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Exploration of variance, autocorrelation, and skewness of deviations from lactation curves as resilience indicators for breeding

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**Interpretive summary**

Exploration of variance, autocorrelation, and skewness of deviations from lactation curves as resilience indicators for breeding. Poppe et al. Cows differ in their ability to cope with diseases and other challenges. We explored methods to describe the ability of a cow to handle unknown challenges by studying the fluctuation pattern in deviations from a lactation curve. Variance of deviations was most heritable and was genetically related to health and functionality. Autocorrelation and skewness had a lower heritability than the variance and had weak or unexpected genetic correlations with health and functionality. Therefore, variance in milk yield is the most promising indicator of resilience.

**MILK FLUCTUATIONS AS A RESILIENCE INDICATOR**

**Exploration of Variance, Autocorrelation, and Skewness of Deviations from Lactation Curves as Resilience Indicators for Breeding**

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**ABSTRACT**

The ability of a cow to cope with environmental disturbances, such as pathogens and heat waves, is called resilience. To improve resilience by breeding we need resilience indicators, which could be based on the fluctuation pattern in milk yield resulting from disturbances. The aim of this study was to explore three traits that describe fluctuations in milk yield as indicators for breeding resilient cows: the variance, autocorrelation, and skewness of the deviations from individual lactation curves. We used daily milk yield records of 198,754 first parity cows, recorded by automatic milking systems. First, we estimated a lactation curve for each cow using 4 different methods: moving average, moving median, quantile regression, and Wilmink curve. We then calculated the log-transformed variance (LnVar), lag-1 autocorrelation ($r_{auto}$), and skewness (Skew) of the daily deviations from these curves as resilience indicators. A genetic analysis of the resilience indicators was performed and genetic correlations between resilience indicators and health, longevity, fertility, metabolic, and production traits were estimated. The heritabilities differed between LnVar (0.20 – 0.24), $r_{auto}$ (0.08 – 0.10) and Skew (0.01 – 0.02), and the genetic correlations among the indicators were weak to moderate. For $r_{auto}$ and Skew, the genetic correlations with the health, longevity, fertility, and metabolic traits were weak or the opposite of what we expected. Therefore, $r_{auto}$ and Skew have limited value as resilience indicators. However, a lower LnVar was genetically associated to a better udder health (genetic correlations from -0.22 to -0.32), a better longevity (-0.28 to -0.34), less ketosis (-0.27 to -0.33), a better fertility (-0.06 to -0.17), a higher BCS (-0.29 to -0.40), and a higher dry matter intake (-0.53 to -0.66) at the same level of milk yield. These correlations support that LnVar is an indicator of resilience. Of all 4 curve fitting methods, LnVar based on quantile regression systematically had the strongest genetic correlations with the health, longevity, and fertility traits. Thus, quantile regression is considered the best curve fitting method. In conclusion,

50   LnVar based on deviations from a quantile regression curve is a promising resilience indicator

51   that can be used to breed cows that are better at coping with disturbances.

52

53   ***Key words:*** resilience, variance, milk yield, automatic milking system, dairy cow

54

55                                    **INTRODUCTION**

56   Cows differ in their ability to cope with environmental disturbances such as pathogens, heat

57   waves, and changes in feed composition and feed quantity. A cow that is unaffected by a

58   disturbance, or that quickly returns to her normal level of functioning, is labelled resilient

59   (Colditz and Hine, 2016; Berghof et al., 2019). Resilience could be improved through genetic

60   selection, but to do so we need to measure it on individual cows. Several studies have quantified

61   the response to and recovery from an experimental disturbance in animals (Friggens et al., 2016;

62   Revilla et al., 2019). However, such challenge experiments cannot be carried out routinely on

63   commercial farms. Moreover, challenge experiments focus on one type of disturbance, whereas

64   our interest is in improving the general resilience to unknown disturbances.

65

66   Alternatively, a data-driven approach can be used. Scheffer et al. (2018) proposed methods to

67   quantify resilience in cows using frequently measured data. These methods rely on the

68   assumption that cows are constantly subject to unknown disturbances, which result in

69   fluctuations in frequently measured traits. Cows with few fluctuations are less affected by

70   disturbances than cows with more fluctuations. Therefore, the fluctuation pattern is expected to

71   be informative about resilience. Several resilience indicators describing fluctuations in

72   frequently measured traits have been suggested, such as the variance of the trait, which indicates

73   the variability of the frequently measured trait, the lag-1 autocorrelation of the trait, which

74   indicates stretches of values above or below the expected level, and skewness of the trait, which

3

75 indicates asymmetry (Scheffer et al., 2018; Berghof et al., 2019). Up to know, it is difficult to

76 validate resilience indicators by relating them to response to disturbances, because of the lack

77 of data on disturbances. However, genetic analysis can be used to better understand the biology

78 of a trait and as such increase our understanding of new resilience indicators, similar to

79 validating subjectively scored traits such as BCS (Veerkamp et al., 2002).

80

81 A trait that is frequently measured and that shows response to disturbances is milk yield.

82 Variance of milk yield has been studied by several researchers. Elgersma et al. (2018) showed

83 that variance of daily recorded milk yield was heritable and that cows with a lower variance

84 had genetically a better udder health, less ketosis and a better longevity. Therefore, variance of

85 daily milk yield has potential as a resilience indicator. However, Elgersma et al. (2018) did not

86 account for the lactation curve shape, which is expected to influence the level of variance in

87 milk yield. Other studies showed genetic variation in environmental variance in milk yield using

88 a random regression model, which did account for lactation curve shape (Rönnegård et al.,

89 2013; Vandenplas et al., 2013; Ehsaninia et al., 2019). However, these authors used test-day

90 records, which are not frequent enough to detect all fluctuations in milk yield. Overall, there is

91 room for improvement of variance in milk yield as a resilience indicator. Furthermore,

92 autocorrelation and skewness of daily recorded milk yield may provide additional information

93 about resilience.

94

95 The aim of this study was to explore the use of variance, autocorrelation and skewness of

96 deviations in daily milk yield level from a lactation curve as indicators for breeding resilient

97 cows. We explored 4 methods to fit the lactation curve: moving average, moving median,

98 quantile regression, and Wilmink curve. The heritabilities of all resilience indicators were

99 estimated, as well as genetic correlations among the resilience indicators and genetic

4

100    correlations among the curve fitting methods. In addition, genetic correlations between the

101    resilience indicators and health, production, longevity, fertility, and metabolic traits were

102    estimated.

**MATERIALS AND METHODS**

104 In this study, we performed a genetic analysis on three potential resilience indicators. The

105 initial data contained 1,782,373,113 milk yield records on 1,120,550 cows obtained during

106 single milk visits of automatic milking systems (**AMS**) and conventional milking systems.

107 The potential resilience indicators were calculated from these data for 198,754 first parity

108 Holstein Friesian cows milked by AMS (see section 'data editing'). The calculation of the

109 potential resilience indicators was performed in 2 steps: (1) fitting of individual lactation

110 curves, (2) defining resilience indicators based on deviations from lactation curves. We will

111 first describe the 2 steps that generated the resilience indicators, followed by the data editing

112 and the genetic analysis.

113

### *Fitting individual lactation curves*

115 The aim of fitting individual lactation curves for each cow based on daily milk yield records,

116 was to get the expected milk yield of a cow at each day. Ideally, a fitted lactation curve would

117 be as close as possible to the curve that a cow would have realized in the absence of

118 disturbances, because then the deviations from the curve would contain most information

119 about responses to disturbances. The deviations from such a curve could thus be used to

120 indicate resilience (see Figure 1 for an example of a fitted lactation curve and the deviations

121 from that lactation curve). Fitting a lactation curve that a cow would have realized in the

122 absence of disturbances was difficult, because information about disturbances was lacking

123 and disturbances may even be cow-specific and unknown. Therefore, different methods were

124 explored for fitting the individual lactation curves using only the daily milk yield records as

125 input. The choice of the best curve fitting method is per definition arbitrary. However, the

126 results of this study will generate insight in which method has most potential and how

127 sensitive genetic parameters are when changing the curve fitting method. There are two

generic ways of fitting a trend through a time series: nonparametric trend estimation and model based estimation (Brockwell and Davis, 2016). Because it was unknown which method would generate the best results, it was decided to explore both. Four methods were used: two nonparametric (moving average and moving median), and two model based methods (the Wilmink lactation curve (Wilmink, 1987) and a quantile polynomial regression method). See Figure 2 for illustrations of the 4 lactation curve fitting methods.

*Nonparametric trend estimation.* The first nonparametric method was a two-sided moving average filter with a window of 21 days. This means that the expected milk yield on a certain day is the average of the milk yield of the 10 days before that day, the 10 days after that day and the day itself. Window sizes different from 21 days were explored as well. However, based on visual inspection of fitted trends for random cows from the data set it was decided to focus only on a window of 21 days. Because a moving average is relatively sensitive to drops in milk yield, it was decided to also fit a moving median filter with a window of 21 days. A moving median is the same as a moving average, but the expected milk yield is the median, and not the average, of a series of milk yield records. Both the moving average and the moving median filter were applied using the rollapply function in the zoo package in R (Zeileis and Grothendieck, 2005). The advantage of a moving average and moving median is that they are flexible, because expected yields are only dependent on the data points that are close in time. However, the risk is that the moving average and moving median are too flexible, which results in lost information on drops in milk yield in the deviations of the curve.

