target trajectory were introduced, and simulation studies identified key conditions under which these resilience indicators correctly distinguish between animals with high and low resilience. In this section, these resilience indicators were applied to the Smarter Alpine goat dataset described in section 4, to investigate the response to a lipopolysaccharide (LPS) challenge to which 45 goats were submitted one month after the nutritional challenge in 2021. LPS serves as a non-infectious component found in the outer membranes of Gram-negative bacteria mimicking mastitis-like inflammation (Zielen, Trischler and Schubert, 2015). The aim of this analysis was to assess whether the two divergently selected lines of goats differ in their resilience to the inflammatory challenge based on the statistical resilience indicators described in section 3.

5.2 Material and methods

5.2.1 Dataset

The data contains performance measures of 45 Alpine goats that had been subjected to the LPS challenge one month after the nutritional challenge described in section 4. The animals were from two divergently selected lines based on their functional longevity, with 27 and 18 animals from the high (high_LGV) and low (low_LGV) lines respectively. The data includes milk yield, protein content (PC) and fat content (FC) of milk, and somatic cell scores (SCS) collected over a 77 day period (21 days before challenge and 54 days after the challenge). There are 15 recorded measurements in this time interval at non-equidistant time points (days -21, -20, -19, -18, -13, -3, 0, 1, 2, 3, 7, 15, 45, 50, 53, 56). Here, day 0 denotes the day animals were challenged. Other factors that were recorded are the litter size of each individual (1, 2 or 3), the age of animal (1 or 2 year-old) and the days in milk.

5.2.2 Estimation of target trajectories

For simplicity, linear (including constant) target trajectories for all 4 traits were assumed for the limited observation period. To estimate the target trajectory for each individual, a quantile regression method was used with different thresholds τ (see section 3.1.1.3 for an explanation of these thresholds). When the deviations are expected to be mostly negative due to the challenge, e.g., milk yield deviations, a high threshold ($\tau = 0.7$) was used. Other high threshold values were also tested ($\tau \in \{0.6, 0.75, 0.8, 0.9\}$). In contrast, a low threshold value of 0.3 was used when the deviations due to the challenge are expected to be positive, i.e., fat content or protein content. Other low values of threshold values were also tested for these two traits, but the choice of the threshold generally did not affect the results. For the fat to protein ratio both low and high values of $\tau \in (0.1, 0.9)$ were tested. The “quantreg” package of R was used for estimation of target trajectories.

After fitting the target trajectory for a given trait for each individual, the deviations over time were estimated for each animal as the residual of the fitting,

$$y_j(t) \sim Y_j(t) + d_j(t),$$

where $y_j(t)$ is the performance of animal j , $Y_j(t)$ is its target trajectory value predicted and $d_j(t)$ is its deviation, all evaluated at time t .

5.2.3 Calculation of individuals' resilience indicators

After calculating individuals' deviations from their target trajectory, i.e., $d_j(t)$, the following resilience indicators were calculated as outlined in section 3.2: logarithm of variance (LV), logarithm of mean of sum of squares (LMS) and the area under the curve (AUC). The log-transformation was applied to variance and mean of sum of squares to normalise their distribution. For AUC, the trapezoidal rule was used to estimate the area bound by the target trajectory and the realised trajectory. In this study, we did not use lag-1 autocorrelation and skewness as resilience indicators. As shown in the first part of this report, the skewness can have strong and non-monotonic dependence on pre- and post-perturbation data. Additionally, lag-1 autocorrelation is not robust when the measurements are not frequent and don't come at equidistance intervals, as was the case here.

5.2.4 Statistical model

The following linear model was used to assess whether the high and low LGV differ in the value of a resilience indicator,

$$P = L + A + A:L + S + D_0 + \epsilon,$$

where P is the value of any of the above three resilience indicators applied to deviation of animals. The terms L , A and S are the line (low_LGV, high_LV), age and the litter size of animals and are considered fixed effects. The term D_0 correspond to the days in milk for animals at day -21 and is treated as a covariate. The residuals ϵ were assumed to follow a normal distribution.

5.2.5 Validation

The above procedure was applied to 2 datasets: 1- considering only the data before challenge, 2- considering all the data during the full 77 day observation window. A similar line difference in both scenarios indicates that both lines respond similar to the LPS challenge. On the other hand, differences in the estimated LGV line effect between the 2 scenarios indicate that the low_LGV and high_LGV lines respond differently to the challenge, i.e. differ in their resilience.