*Model building.* The first model based method was the Wilmink lactation curve (Wilmink, 1987):

$$yield_t = \beta_0 + \beta_1 t + \beta_2 e^{-0.05t} + \varepsilon \,,$$

where $yield_t$ is the observed milk yield on day in milk (**DIM**) $t$, $\beta_0$ is related to the level of production, $\beta_1$ describes the production decrease after the peak yield, $\beta_2$ describes the increase in milk yield at the start of the lactation, and $\varepsilon$ is the error term. The regression coefficients were estimated for each cow using the lm function in R and they were used to calculate the expected lactation curves. The advantage of the Wilmink curve is that it is a commonly used regression method for fitting lactation curves (Schaeffer et al., 2000; CRV, 2018a), and is therefore easy to understand. However, it might not fit the data for individual cows well enough, resulting in incomplete removal of the general trend.

The second model based method was fourth order polynomial quantile regression using a 0.7 quantile:

$$yield_t = \beta_0 + \beta_1 t + \beta_2 t^2 + \beta_3 t^3 + \beta_4 t^4 + \varepsilon$$

where $yield_t$ is the observed milk yield on DIM $t$ and $\varepsilon$ is the error term. Polynomial regression is commonly used in time series analysis (Brockwell and Davis, 2016). Similarly, most test-day models used in genetic evaluation use Legendre polynomials with random regression (Van der Werf et al., 1998; Pool and Meuwissen, 2000; Swalve, 2000; CRV, 2018a). The advantage of fourth order polynomial regression is that it is more flexible than a Wilmink curve, partly because of additional parameters, but the risk of being too flexible is smaller than for the trend estimation methods. Quantile regression was used instead of classical linear regression, to make the resulting curves less sensitive to drops in milk yield and thus closer to the potential curves in absence of disturbances. Whereas classical regression models estimate the conditional mean

178　milk yield given certain values of DIM, quantile regression models estimate the conditional

179　median or other quantile (Koenker, 2005). By using a quantile higher than 0.5, low milk yield

180　values have less influence on the predicted milk yield curve than high milk yield values. In

181　other words, drops in milk yield have less influence on the predicted milk yield curve when

182　using quantile regression with a quantile >0.5 than when using classical linear regression, and

183　the negative deviations from the quantile regression curve are larger. As a result, a quantile

184　regression curve using a quantile >0.5 was expected to better match the potential milk yield in

185　absence of disturbances than classical linear regression and thus to generate deviations that

186　contain more information on resilience. Different quantiles higher than 0.5 were explored, but

187　upon visual inspection of fitted curves for random cows from the data set it was decided to

188　focus on only the 0.7 quantile. The regression coefficients of the fourth order polynomial

189　quantile regression model using the 0.7 quantile were estimated for each cow using the quantreg

190　package (Koenker, 2018) and the poly function in R. The estimated regression coefficients for

191　each cow were then used to calculate individual expected lactation curves.

192

### *Defining resilience indicators based on deviations from lactation curves*

194　The deviations from the fitted lactation curves ($yield - \widehat{yield}$) were expected to contain

195　information about responses to environmental disturbances, and they were therefore used to

196　calculate 3 potential resilience indicators: the variance, the lag-1 autocorrelation, and the

197　skewness of the deviations. A low variance of the deviations was expected to indicate a good

198　resilience, because resilient cows have a smaller range of deviations from their lactation curve

199　than less resilient cows. A low lag-1 autocorrelation of the deviations was expected to indicate

200　a good resilience, because resilient cows have less and shorter stretches of negative deviations

201　than less resilient cows. A close to zero skewness of the deviations was expected to indicate a

202　good resilience, because resilient cows have as many positive as negative deviations, whereas

less resilient cows have more negative than positive deviations (Scheffer, 2009; Scheffer et al., 2018; Berghof et al., 2019). Because the lactation curve models had a poor fit in the beginning and end of lactation, and because the moving average and moving median were based on less than 21 days in the beginning and end of lactation, the first and last 10 DIMs of each cow were excluded from the calculation of the resilience indicators.

The variance of the deviations was transformed with a natural logarithm, which made the trait normally distributed upon visual inspection. The transformation made the resulting genetic variance directly comparable to previous work on heritable variance in residual variance, that used an exponential model on the variance (SanCristobal-Gaudy et al., 1998; Hill and Mulder, 2010; Sell-Kubiak et al., 2015). From now on, log-transformed variance of deviations from a lactation curve will be referred to as LnVar, lag-1 autocorrelation will be referred to as $r_{auto}$, and skewness will be referred to as Skew. Because each resilience indicator was calculated for 4 curve fitting methods, each cow had in total 12 potential resilience indicators. In addition to LnVar, $r_{auto}$, and Skew, the average daily milk yield and the natural log of the variance of the raw daily milk yield records (RawVar) were calculated for each cow. RawVar was used to compare our results to Elgersma et al. (2018) and the average daily milk yield was used to adjust genetic correlations between the resilience indicators and the health, longevity, fertility, and metabolic traits for milk yield level (see section "Genetic analysis").

### *Data editing*

The initial dataset was provided by Cooperation CRV and CRV BV (Arnhem, The Netherlands), and contained milk yield records obtained during single milk visits of AMS and conventional milking systems, resulting in multiple records per day for each cow. The data consisted of 1,782,373,113 milk yield records on 1,120,550 cows, recorded between 1998 and

228 2018. However, the resilience indicators were calculated only for first parity Holstein Friesian

229 cows that were milked by AMS, that were herd-book registered, that calved after 640 days of

230 age and before the $1^{st}$ of June 2017, and that had not more than 5% missing daily milk yield

231 records. Moreover, the resilience indicators were only based on the first 350 DIM. Daily milk

232 yield records were obtained from the records on single AMS visits by summing the milk yield

233 of the single AMS visits per day for each cow. However, the milk yield of the first AMS visit

234 of each day was partly assigned to the previous day depending on the milk produced per minute

235 since the previous AMS visit and the time between the previous AMS visit and midnight. After

236 calculating the resilience indicators, resilience indicator records of individual cows were set to

237 missing if they deviated more than 4 standard deviations from the mean of that resilience

238 indicator. To adjust for herd, year of calving, and season of calving, herd-year-season (**HYS**)

239 classes were made with 4 seasons (January-March, April-June, July-September, October-

240 December). HYS classes with less than 5 cows were removed. Finally, 198,754 cows were used

241 for the genetic analysis of the resilience indicators. Data editing was performed using the AWK

242 programming language (Aho et al., 1988) and R (R v 3.2.2; R Project for Statistical Computing,

243 Vienna, Austria). All data editing steps, with information on the number of remaining records

244 and number of cows after each editing step, are shown in Table 1.

245

246 ***Genetic analysis***

247 For all resilience indicators and average daily milk yield, heritabilities and EBV were estimated

248 with univariate analyses, and genetic correlations among traits were estimated with bivariate

249 analyses using ASReml 4.1 (Gilmour et al., 2015). The pedigree included 5 generations of

250 ancestors.

251

252     ***Univariate Analysis.*** Heritabilities and EBV were estimated using the following

253     univariate linear mixed animal model:

254

255                              $$\mathbf{y} = \mathbf{Xb} + \mathbf{Za} + \mathbf{e} \,,$$

256

257     where $\mathbf{y}$ was a vector with observations of a certain resilience indicator; $\mathbf{b}$ was a vector

258     containing fixed effects, which were HYS, age at first calving in months, and lactation length

259     (remaining number of days after removing the first and last 10 DIM) in 7 classes, each

260     containing a range of 40 days (50-90 days, 91-130 days etc.); $\mathbf{a}$ was a vector containing the

261     additive genetic effects, $\mathbf{a} \sim \mathrm{N}(\mathbf{0}, \mathbf{A}\sigma_a^2)$, where $\mathbf{A}$ is the additive genetic relationship matrix and

262     $\sigma_a^2$ is the additive genetic variance; and $\mathbf{e}$ was a vector containing the residuals, $\mathbf{e} \sim \mathrm{N}(\mathbf{0}, \mathbf{I}\sigma_e^2)$,

263     where $\mathbf{I}$ is the identity matrix and $\sigma_e^2$ is the residual variance. $\mathbf{X}$ and $\mathbf{Z}$ were incidence matrices

264     linking the records in $\mathbf{y}$ to the fixed effects and additive genetic effects, respectively. For the

265     LnVar traits and RawVar a genetic coefficient of variation (GCV) was calculated as $\sigma_a$, because

266     using the ln-transformation of the variance assumes an exponential model and GCV in the

267     exponential model for variance is equal to $\sigma_a$ (see Mulder et al., 2007). For the other resilience

268     indicators a GCV was calculated as $\frac{\sigma_a}{\mu}$.

269

270     ***Bivariate Analysis.*** Genetic correlations between the different resilience indicators,

271     between the same resilience indicators based on different lactation curve fitting methods, and

272     between the resilience indicators and average daily milk yield, were estimated using the

273     following bivariate mixed animal model:

274

275
$$\begin{bmatrix} \mathbf{y_1} \\ \mathbf{y_2} \end{bmatrix} = \begin{bmatrix} \mathbf{X_1} & \mathbf{0} \\ \mathbf{0} & \mathbf{X_2} \end{bmatrix} \begin{bmatrix} \mathbf{b_1} \\ \mathbf{b_2} \end{bmatrix} + \begin{bmatrix} \mathbf{Z_1} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z_2} \end{bmatrix} \begin{bmatrix} \mathbf{a_1} \\ \mathbf{a_2} \end{bmatrix} + \begin{bmatrix} \mathbf{e_1} \\ \mathbf{e_2} \end{bmatrix},$$

276

277    where $\mathbf{y}_i$ was a vector with observations on trait $i$; $\mathbf{b}_i$ was a vector with the fixed effects for

278    trait $i$, which were the same as in the univariate analysis; $\mathbf{a}_i$ was a vector with the additive

279    genetic effects for trait $i$; and $\mathbf{e}_i$ was a vector with the residuals for trait $i$. $\mathbf{X}_i$ and $\mathbf{Z}_i$ were

280    incidence matrices linking the records in $\mathbf{y}_i$ to the fixed effects and additive genetic effects,

281    respectively. The additive genetic effects for all traits were assumed normally distributed with

282    a mean of zero, a genetic variance of $\sigma_{a_i}^2$ for trait $i$ and a genetic covariance between traits of

283    $\sigma_{a_1 a_2}$: $\begin{bmatrix} \mathbf{a_1} \\ \mathbf{a_2} \end{bmatrix} \sim \mathrm{N}\left( \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{A} \otimes \begin{pmatrix} \sigma_{a_1}^2 & \sigma_{a_1 a_2} \\ \sigma_{a_1 a_2} & \sigma_{a_2}^2 \end{pmatrix} \right)$. The residuals were assumed normally distributed

284    as well, with a mean of zero, a residual variance of $\sigma_{e_1}^2$ for trait $i$, and a residual covariance

285    between traits of $\sigma_{e_1 e_2}$: $\begin{bmatrix} \mathbf{e_1} \\ \mathbf{e_2} \end{bmatrix} \sim \mathrm{N}\left( \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{e_1}^2 & \sigma_{e_1 e_2} \\ \sigma_{e_1 e_2} & \sigma_{e_2}^2 \end{pmatrix} \right)$.

286

287    Because of long computing times for the bivariate analyses, the dataset was randomly split into

288    5 subsets based on herd. The bivariate analyses were then performed on the 5 subsets and

289    weighted averages of the parameters were calculated. See Appendix for an explanation of the

290    weighting of the parameters resulting from the bivariate analyses on the subsets.

291

292    ***Genetic Correlations with Health, Longevity, Fertility, Metabolic, and Production***

293    ***Traits.*** Genetic correlations between the resilience indicators and several health, longevity,

294    fertility, metabolic, and production traits were estimated using the Multiple trait Across Country

295    Evaluation (**MACE**) procedure: the MACE procedure is used by Interbull (Interbull, 2017) to

296    evaluate bulls in different countries for the same trait, but can also be used to estimate genetic

297    correlations between de-regressed sire EBV of different traits (Schaeffer, 1994; Klei, 1998;

298    Larroque and Ducrocq, 1999). De-regressed EBV are used to make the variance of the EBV

independent from their reliabilities and to take out the contribution by the parents (Larroque and Ducrocq, 1999). The MACE procedure was used instead of bivariate analysis because it allows for inclusion of all available records on health, longevity, fertility, metabolic, and production traits in the national population, without the need for the actual data and models that accompany these traits. For the resilience indicators, de-regressed sire EBV resulting from the univariate analyses were used as input for the MACE procedure. For the health, longevity, fertility, metabolic, and production traits, de-regressed sire EBV from Cooperation CRV and CRV BV from the official run of December 2018 were used as input. All available health indexes and EBV, which were the udder health index (CRV, 2017b), the hoof health index (CRV, 2015), and ketosis resistance in first lactation (Vosman et al., 2015), were included because resilient cows are expected to be healthier than less resilient cows. For these three traits, a higher value means a better health or less ketosis. Productive longevity (CRV, 2018c) and the fertility index (CRV, 2017a), were also included because resilient cows are expected to live longer and to be more fertile than less resilient cows. For these two traits, a higher value means a better fertility or longevity. In addition, the metabolic traits BCS (CRV, 2018b) and dry matter intake (CRV, 2018e) were included because of the expected relation between resilience and the amount of resources a cow has available to respond to disturbances. For these two traits, a higher value means a higher BCS or a higher dry matter intake. The production trait fat-protein persistency in first lactation was included to investigate the differences in effect of persistency on RawVar and LnVar. The sire EBV for fat-protein persistency were based on daily EBV for kilograms of fat and protein resulting from a random regression model (CRV, 2018a). For this trait, a higher value means a flatter lactation curve. Finally, the production trait milk yield (CRV, 2018a) was included to compare the average daily milk yield calculated in the current AMS dataset to the official breeding value for milk yield based on the total Dutch-Flemish cow population.

324

325    ***Genetic Correlations Adjusted for Milk Yield.*** Considerable genetic correlations

326    between some of the resilience indicators and average daily milk yield were observed.

327    Therefore, partial genetic correlations between the resilience indicators and the health,

328    longevity, fertility, and metabolic traits, adjusted for average daily milk yield ($r_{xy,z}$), were

329    calculated as:

330

331    $$r_{xy,z} = \frac{r_{xy} - r_{xz}r_{yz}}{\sqrt{1 - r_{xz}^2}\sqrt{1 - r_{yz}^2}},$$

332

333    where $x$ is the resilience indicator, $y$ is the existing trait, and $z$ is average daily milk yield. The

334    correlations between the resilience indicators and average daily milk yield were genetic

335    correlations obtained from the bivariate analyses. The other correlations were genetic

336    correlations estimated using the MACE procedure.

# RESULTS

## *Comparison of Resilience Indicators*

The resilience indicators LnVar and RawVar had the highest heritability (0.20 to 0.24) and genetic coefficient of variation (0.23 to 0.26), whereas Skew had the lowest heritability (0.01 to 0.02) and genetic coefficient of variation (0.05 to 0.10; Table 3). Although RawVar had a comparable heritability to LnVar, they were genetically different traits, because the genetic correlations between RawVar and LnVar based on all curve fitting methods were 0.45 and lower. In addition to LnVar and RawVar, also LnVar, $r_{auto}$, and Skew genetically differed from each other. The genetic correlations between LnVar and $r_{auto}$ ranged from -0.12 to 0.05, the genetic correlations between LnVar and Skew ranged from 0.06 to 0.65 and the genetic correlations between $r_{auto}$ and Skew ranged from -0.35 to 0.37 (Table 4). In summary, the genetic correlations show that RawVar, LnVar, $r_{auto}$, and Skew are genetically different traits.

## *Comparison of Lactation Curve Fitting Methods*

The four lactation curve fitting methods resulted in different means of the resilience indicators (Table 2). We observed the most extreme difference between means for Skew based on a moving median and a Wilmink curve, where the deviations from a Wilmink curve were less skewed than the deviations from a moving median curve. In addition to the mean, also the genetic variance and heritability differed between the curve fitting methods, especially for Skew (Table 3). Skew based on a Wilmink curve genetically differed from the other curve fitting methods, with genetic correlations ranging from 0.31 to 0.60 (Table 5). The other curve fitting methods resulted in Skew traits that were genetically more similar, with genetic correlations ranging from 0.81 to 0.95. In comparison to Skew, LnVar and $r_{auto}$ had stronger genetic correlations between the curve fitting methods (>0.89). In summary, for LnVar and $r_{auto}$ different

361 curve fitting methods resulted in genetically similar traits, whereas for Skew the different curve

362 fitting methods resulted in genetically less similar traits.

363

364 ***Genetic Correlations with Health, Longevity, Fertility, Metabolic, and Production Traits***

365 LnVar and RawVar were the resilience indicators with the strongest genetic correlations with

366 the health, longevity, fertility, metabolic, and production traits (Table 6). Both a lower LnVar

367 and a lower RawVar were genetically related to a better udder health, a better hoof health, a

368 better longevity, a better fertility, a higher BCS, less ketosis and a lower milk yield level.

369 However, LnVar and RawVar differed in the sign of their genetic correlations with persistency

370 and dry matter intake. LnVar had a positive genetic correlation of only 0.08 to 0.14 with

371 persistency, whereas RawVar had a negative genetic correlation with persistency of -0.51.

372 LnVar had a positive genetic correlation of 0.24 to 0.29 with dry matter intake, whereas RawVar

373 had a negative genetic correlation with dry matter intake of only -0.04. If we now turn to $r_{auto}$,

374 we see that its genetic correlations with the health, longevity, fertility, metabolic, and

375 production traits were generally in the same direction as for LnVar: a lower $r_{auto}$ was genetically

376 related to a better health, fertility, and longevity, a higher dry matter intake and BCS, and a

377 lower milk yield level. However, $r_{auto}$ had weaker genetic correlations (-0.21 to 0.20) with the

378 health, longevity, fertility, metabolic, and production traits than LnVar. For Skew, the genetic

379 correlations with the health, longevity, fertility, and metabolic traits were in general negligible

380 or weak (-0.25 to 0.17), where a higher Skew was weakly genetically associated to more ketosis,

381 a lower BCS, and a lower longevity (Table 6). The genetic correlations between Skew and

382 average daily milk yield were moderate, and negative for Skew based on a Wilmink curve (-

383 0.40) and positive for Skew based on the other curve fitting methods (0.19 to 0.30).

384

Average daily milk yield had a strong genetic correlation (0.95) with official milk yield produced in 305 days in first lactation (Table 6). This strong genetic correlation indicates that the studied dataset is a good representation of the total Dutch-Flemish population. The genetic correlations between LnVar and average daily milk yield were positive and strong (0.75 to 0.79), and for both LnVar and average daily milk yield the genetic correlations with the health traits and fertility, BCS, dry matter intake, and ketosis resistance were in the same direction. Interestingly though, LnVar and average daily milk yield had an opposite but weak genetic correlation with productive longevity.