5.3 Results

Figure 1 shows the data before and after the LPS challenge for all the four traits measured. A visual inspection on these plots indicates that the majority of individuals, return back to their target trajectories after experiencing a shock due to the injection of LPS. Hence,

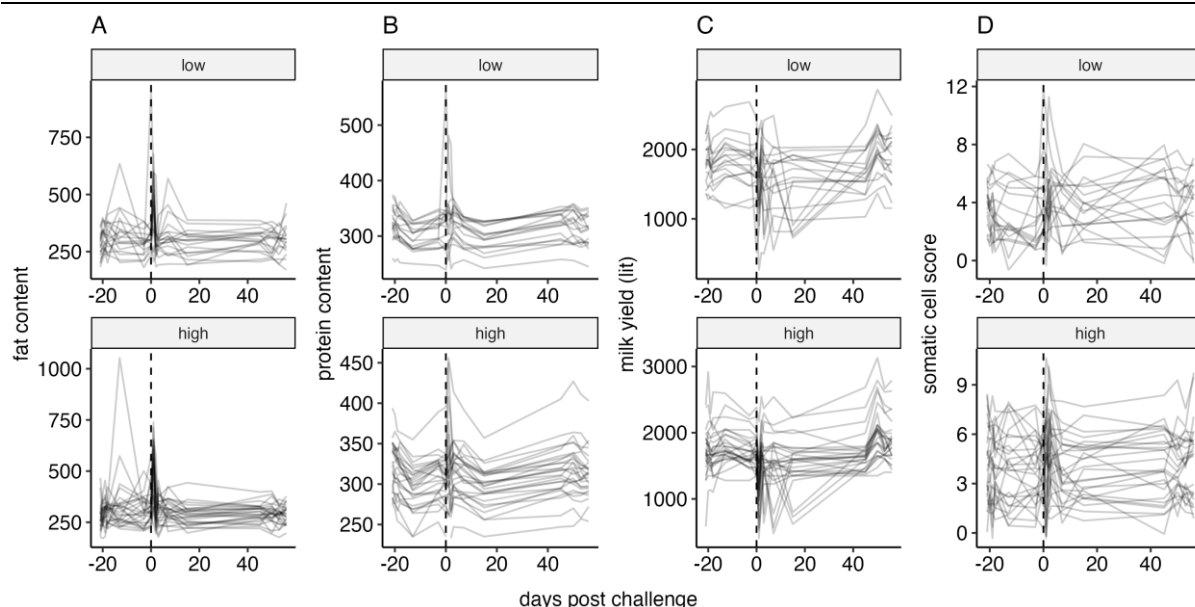


Figure 1. Profile of milk composition (A and B), milk yield (C) and somatic cell score before and after the LPS challenge for the two different lines (high: high_LGV, low: low_LGV). Day 0, represented by vertical dashed line, indicates the day of the challenge. Each animal is shown by a separate grey line.

The p-values for the F-statistics corresponding to LGV line effects on the diverse resilience indicators are provided in the Table 1 for the pre-challenge and full dataset, respectively. In general, the results were consistent across different resilience indicators. Furthermore, the results were similar when linear or constant target trajectories were assumed and for different threshold values used in the quantile regression (results not shown). Hence, only results for linear target trajectories and baseline threshold values for the quantile regression are shown.

Table 1. P-value (F-statistics) for the LGV line effect on the resilience indicators

trait	Before challenge			Full 77 day observation period		
	AUC	LV	LMS	AUC	LV	LMS
Milk yield	0.48	0.76	0.65	0.23	0.57	0.61
Fat content	0.58	0.40	0.52	0.65	0.08	0.12
Protein content	0.58	0.11	0.07	0.04 *	0.03 *	0.02 *
SCS (line:age)	0.02 *	0.04 *	0.04 *	0.07	0.95	0.17

No statistically significant difference was found between the two LGV lines prior to the challenge or considering all time points using any of the resilience indicators for milk yield or fat content (Table 1). In contrast, significant LGV line differences were observed for all three resilience indicators associated with milk protein content based on data from the full 77 day observation period. Interestingly, the values of these resilience indicators did not differ significantly between the LGV lines when only pre-challenge data were used, thus indicating that the LGV longevity lines differ significantly in their

resilience to the LPS challenge. Least square mean differences between the low_LGV and high_LGV lines were 4.24, 0.51 and 0.45 for AUC, LMS and LV, respectively, indicating that the high_LGV line is more resilient to the LPS challenge.

For resilience indicators associated with SCS, there was no significant LGV line difference when data from the full observation period were considered (Table 1). However, the interaction effect of LGV line by age was significantly before animals were challenged. For that period, least square mean differences between low_LGV and high_LGV goats for AUC, LMS and LV were -0.261, -0.49 and -0.49 for 1-year-old goats and -0.261, 1.38 and 1.425 for 2-year-old, respectively. This indicates that high_LGV goats experienced on average less deviations in SCS from the estimated target trajectory than low_LGV goats prior to challenge. The line by age interaction was no longer significantly different when considering all the time points, indicating that the LPS challenge reduced LGV line differences in SCS fluctuations.