To disentangle the effect of milk yield level and variance in milk yield on the genetic correlations between LnVar and the health, longevity, fertility, and metabolic traits, the original genetic correlations were converted to partial genetic correlations, adjusted for milk yield level. Most partial genetic correlations between LnVar and the health, longevity, fertility, and metabolic traits were weaker (Table 7) than the original genetic correlations (Table 6). However, the partial genetic correlations between LnVar and longevity were stronger (-0.28 to -0.34) than the original genetic correlations. Moreover, the partial genetic correlations between LnVar and dry matter intake were negative (-0.53 to -0.66), whereas the original genetic correlations were positive: at an equal milk yield across cows, a less variable milk was genetically related to a higher dry matter intake. Although $r_{auto}$ and Skew had weaker genetic correlations with average daily milk yield than LnVar (Table 6), their partial genetic correlations with dry matter intake were stronger and in most cases had a different sign than their original genetic correlations with dry matter intake (Table 7). In summary, of the three resilience indicators, LnVar had the strongest genetic correlations with the health, longevity, fertility, and metabolic traits, where at an equal level of milk yield across cows, a lower LnVar

409    was genetically related to a better health, longevity, and fertility, and a higher BCS and dry

410    matter intake.

**DISCUSSION**

We explored the use of LnVar, $r_{auto}$, and Skew of deviations in daily milk yield from different types of lactation curves as indicators of resilience that can be used for breeding. LnVar had the highest heritability and the strongest genetic correlations with health, longevity, fertility, metabolic, and production traits. In addition, the three potential resilience indicators were genetically different from each other, whereas the different lactation curve fitting methods resulted in genetically similar traits for LnVar and $r_{auto}$, and to a lesser extent Skew.

As far as we know, we are the first to perform a genetic analysis on autocorrelation and skewness of a production trait in dairy cattle. However, a similar analysis has been performed on deviations in body weight in layer chickens (Berghof et al., submitted). Although the heritability of autocorrelation based on body weight deviations in chickens was similar to the heritability of autocorrelation based on milk yield deviations in cattle, the rest of the results differed between the two studies. In chickens, the heritability of skewness was ~10 times higher and the heritability of variance was ~2 times lower than in cattle. In addition, the genetic correlations among the three resilience indicators differed largely between the two species. The main reason for the differences between the traits in the two studies is likely that we used deviations from individually fitted lactation curves, whereas deviations from cohort averages were used in the chicken study. Therefore, the interpretation of autocorrelation and skewness differs between the studies. In addition, in this study we had many more records available per animal than in the chicken study.

Whereas autocorrelation and skewness of milk yield have not been studied genetically before, the variance has. Compared to previous studies on variance in milk yield, our study provided two novelties. The first novelty was that we analyzed the variance in deviations from a lactation

curve instead of the variance of raw milk yield values (Elgersma et al., 2018). As expected, fitting a lactation curve removed the effect of persistency on variance: LnVar had only a weak and positive genetic correlation with persistency (0.08 to 0.14), whereas RawVar had a considerable negative genetic correlation with persistency (-0.51). In addition, the genetic correlation between RawVar and LnVar was only moderate. Because of the removed effect of persistency, LnVar has improved value as a resilience indicator compared to variance in raw milk yield as studied by Elgersma et al. (2018). The second novelty of this study compared to most previous studies (Rönnegård et al., 2013; Vandenplas et al., 2013; Ehsaninia et al., 2019), but in line with Elgersma et al. (2018), was that we used daily recorded milk yield instead of test-day records to calculate the variance of deviations in milk yield. As expected, the higher number of records per cow used in our study than in the previous studies resulted in a lower environmental variance and a higher heritability of LnVar (Berghof et al., 2019). Rönnegård et al. (2013), Vandenplas et al. (2013), and Ehsaninia et al. (2019) analyzed their milk yield records with a double hierarchical generalized linear model (**DHGLM**), which effectively means they did a genetic analysis immediately on test day milk yield records. This genetic analysis gave them genetic parameters for the mean milk yield and the variance of the deviations from an estimated lactation curve simultaneously. On the contrary, we used a two-step approach and first estimated individual lactation curves and then summarized the deviations into one resilience indicator per cow, on which we performed a genetic analysis. In theory, the DHGLM could be applied to our daily milk yield records as well, but is expected to yield similar EBV and genetic variance in residual variance as our LnVar (Berghof et al., submitted), whereas it is computationally much more challenging to apply and more difficult to understand.

Our research focused on fluctuations in milk yield level for defining resilience indicators. However, fluctuations in milk components may also be related to resilience. For example,

461   fluctuations in fat content may indicate resilience to ketosis or rumen acidosis, and fluctuations

462   in somatic cell score may indicate resilience to mastitis (De Haas et al., 2008; Urioste et al.,

463   2012). Rönnegård et al. (2013) and Vandenplas et al. (2013) showed genetic variation in

464   variability of somatic cell count measured on test-days, and Vandenplas et al. (2013) also

465   showed genetic variation in variability of different types of fatty acids. Furthermore, Ehsaninia

466   et al. (2019) showed genetic variation in variability of fat and protein content measured on test-

467   days. It would be interesting to also analyze variability of these traits using daily records and to

468   investigate their genetic correlations with health traits. However, until now daily measurements

469   of milk components are not available on a large scale.

470

471   In our study, as well as in Rönnegård et al. (2013), Vandenplas et al. (2013), Elgersma et al.

472   (2018), and Ehsaninia et al. (2019), the variance of (deviations in) milk yield was studied as a

473   resilience indicator. Alternative measures could be the mean of absolute deviations or using the

474   variance of only negative deviations. The mean of absolute deviations may give similar

475   information as the variance, but a variance gives more weight to large deviations than to small

476   deviations, because a variance is essentially the mean of squared deviations. Because small

477   deviations can be just due to noise, we expect that the variance is more powerful as a resilience

478   indicator than the mean of absolute deviations. The use of only negative deviations to calculate

479   the variance may seem better than using also positive deviations because disturbances cause

480   drops in milk yield and not peaks. However, work on daily feed intake in turkeys has shown

481   that variance based on only negative deviations had a considerably smaller heritability than the

482   variance based on all deviations, while the genetic correlation between them was 0.98 (H. A.

483   Mulder, unpublished data). Thus, we expect the variance of all deviations to be more

484   informative about resilience than the mean of absolute deviations or the variance of only

485   negative deviations.

22

486

487  All our resilience indicators were based on data from complete lactations up to DIM 350.

488  However, resilience may differ between lactation stages because of differences in disease

489  susceptibility (Ingvartsen et al., 2003). Therefore, it would be interesting to test if resilience

490  indicators based on data from different lactation stages are genetically different from each other

491  and if they differ in their genetic correlations with health, longevity, fertility, metabolic, and

492  production traits.

493

494  ***The Suitability of Traits Used as Resilience Indicators***

495  The suitability of a resilience indicator depends on its heritability and its genetic correlations

496  with health, longevity, fertility, metabolic, and production traits. A high heritability indicates

497  that family members are more alike than other animals, and indicates therefore that the indicator

498  is not simply random noise. Furthermore, resilience is expected to be genetically correlated to

499  a better health, longevity, and fertility (Elgersma et al., 2018; Berghof et al., 2019), and a higher

500  dry matter intake, a higher BCS, and a lower milk yield level. The expected correlations with

501  dry matter intake, BCS, and milk yield level can be explained by resource allocation theory. If

502  the demand for resources for milk yield is high, less resources are left for coping with

503  disturbances than when demand for resources for milk yield is low. Therefore, a high milk yield

504  can make a cow less resilient. Alternatively, a high dry matter intake or a high BCS can cause

505  a cow to have enough resources to cope with disturbances, even at a high milk yield, which

506  makes her more resilient (Rauw, 2008). If a lower LnVar and $r_{auto}$ indicate a better resilience,

507  they are expected to have negative genetic correlations with udder health, hoof health,

508  longevity, fertility, ketosis resistance, dry matter intake, and BCS, and positive correlations

509  with milk yield level. If a higher (more positive) Skew indicates a better resilience, it is expected

510  to have positive genetic correlations with udder health, hoof health, longevity, fertility, ketosis

23

resistance, dry matter intake, and BCS, and negative correlations with milk yield level. In the following sections we will discuss which of the resilience indicators best behaves according to these expectations.

*Variance.* In our results, LnVar based on all curve fitting methods had a considerable heritability. In addition, a lower LnVar was genetically correlated with a better health, longevity, and fertility, and to a higher BCS, which was as expected. These results support that LnVar indicates resilience. Most of the genetic correlations with the health, longevity, fertility, and metabolic traits were only moderate, but this is favorable: LnVar should indicate general resilience, and not resilience to specific diseases (Putz et al., 2019). Other studies that investigated resilience indicators also found moderate genetic correlations with health and functional traits (Elgersma et al., 2018; Putz et al., 2019). More importantly, all genetic correlations consistently showed that a low LnVar was related to a good health and functionality.

Although the health, longevity, fertility, and metabolic traits did not have strong genetic correlations with LnVar, the average daily milk yield did have strong positive correlations. There are two possible explanations for these strong genetic correlations. The first explanation is that cows with a higher milk yield level have a worse resilience than cows with a lower milk yield level. High producing cows are expected to have fewer resources available to respond to disturbances than low producing cows due the high resource demand for their milk yield, and thus have a larger tendency to take resources away from production (Rauw, 2008; Berghof et al., 2019). The second explanation for the strong genetic correlation between LnVar and average daily milk yield is a scale effect (Falconer and Mackay, 1996; Berghof et al., 2019). A scale effect means that the same disturbance results in a larger drop in milk yield in high

producing cows than in low producing cows, whereas the size of the drop relative to the

production level is equal for cows with different production levels.