5.4 Discussion

Previous studies have postulated high functional longevity is associated high resilience (Rostellato *et al.*, 2021). Indeed, previous analyses on data from the same goats have shown that the two goat lines divergently selected for functional longevity differ in their response to nutritional challenge (Ithurbide *et al.*, 2022 and section 4). In particular, the analyses in section 4 concluded that high_LGV goats allocate more for structural mass and better cope with an unexpected environmental change such as short-term underfeeding. The results of in this section complement these results by indicating that the the high_LGV goats also tend to cope better with short-term immune challenges. In line with the results for the nutritional challenge, our results did not indicate LGV line differences in the milk yield or fat content trajectories. However, significant differences were observed across all resilience indicators in terms of resilience indicators associated with milk protein content and SCS.

Compared to section 4, the analysis in this section involves fewer data and is far less comprehensive as it only focuses on LGV line differences in resilience to the LPS challenge, as manifested through the statistical resilience indicators associated with milk yield, milk fat and protein content, and SCS. The analysed dataset is relatively small with limited non-equidistance timepoint measurements. In fact, the frequency of measurement is smaller than the minimum postulated by the simulation studies in section 3. However, the trend for most of the traits appears constant or at least linear for the period after 10 days post-infection. Therefore, we believe the indicators can be applied to this dataset. In addition, screening the data did not reveal presence of any *Non-resilient* individuals, which has shown to cause potential bias in the resilience indicators in section 3.

A LGV line difference in the resilience indicators associated with milk protein content could only be observed when considering data that captured the pre- and post-challenge period, but not the pre-challenge period only. Therefore, it can be argued that this line difference indicates differential response to the LPS challenge. The difference was in the direction such that the high_LGV animals were more resilient than the low_LGV ones. Note however, that this does not mean that, on average, the high_LGV animals have higher milk protein content than the low LGV animals, as the resilience indicators are applied to the deviation of each individual with respect to its own target trajectory. Hence, the difference should be interpreted as the ability of the animal to control the effect of the challenge on the changes in the protein level.

It is expected that an LPS challenge affects the SCS of animals. However, the results associated with resilience based on this traits are difficult to interpret. Interestingly, the low_LGV and high_LGV lines differed significantly in their SCS resilience indicators prior to the LPS challenge, but the difference

reduced after challenge. Furthermore, the high_LGV line had higher values for the SCS resilience indicators than the low_LGV line for the 2-year-old goats. However, for the 1-year-old animals the estimated marginal means were higher for high_LGV animals, when using LMS or LV. Since the number of animals in the 2-year-old is relatively small (4 LGV- and 5 LGV+), and there is inconsistency between the resilience indicators in this particular case, caution is advised when interpreting the results.

Another important consideration is that these animals were subject to a nutrition challenge one month before the initiation of the LPS challenge. Therefore, the earlier challenge experiment may have had an impact on the response of animals prior to day 0.

Future studies that combine the data associated with the nutritional and LPS challenge, and apply the same statistical methods to assess resilience trajectory characteristics associated with both challenges are warranted.

5.5 Conclusions

The ability to record individual milk yield in dairy livestock is becoming increasingly accessible thanks to the advent of advanced monitoring systems. Previous studies have indicated that variations in milk yield can provide valuable insights into animals' resilience to diverse temporary environmental challenges. However, this dataset demonstrates that resilient and non-resilient animals may exhibit differences in the variability of milk compositions, particularly in terms of protein content, rather than in milk yield.

6 General conclusions and recommendations

We conclude with a summary of the key findings of the modelling studies and data analyses presented in this report, and implications:

1. Statistical resilience indicators based on individuals' deviations in performance measures from their target performance trajectory can reliably distinguish highly resilient animals from less resilient animals. However, there is a risk that these indicators wrongly classify animals that don't recover from a disturbance as more resilient than animals that do recover. To avoid misclassification, it is recommended to record animals' performance frequently over a prolonged period of time that covers both challenge and non-challenge periods.
2. Modelling studies show that it is possible to improve resilience of animals to infectious challenges through genetic selection using statistical resilience indicators from performance records as breeding goal. However, the models also demonstrate that genetic selection for resistance may be more efficient in improving animal health and performance in both challenge and non-challenge conditions. It is recommended that breeders and livestock producers carefully consider disease resistance versus disease resilience as alternative breeding objective to genetically improve animal health and productivity. This is in line with a previous literature review on disease resilience (D3.1 and <https://doi.org/10.1016/j.animal.2021.100286>) that warns that genetic selection of individuals with high resilience may not necessarily improve herd resilience.
3. Smarter data analyses provide evidence that animals vary substantially in their resilience to short-term nutritional and immune challenges. Experimental studies that exposing animals from divergently selected lines to short-term nutritional and immune challenges, combined

with statistical and mechanistic modelling, provides a useful approach to identify animals' adaptive strategies under challenging environments. The studies also highlight the importance of collecting a range of phenotypic performance measures to identify differences in resilience and adaptive strategies. For example, non-invasive measurements of body or milk metabolites may reveal differences in resilience better than body weight or milk yield measures.

7 Deviations or delays

No delay nor deviation