Because of the strong positive genetic correlations between LnVar and average daily milk yield

and the generally unfavorable genetic correlation between milk yield and functionality, one

could argue that the genetic correlations between LnVar and the health, longevity, fertility, and

metabolic traits were mainly caused by milk yield level and not by variability in milk yield.

However, the partial genetic correlations between LnVar and most functional traits, adjusted

for milk yield, were still considerable and in the expected direction (a low LnVar was related

to good health and functionality). These considerable partial genetic correlations indicate that

LnVar does contain information about health and functionality that is not covered by milk yield

level. Moreover, the partial genetic correlations between LnVar and both dry matter intake and

longevity were closer to our expectations of LnVar as a resilience indicator than the original

genetic correlations. The negative partial genetic correlation between LnVar and longevity was

stronger than the original one, which was closer to our expectation because we expected a lower

LnVar to be related to a higher longevity (resilient cows live longer). The change in strength of

the genetic correlation between LnVar and longevity after adjustment for milk yield level is

caused by the weak genetic correlation between average daily milk yield and longevity: the

genetic correlation between LnVar and longevity was "suppressed" by the weak genetic

correlation between average daily milk yield and longevity. The partial genetic correlation

between LnVar and dry matter intake was quite strong and negative, which means that at an

equal level of milk yield across all cows, cows with a low variance in milk yield tend to have a

higher dry matter intake than cows with a high variance, which probably gives the low variance

cows the resources they need to respond to disturbances. The partial genetic correlation between

LnVar and dry matter intake was opposite from the original positive genetic correlation that

561 indicated that a higher LnVar was related to a higher dry matter intake. This difference is caused

562 by the positive genetic correlation between milk yield level and dry matter intake: cows with a

563 genetically higher milk yield tend to eat more than less productive cows, but they also have a

564 higher variance in milk yield. The negative partial genetic correlations between LnVar and dry

565 matter intake and the negative partial genetic correlations between LnVar and longevity confirm

566 that LnVar corrected for milk yield is informative about resilience.

567

568 Although most genetic correlations between LnVar and the functional traits became only

569 slightly weaker after adjusting them for milk yield level, the genetic correlations between LnVar

570 and hoof health became negligible. Apparently, LnVar does not contain information about hoof

571 health that is not covered yet by milk yield level. The negligible partial correlation is probably

572 caused by the inability of the curve fitting methods to capture long-term declines in milk yield

573 that are typical for lameness (Green et al., 2002). LnVar based on the curve fitting methods

574 applied in this study is therefore not suitable for long-term disturbances such as claw disorders.

575

576 In summary, LnVar contains information about health and functionality that is not covered by

577 milk yield level. Therefore, LnVar is a promising resilience indicator and seems a good

578 candidate to include in breeding goals. The economic value of resilience is already partly

579 accounted for in breeding goals by health traits. However, resilience has an additional economic

580 value, because resilient cows require less time from farmers for checking and monitoring than

581 less resilient cows. In addition, resilience may account for the costs of diseases that are not yet

582 included in the breeding goal (Berghof et al., 2019), such as ketosis and rumen acidosis in the

583 Netherlands (CRV, 2018d). Additional research is needed to determine the correct economic

584 value of LnVar in the breeding goal. Alternatively, a desired gains approach could be used

585    (Brascamp, 1984). Such an approach should aim for a decrease in LnVar while simultaneously

586    increasing milk yield level, health, longevity, and fertility, and decreasing dry matter intake.

587

588    ***Autocorrelation.*** The heritability of $r_{auto}$ was not high, but was still considerable, which

589    suggests that $r_{auto}$ contains information and is not just random noise. We expected that the

590    information that $r_{auto}$ contained would be mostly about the recovery aspect of resilience

591    (Berghof et al., 2019). A higher $r_{auto}$ was expected to indicate longer stretches of negative (or

592    positive) deviations and thus a slower recovery. Because the EBV for the health traits are more

593    informative about resistance to diseases than recovery from diseases, the genetic correlations

594    between $r_{auto}$ and the disease traits may be of limited value for validating $r_{auto}$ as an indicator of

595    recovery time. Indeed, the genetic correlations between $r_{auto}$ and udder health and hoof health

596    were weak and negligible, respectively. Nevertheless, they were in the expected direction,

597    where a lower $r_{auto}$ indicated a better health. The association between $r_{auto}$ and udder health

598    could be caused by the positive genetic association between mastitis resistance and recovery

599    rate (Welderufael et al., 2018). Based on this observation one may expect a positive genetic

600    correlation between $r_{auto}$ and LnVar, but we found a weak and negative genetic correlation. In

601    summary, we cannot conclude from our results whether $r_{auto}$ is informative about recovery time,

602    and more research is needed. If $r_{auto}$ turns out to contain information about recovery time that

603    LnVar lacks, the two traits could be combined in a resilience index. However, as a single

604    indicator of overall resilience, $r_{auto}$ is less suitable than LnVar.

605

606    ***Skewness.*** Skew contained less genetic variation than LnVar and $r_{auto}$, indicated by the

607    low GCV, and more noise, indicated by the low heritability. In addition, Skew had weak or

608    unexpected genetic correlations with both LnVar and the health, longevity, fertility, and

609    metabolic traits. For instance, a higher (closer to 0) Skew was expected to indicate a better

610 resilience, but was weakly genetically related to a shorter longevity, a lower BCS, more ketosis,

611 and a higher LnVar. Therefore, Skew is not considered a good resilience indicator. The reason

612 that Skew was unable to reflect resilience could be that this trait was too sensitive to incorrect

613 milk yield records: only one outlier could have a large effect on Skew. We were not able to

614 remove all outliers from the data, because if we would be too strict, we would also remove

615 extreme records that were informative about resilience. Because of the sensitivity to outliers,

616 Skew is not suitable as a resilience indicator using commercial data.

617

618 ***Which curve fitting method is best?***

619 Because of its heritability and genetic correlations with health, longevity, fertility, metabolic,

620 and production traits, LnVar is the most promising resilience indicator. However, we should

621 also decide which curve fitting method generates the best LnVar. All 4 curve fitting methods

622 resulted in genetically similar LnVar traits (Table 5), which indicates that for LnVar it is not

623 important which curve fitting method is used. However, small differences were observed in the

624 genetic parameters. Moving average and moving median resulted in the highest heritability,

625 whereas polynomial quantile regression generated the strongest genetic correlations with the

626 health, longevity, fertility, and metabolic traits. To decide which method is best, we can

627 calculate the indirect response in a health trait, such as udder health, that results from selection

628 on reduced LnVar based on the 4 curve fitting methods. If we consider genomic selection using

629 20,000 cows in the reference population and we assume that the number of independent

630 chromosomal segments is 1,200, then the accuracy of a genomic EBV (Daetwyler et al., 2010)

631 for LnVar would be ~0.90 based on moving average and moving median, and ~0.88 based on

632 polynomial quantile regression and a Wilmink curve. Note that this comparison is not affected

633 by the assumption on the number of independent chromosomal segments; getting an appropriate

634 value is an unresolved scientific issue (Brard and Ricard, 2014). Assuming the selection

635 intensity to be 1, the genetic improvement in udder health would be 0.24, 0.23, 0.28 and 0.25

636 genetic standard deviations when selection is on LnVar based on moving average, moving

637 median, polynomial quantile regression, and Wilmink curve, respectively. This shows that

638 polynomial quantile regression would lead to the highest genetic improvement in udder health

639 if selection is on LnVar. The same was observed for hoof health, ketosis, longevity, and fertility.

640 Therefore, polynomial quantile regression is considered the best curve fitting method among

641 the methods studied here.

**CONCLUSION**

643 All potential resilience indicators explored in this study were heritable, although the

644 heritabilities ranged from low to moderate. LnVar had the largest heritability and the strongest

645 genetic correlations with health, longevity, fertility, and metabolic traits, in the expected

646 direction. Therefore, it has most potential as a resilience indicator. The genetic correlations of

647 $r_{auto}$ with the health, longevity, fertility, and metabolic traits were weak, but more research is

648 needed to investigate whether $r_{auto}$ could indicate recovery time. Skew had a negligible

649 heritability and had unexpected genetic correlations with the health, longevity, fertility, and

650 metabolic traits. Skew is thus not considered a good resilience indicator. The lactation curve

651 fitting methods on which LnVar was based resulted in genetically similar traits, but selection

652 on LnVar based on quantile regression would consistently result in the largest correlated

653 responses in health, longevity, and fertility traits. Therefore, this curve fitting method is

654 recommended. This research is an important stepping stone to further explore the use of log-

655 transformed variance of deviations in milk yield as an indicator that can be used to breed

656 resilient cows.

657

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**APPENDIX**

814

815 *Bivariate analyses using subsets*

816 Because of the long computing time, genetic correlations between the resilience indicators were

817 estimated on subsets of the complete data. Weighted averages were subsequently estimated,

818 which are presented in this paper. In this appendix we provide additional information about the

819 aggregation of the genetic correlations estimated on subsets of the data.

820

821 The complete data set was randomly split into 5 subsets based on herd. On each subset, genetic

822 correlations between resilience indicators were estimated. Weighted averages of the genetic

823 correlations ($\bar{x}$) were estimated as:

824

825
$$\bar{x} = \frac{\sum_{i=1}^{5} w_i x_i}{\sum_{i=1}^{5} w_i},$$

826

827 where $w_i$ was the number of animals in subset $i$ and $x_i$ was the estimated genetic correlation of

828 subset $i$. Weighted standard deviations of the genetic correlations ($s$) were estimated as:

829

830
$$s = \sqrt{\frac{\sum_{i=1}^{5} w_i (x_i - \bar{x})^2}{\frac{4 \sum_{i=1}^{5} w_i}{5}}}.$$

831

832 To calculate the standard error of the weighted average genetic correlations, the weighted

833 standard deviations were divided by the square root of 5. In addition to the weighted genetic

834 correlations, also weighted residual and phenotypic correlations were calculated, which are

835 shown in Table A1.

836                                              **TABLES**

837     Table 1. Data editing steps and the number of records, the number of missing records, and the

838     number of cows present after each editing step

| Editing step | Number of records | Number of missing records | Number of cows |
|---|---|---|---|
| Original dataset | 1,782,373,113 | 0 | 1,120,550 |
| Select cows with parity 1 | 537,289,288 | 0 | 774,241 |
| Select cows milked by AMS | 450,627,626 | 0 | 588,541 |
| Select cows that are registered and at least 87.5% Holstein Friesian | 354,900,725 | 0 | 457,607 |
| Remove records with 0 milk yield | 354,899,345 | 0 | 457,607 |
| Remove cows that moved between herds | 351,722,320 | 0 | 453,535 |
| Remove duplicate records | 345,144,971 | 0 | 453,535 |
| Calculate daily milk yield | 128,155,982 | 14,171,909 | 453,251 |
| Remove records at more than 350 days in milk | 116,450,351 | 13,038,628 | 453,251 |
| Remove cows with less than 20 records[1] | 116,388,475 | 12,670,122 | 446,158 |
| Remove cows that calved before 640 days of age | 115,913,747 | 12,608,713 | 444,281 |
| Set outliers to missing based on Wilmink curve (CRV, 2018a) | 115,747,841 | 12,774,619 | 444,281 |
| Set milk yield >100kg to missing | 115,747,816 | 12,774,644 | 444,281 |

| | | | |
|---|---|---|---|
| Remove cows that have their first milk yield record after 14 days in milk | 108,031,488 | 8,005,087 | 402,054 |
| Fit lactation curves and remove cows with less than 50 records | 100,171,599 | 7,002,276 | 378,480 |
| Aggregate daily milk yield records to resilience indicators | 378,480 | 0 | 378,480 |
| Remove cows with an average milk yield less than the average herd yield +/- 4 SD | 378,364 | 0 | 378,364 |
| Remove cows that calved after the 1st of June 2017 | 334,387 | 0 | 334,387 |
| Remove cows for which more than 5% of their entire lactation consisted of missing records | 255,096 | 0 | 255,096 |
| Set resilience indicator records to missing if they exceed mean +/- 4 SD and remove cows with a missing resilience indicator based on all curve fitting methods | 254,788 | 0 | 254,788 |
| Remove herd*year*season classes with less than 5 cows | 198,754 | 0 | 198,754 |

839    [1]To fit a Wilmink curve, a sufficient amount of records was needed.

Table 2. Descriptive statistics of resilience indicators based on different lactation curve fitting methods, and average daily milk yield

| Trait[1] | Curve[2] | Mean | SD | Minimum | Maximum | Number of cows |
|---|---|---|---|---|---|---|
| LnVar | ma | 0.90 | 0.59 | -1.38 | 3.27 | 198,702 |
| | mm | 0.87 | 0.61 | -1.59 | 3.33 | 198,712 |
| | wilm | 1.69 | 0.57 | -0.60 | 3.97 | 198,728 |
| | quant | 1.39 | 0.57 | -0.89 | 3.69 | 198,725 |
| RawVar | - | 2.85 | 0.64 | 0.28 | 5.36 | 198,723 |
| $r_{auto}$ | ma | 0.32 | 0.19 | -0.43 | 0.91 | 198,736 |
| | mm | 0.30 | 0.18 | -0.43 | 0.89 | 198,746 |
| | wilm | 0.65 | 0.18 | -0.10 | 0.98 | 198,343 |
| | quant | 0.56 | 0.19 | -0.22 | 0.98 | 198,580 |
| Skew | ma | -1.26 | 0.83 | -4.88 | 2.37 | 197,731 |
| | mm | -1.60 | 1.04 | -6.10 | 2.92 | 197,838 |
| | wilm | -0.82 | 0.65 | -3.48 | 1.85 | 198,452 |
| | quant | -1.27 | 0.74 | -4.38 | 1.87 | 198,197 |
| AMY | - | 26.60 | 4.99 | 6.34 | 46.29 | 198,736 |

[1]Trait: LnVar = variance of deviations from lactation curve, RawVar = variance of raw milk yield, $r_{auto}$ = lag-1 autocorrelation of deviations, Skew = skewness of deviations, AMY = average daily milk yield.

[2]Curve: ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

Table 3. Variance components ($\sigma_a^2$ = additive genetic variance; $\sigma_e^2$ = error variance; $\sigma_p^2$ = phenotypic variance) and heritabilities ($h^2$) from the univariate analyses of the resilience indicators (SE in parentheses)

| Trait[1] | Curve[2] | $\sigma_a^2$ | $\sigma_e^2$ | $\sigma_p^2$ | $h^2$ | GCV |
|---|---|---|---|---|---|---|
| LnVar | ma | 0.062 (0.002) | 0.192 (0.002) | 0.254 (0.001) | 0.244 (0.009) | 0.25 |
|  | mm | 0.065 (0.003) | 0.209 (0.002) | 0.274 (0.001) | 0.236 (0.009) | 0.25 |
|  | wilm | 0.054 (0.002) | 0.218 (0.002) | 0.272 (0.001) | 0.198 (0.008) | 0.23 |
|  | quant | 0.056 (0.002) | 0.207 (0.002) | 0.264 (0.001) | 0.213 (0.009) | 0.24 |
| RawVar | - | 0.065 (0.003) | 0.245 (0.002) | 0.310 (0.001) | 0.209 (0.009) | 0.26 |
| $r_{auto}$ | ma | 0.003 (0.000) | 0.028 (0.000) | 0.030 (0.000) | 0.095 (0.006) | 0.17 |
|  | mm | 0.003 (0.000) | 0.027 (0.000) | 0.029 (0.000) | 0.090 (0.006) | 0.17 |
|  | wilm | 0.002 (0.000) | 0.025 (0.000) | 0.027 (0.000) | 0.083 (0.006) | 0.07 |
|  | quant | 0.003 (0.000) | 0.028 (0.000) | 0.030 (0.000) | 0.085 (0.006) | 0.09 |
| Skew | ma | 0.007 (0.001) | 0.571 (0.002) | 0.578 (0.002) | 0.011 (0.002) | 0.06 |
|  | mm | 0.011 (0.002) | 0.906 (0.003) | 0.917 (0.003) | 0.012 (0.002) | 0.07 |
|  | wilm | 0.006 (0.001) | 0.356 (0.001) | 0.362 (0.001) | 0.017 (0.002) | 0.10 |
|  | quant | 0.004 (0.001) | 0.475 (0.002) | 0.479 (0.002) | 0.009 (0.002) | 0.05 |
| AMY | - | 8.467 (0.198) | 9.486 (0.130) | 17.953 (0.093) | 0.472 (0.009) | 0.11 |

[1]Trait: LnVar = variance of deviations from lactation curve, RawVar = variance of raw milk yield, $r_{auto}$ = lag-1 autocorrelation of deviations, Skew = skewness of deviations, AMY = average daily milk yield.

[2]Curve: ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

Table 4. Genetic correlations between the resilience indicators variance, autocorrelation, and skewness for each of the 4 lactation curve fitting methods, and genetic correlations between variance of deviations from lactation curves and variance of raw milk yield records (SE in parentheses)

| | Resilience indicator[1] | | | |
|---|---|---|---|---|
| Curve[2] | LnVar & $r_{auto}$ | LnVar & Skew | $r_{auto}$ & Skew | LnVar & RawVar[3] |
| ma | -0.12 (0.04) | 0.51 (0.12) | -0.20 (0.06) | 0.39 (0.02) |
| mm | -0.12 (0.03) | 0.65 (0.10) | -0.35 (0.05) | 0.37 (0.02) |
| wilm | 0.05 (0.02) | 0.06 (0.08) | 0.37 (0.08) | 0.45 (0.02) |
| quant | -0.04 (0.02) | 0.49 (0.11) | -0.01 (0.05) | 0.45 (0.02) |

[1]Resilience indicator: LnVar = variance of deviations from lactation curve, $r_{auto}$ = lag-1 autocorrelation of deviations, Skew = skewness of deviations, RawVar = variance of raw milk yield

[2]Curve: ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

[3]RawVar is not based on deviations from lactation curves. Therefore, the comparison is between LnVar based on different curves and RawVar.

Table 5. Genetic correlations between 4 lactation curve fitting methods for each resilience indicator (SE in parentheses)

| | Resilience indicator[2] | | |
|---|---|---|---|
| Curve[1] | LnVar | $r_{auto}$ | Skew |
| ma & mm | 1.00 (0.00) | 0.99 (0.01) | 0.95 (0.01) |
| ma & wilm | 0.94 (0.01) | 0.92 (0.01) | 0.46 (0.07) |

| | | | |
|---|---|---|---|
| ma & quant | 0.98 (0.00) | 0.97 (0.00) | 0.81 (0.07) |
| mm & wilm | 0.94 (0.01) | 0.90 (0.01) | 0.31 (0.06) |
| mm & quant | 0.98 (0.00) | 0.95 (0.01) | 0.83 (0.06) |
| wilm & quant | 0.98 (0.00) | 0.96 (0.01) | 0.60 (0.03) |

871    [1]Curve fitting methods: ma = moving average, mm = moving median, wilm = Wilmink curve,

872    quant = quantile regression.

873    [2]Resilience indicator: LnVar = variance, $r_{auto}$ = autocorrelation, Skew = skewness.

Table 6. Genetic correlations between resilience indicators based on different lactation curve fitting methods and average daily milk yield, and

health, functional, and production traits, estimated using the MACE procedure. Standard errors are not provided, because the MACE procedure

does not give any

| Indicator/Trait[1] | Curve[2] | Health, longevity, fertility, metabolic, and production traits[3] | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | UH | HH | KET | LON | FER | BCS | DMI | AMY (SE)[4] | OMY | PER |
| LnVar | ma | -0.27 | -0.13 | -0.46 | -0.14 | -0.35 | -0.36 | 0.26 | 0.76 (0.02) | 0.62 | 0.14 |
| | mm | -0.26 | -0.13 | -0.45 | -0.14 | -0.34 | -0.35 | 0.25 | 0.75 (0.02) | 0.61 | 0.14 |
| | wilm | -0.29 | -0.14 | -0.45 | -0.13 | -0.34 | -0.38 | 0.29 | 0.79 (0.02) | 0.64 | 0.08 |
| | quant | -0.32 | -0.14 | -0.48 | -0.16 | -0.40 | -0.41 | 0.24 | 0.79 (0.02) | 0.64 | 0.12 |
| RawVar | - | -0.31 | -0.10 | -0.21 | -0.29 | -0.12 | -0.32 | -0.04 | 0.20 (0.03) | 0.15 | -0.51 |
| $r_{auto}$ | ma | -0.19 | -0.02 | -0.17 | 0.01 | -0.06 | -0.07 | 0.03 | 0.19 (0.04) | 0.16 | -0.05 |
| | mm | -0.18 | -0.01 | -0.18 | 0.02 | -0.06 | -0.06 | 0.05 | 0.20 (0.03) | 0.18 | -0.04 |
| | wilm | -0.12 | -0.02 | -0.08 | 0.01 | 0.01 | -0.06 | 0.05 | 0.15 (0.04) | 0.10 | -0.09 |
| | quant | -0.21 | -0.03 | -0.15 | -0.02 | -0.09 | -0.10 | -0.03 | 0.16 (0.04) | 0.12 | -0.09 |
| Skew | ma | 0.06 | 0.02 | -0.20 | -0.14 | -0.01 | -0.17 | 0.03 | 0.23 (0.07) | 0.09 | -0.08 |
| | mm | 0.05 | -0.01 | -0.22 | -0.15 | -0.05 | -0.17 | 0.02 | 0.30 (0.07) | 0.04 | -0.04 |

| | UH | HH | KET | LON | FER | DMI | AMY | OMY | PER | |
|---|---|---|---|---|---|---|---|---|---|---|
| wilm | 0.04 | 0.02 | 0.06 | -0.10 | 0.17 | -0.17 | -0.15 | -0.40 (0.06) | -0.24 | -0.32 |
| quant | 0.00 | -0.05 | -0.17 | -0.14 | -0.02 | -0.25 | -0.10 | 0.19 (0.06) | 0.07 | -0.17 |
| AMY | - | -0.15 | -0.15 | -0.37 | 0.07 | -0.38 | -0.22 | 0.68 | - | 0.95 | 0.37 |

[1] Indicator/Trait: LnVar = variance of deviations from lactation curve, RawVar = variance of raw milk yield, $r_{auto}$ = lag-1 autocorrelation of deviations, Skew = skewness of deviations, AMY = average daily milk yield

[2] Curve: ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

[3] Health, longevity, fertility, metabolic, and production traits: UH = udder health, HH = hoof health, KET = ketosis resistance in first lactation, LON = productive longevity, FER = fertility, DMI = dry matter intake, AMY = average daily milk yield from automatic milking system data, OMY = official milk yield produced in 305 days in first lactation, PER = persistency in first lactation.

[4] Genetic correlations between the resilience indicators and average daily milk yield were estimated using a bivariate mixed animal model.

Table 7. Partial genetic correlations between resilience indicators based on different lactation curve fitting methods and commercial traits,

estimated using the MACE procedure and adjusted for average daily milk yield

| Indicator/Trait[1] | Curve[2] | Health, longevity, fertility, metabolic, and production traits[3] | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | UH | HH | KET | LON | FER | BCS | DMI | PER |
| LnVar | ma | -0.23 | -0.03 | -0.29 | -0.29 | -0.10 | -0.31 | -0.54 | -0.18 |
| | mm | -0.22 | -0.03 | -0.28 | -0.28 | -0.09 | -0.29 | -0.53 | -0.17 |
| | wilm | -0.27 | -0.04 | -0.27 | -0.31 | -0.06 | -0.35 | -0.56 | -0.31 |
| | quant | -0.32 | -0.04 | -0.33 | -0.34 | -0.17 | -0.40 | -0.66 | -0.24 |
| RawVar | - | -0.29 | -0.07 | -0.15 | -0.31 | -0.04 | -0.29 | -0.25 | -0.62 |
| $r_{auto}$ | ma | -0.16 | 0.01 | -0.11 | -0.00 | 0.02 | -0.03 | -0.13 | -0.12 |
| | mm | -0.16 | 0.02 | -0.11 | 0.01 | 0.02 | -0.01 | -0.12 | -0.12 |
| | wilm | -0.09 | 0.01 | -0.02 | -0.00 | 0.08 | -0.03 | -0.07 | -0.15 |
| | quant | -0.19 | -0.01 | -0.10 | -0.03 | -0.03 | -0.07 | -0.19 | -0.15 |
| Skew | ma | 0.10 | 0.05 | -0.13 | -0.16 | 0.09 | -0.13 | -0.17 | -0.17 |
| | mm | 0.11 | 0.04 | -0.12 | -0.18 | 0.07 | -0.12 | -0.26 | -0.15 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| wilm | -0.02 | -0.04 | -0.11 | -0.08 | 0.02 | -0.29 | 0.18 | -0.22 |
| quant | 0.03 | -0.03 | -0.11 | -0.15 | 0.06 | -0.21 | -0.31 | -0.25 |

886 [1]Indicator/Trait: LnVar = variance of deviations from lactation curve, RawVar = variance of raw milk yield, $r_{auto}$ = lag-1 autocorrelation of

887 deviations, Skew = skewness of deviations, AMY = average daily milk yield

888 [2]Curve: ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

889 [3]Health, longevity, fertility, metabolic, and production traits: UH = udder health, HH = hoof health, KET = ketosis resistance in first lactation,

890 LON = productive longevity, FER = fertility, DMI = dry matter intake, PER = persistency in first lactation.

Table A1. Residual (above diagonal) and phenotypic correlations (below diagonal) among the resilience indicators and average daily milk yield.

A dash means that no genetic correlation was estimated for this combination

| Trait[1] | | LnVar | | | | RawVar | $r_{auto}$ | | | | Skew | | | | AMY |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Curve[2] | ma | mm | wilm | quant | - | ma | mm | wilm | quant | ma | mm | wilm | quant | - |
| LnVar | ma | - | 0.99 | 0.68 | 0.85 | 0.28 | -0.18 | - | - | - | -0.13 | - | - | - | 0.04 |
| | | | (0.00) | (0.00) | (0.00) | (0.00) | (0.00) | | | | (0.00) | | | | (0.01) |
| | mm | 0.99 | - | 0.63 | 0.80 | 0.24 | - | -0.15 | - | - | - | -0.14 | - | - | 0.04 |
| | | (0.00) | | (0.01) | (0.00) | (0.00) | | (0.00) | | | | (0.00) | | | (0.01) |
| | wilm | 0.73 | 0.69 | - | 0.79 | 0.46 | - | - | 0.25 | - | - | - | -0.06 | - | 0.03 |
| | | (0.00) | (0.00) | | (0.00) | (0.00) | | | (0.01) | | | | (0.00) | | (0.01) |
| | quant | 0.87 | 0.84 | 0.82 | - | 0.37 | - | - | - | 0.12 | - | - | - | -0.23 | 0.02 |
| | | (0.00) | (0.00) | (0.00) | | (0.00) | | | | (0.01) | | | | (0.00) | (0.01) |
| RawVar | - | 0.30 | 0.27 | 0.46 | 0.38 | - | - | - | - | - | - | - | - | - | 0.06 |
| | | (0.00) | (0.00) | (0.00) | (0.00) | | | | | | | | | | (0.00) |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $r_{auto}$ | ma | -0.17 | - | - | - | - | - | 0.97 | 0.74 | 0.85 | -0.08 | - | - | - | 0.10 |
| | | (0.01) | | | | | | (0.00) | (0.00) | (0.00) | (0.00) | | | | (0.00) |
| | mm | - | -0.14 | - | - | - | 0.97 | - | 0.67 | 0.79 | - | -0.19 | - | - | 0.10 |
| | | | (0.01) | | | | (0.00) | | (0.00) | (0.00) | | (0.00) | | | (0.00) |
| | wilm | - | - | 0.23 | - | - | 0.75 | 0.69 | - | 0.82 | - | - | 0.14 | - | 0.06 |
| | | | | (0.01) | | | (0.00) | (0.00) | | (0.00) | | | (0.00) | | (0.01) |
| | quant | - | - | - | 0.10 | - | 0.86 | 0.80 | 0.83 | - | - | - | - | -0.09 | 0.06 |
| | | | | | (0.01) | | (0.00) | (0.00) | (0.00) | | | | | (0.00) | (0.01) |
| Skew | ma | -0.09 | - | - | - | - | -0.08 | - | - | - | - | 0.96 | 0.59 | 0.75 | -0.04 |
| | | (0.01) | | | | | (0.00) | | | | | (0.00) | (0.00) | (0.00) | (0.00) |
| | mm | - | -0.09 | - | - | - | - | -0.19 | - | - | 0.96 | - | 0.60 | 0.77 | -0.04 |
| | | | (0.01) | | | | | (0.00) | | | (0.00) | | (0.00) | (0.00) | (0.00 |
| | wilm | - | - | -0.05 | - | - | - | - | 0.15 | - | 0.59 | 0.59 | - | 0.72 | -0.02 |
| | | | | (0.00) | | | | | (0.00) | | (0.00) | (0.00) | | (0.00) | (0.01) |
| | quant | - | - | - | -0.19 | - | - | - | - | -0.09 | 0.75 | 0.77 | 0.71 | - | 0.00 |
| | | | | | (0.01) | | | | | (0.00) | (0.00) | (0.00) | (0.00) | | (0.00) |

| AMY | - | 0.27 | 0.26 | 0.25 | 0.25 | 0.10 | | 0.11 | 0.11 | 0.07 | 0.07 | -0.02 | -0.01 | -0.05 | 0.01 | - |
| | | (0.00) | (0.00) | (0.00) | (0.00) | (0.01) | | (0.01) | (0.00) | (0.00) | (0.00) | (0.00) | (0.00) | (0.00) | (0.00) | |

[1]Trait: LnVar = Variance of deviations from lactation curve, RawVar = Variance of raw milk yield, $r_{auto}$ = autocorrelation of deviations, Skew = skewness of deviations, AMY= average daily milk yield

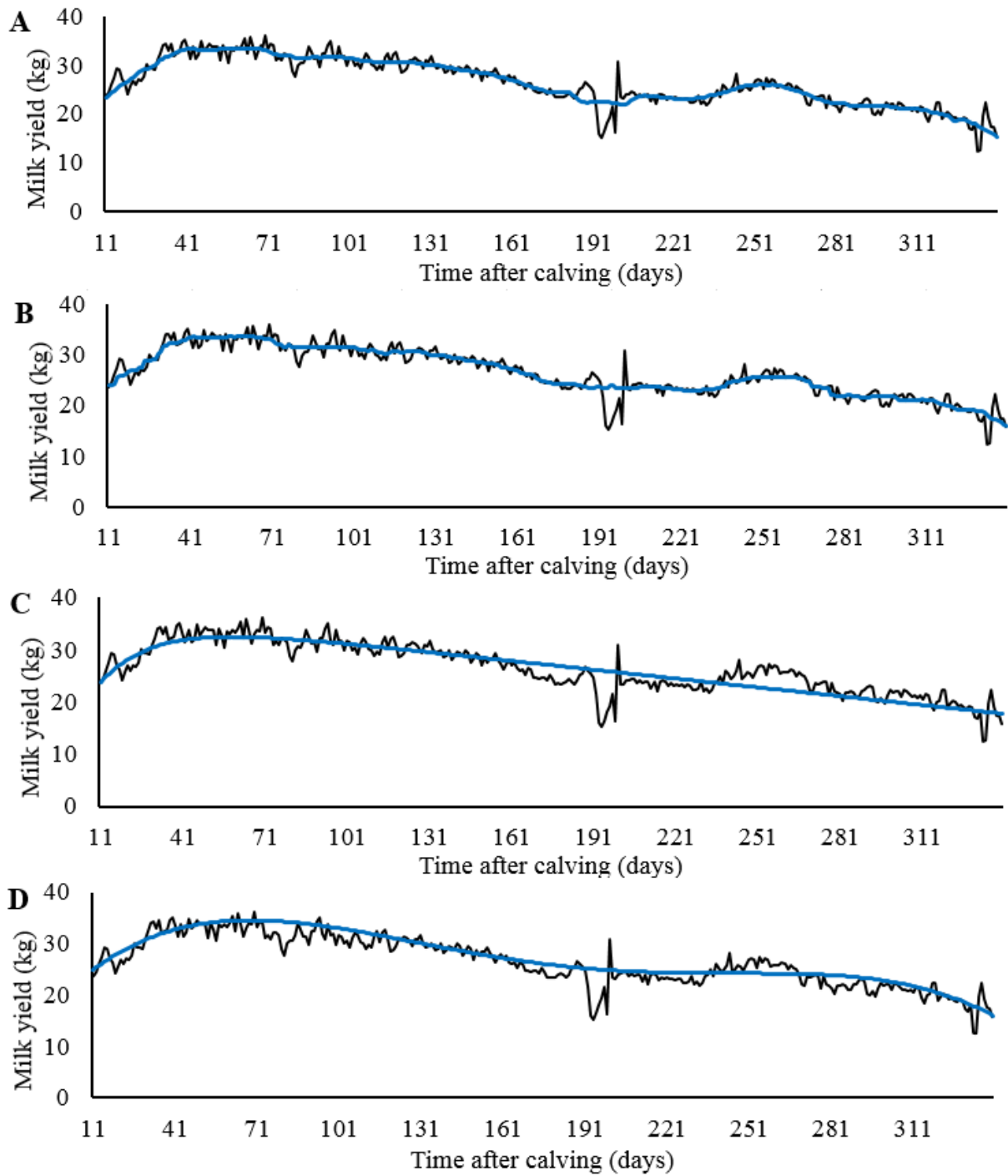[2]curve: ma = moving average, mm = moving median, quant = quantile regression, wilm = wilmink curve

**FIGURES**

898     Figure 1: A: Observed (black line) and predicted (blue line) daily milk yield as a function of

899     time after calving in days of an example cow. B: Deviations from predicted milk yield as a

900     function of time after calving in days of the same example cow.



901
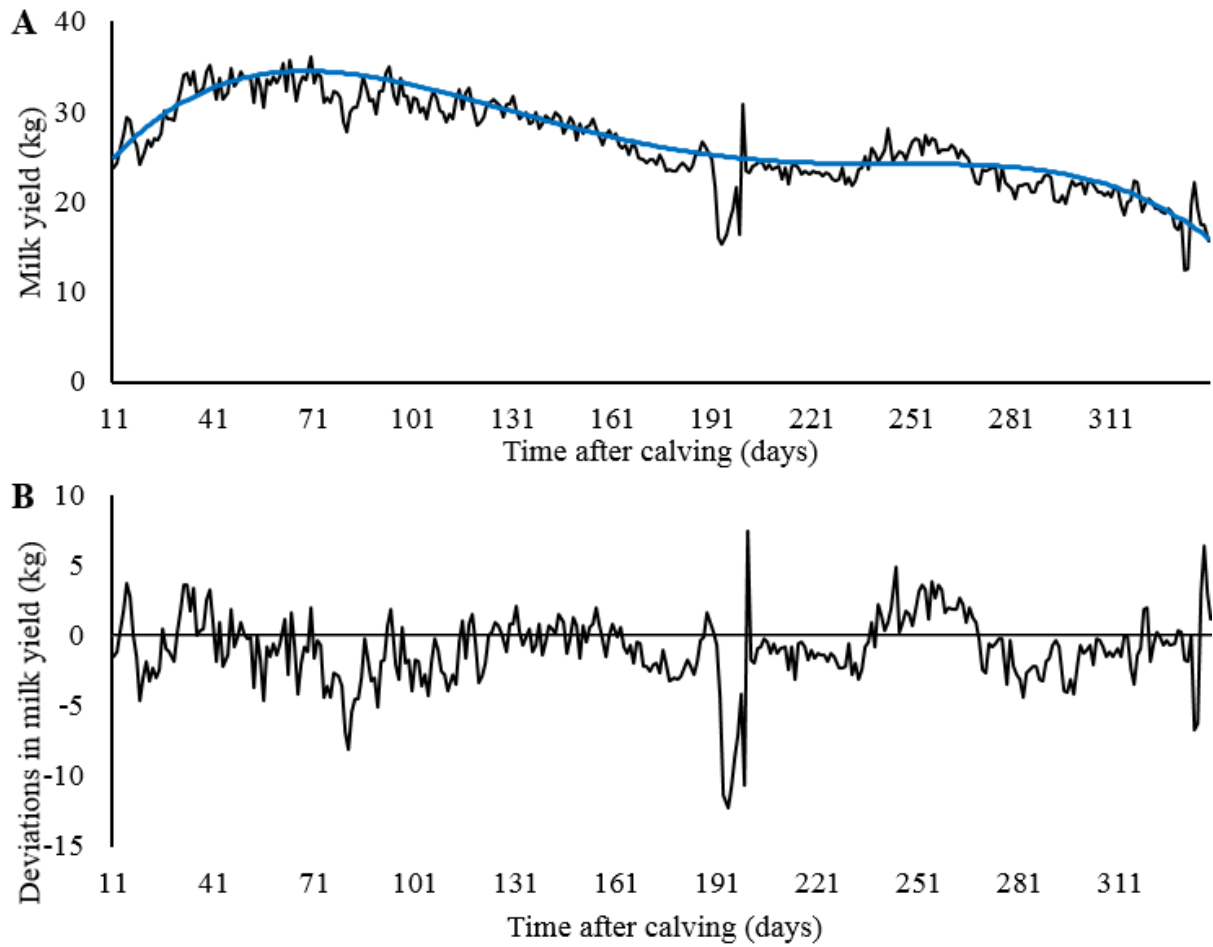
902     Poppe – Figure 1

903    Figure 2: Examples of lactation curve fitting methods for an example cow. Black lines show

904    observed milk yield and blue lines show predicted milk yield. A: moving average, B: moving

905    median, C: Wilmink curve, D: quantile regression



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907    Poppe – Figure 2