

Genetic improvement of resilience in dairy cattle using longitudinal data

Marieke Poppe



Propositions

1. Daily milk yield is the only phenotype needed to breed for improved resilience.
(this thesis)
2. The second best option to select for resilience is the breeding value for body condition score.
(this thesis)
3. Governmental funding of research without clear application is a frivolous activity we cannot afford facing the challenges of today.
4. The request of scientific journals for potential reviewers threatens the objectivity of their peer review process.
5. Transferring personnel between departments within a hospital decreases resilience of that hospital.
6. Exposure makes resilient.

Propositions belonging to the thesis, entitled

Genetic improvement of resilience in dairy cattle using longitudinal data

Marieke Poppe
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Genetic improvement of resilience in dairy cattle using longitudinal data

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Genetic improvement of resilience in dairy cattle using longitudinal data

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Abstract

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Resilience is the ability of cows to be minimally affected by, and to quickly recover from environmental disturbances, such as pathogens, extreme weather, or changes in feed quality. Resilience is important for welfare of cows and work pleasure of farmers, especially given an expected increase of disturbances in the future. This thesis focuses on developing indicators of resilience from longitudinal data, based on the expectation that longitudinal data records show response patterns to disturbances, informative about resilience. Resilience indicators based on response patterns can potentially assist in selecting the genetically most resilient animals for breeding, and in identifying resilience at herd level. The main focus of this thesis was on the resilience indicators 'variance' and 'autocorrelation' of daily deviations from expected values of milk yield and step count. Resilience is indicated by low variance (small deviations from baseline) and low lag-1 autocorrelation (weak dependency between subsequent deviations - quick recovery). Variance and autocorrelation of daily deviations from expected milk yield were heritable (0.21 and 0.09, respectively) and both were genetically similar within and between lactations. Variance seems informative about vulnerability and strength of response to disturbances, based on genetic correlations with milk loss upon real-life disturbances and with health, longevity and fertility. Autocorrelation had a favorable genetic correlation with recovery rate upon disturbances. Furthermore, variance was associated with lifetime gross margin, which confirms its economic importance. Levels of variance and autocorrelation differed considerably between herds, suggesting herd management plays a role in resilience. When based on step count instead of milk yield, variance and autocorrelation were heritable (0.14 and 0.04), and autocorrelation was favorably genetically correlated with health traits and fertility. However, variance had unfavorable genetic correlations with health. Additional traits based on step count were also heritable (especially mean step count; 0.45), but more research is needed into their relations with resilience. Genetic selection on a resilience index based on variance and autocorrelation of milk yield deviations, and potentially autocorrelation based on step count deviations, is expected to result in more resilient cows, that are less affected by disturbances and that recover more quickly.

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General introduction

1.1 Introduction

For many decades, focus has been on improving productivity of livestock, both through genetic selection and optimization of the environment (Ge et al., 2016). Despite more recent focus on improving resistance to individual diseases, society still expresses concerns about animal welfare (Ge et al., 2016; Clay et al., 2020) and farmers express a desire for problem-free cows (Elgersma et al., 2018; Berghof et al., 2019b; Egger-Danner and Heringstad, 2020). Especially in the light of climate change, which will likely lead to more environmental disturbances in the near future (Boichard and Brochard, 2012; Urruty et al., 2016), we need animals that can cope with disturbances well (Phocas et al., 2016). Such animals are called ‘resilient’, and likely have good welfare and are easy to manage for the farmer (Colditz and Hine, 2016).

There are several ways to improve resilience of animals, and one of them is through genetic selection. Genetic selection is the selection of the genetically ‘best’ animals as parents for the next generation (Falconer and Mackay, 1996). In case of resilience, the ‘best’ animals would be the most resilient animals. By selecting the genetically most resilient animals as parents, the next generation will be on average more resilient than the previous generation. However, as resilience is a broad concept, it is difficult to quantify it and thus to identify which animals are genetically most resilient.

When traits are difficult to measure on selection candidates, breeding programs often make use of ‘indicator traits’ (Falconer and Mackay, 1996; Miglior et al., 2017). Indicator traits are easily measurable traits that are heritable and are genetically correlated with the trait of interest. Selection on the easily measurable indicator trait will then result in improvement of the trait of interest as well. This thesis focuses on the development of indicator traits for the complex trait resilience from easily available, automatically measured longitudinal traits in dairy cattle.

In this introduction, I will first describe the history of genetic selection, and how this led to the current need for genetic selection for resilience. I will then focus on previous research into selection for resilience. Finally, I will introduce new opportunities for quantifying resilience, which lead to the main research topics of this thesis.

1.2 History of genetic selection in livestock

To understand the need for genetic selection for more resilient livestock, it is useful to first get an overview of the genetic selection in the past that led to the livestock populations we have today. Genetic selection started off with selection on

only production traits, which carried on until the '90s in most countries. Focus was on milk yield in dairy cattle (Miglior et al., 2005), growth and carcass traits in pigs (Rauw et al., 1998; Knap and Rauw, 2009), and either meat or egg production in poultry (Siegel et al., 2009). This selection was successful, because together with improved feed quality and management, it resulted in a yearly increase in milk yield of around 100-125 kg per lactation (Veerkamp et al., 2009), a yearly increase in growth rate in Dutch pigs of about 5 grams per day (Rauw et al., 1998), and a yearly decrease in age at a given body weight in broilers of about 1 day (Rauw et al., 1998).

Although selection on production was successful, negative consequences of increased productivity on other life functions were observed through unfavorable genetic correlations. In dairy cattle, negative trends were reported for fertility (Rauw et al., 1998; Veerkamp et al., 2009) and health (Rauw et al., 1998; Miglior et al., 2005). In pigs, a reduced ability to deal with suboptimum conditions was reported (Knap and Rauw, 2009). In poultry, decreased fertility and increased heart failure, ascites, bone disorders, and mortality were observed (Rauw et al., 1998). To mitigate the negative effects of selection for production on other life functions and to improve 'robustness' (Veerkamp et al., 2013), traits related to fertility, health, and survival were added to the breeding goal (Miglior et al., 2005, 2017; Neeteson-van Nieuwenhoven et al., 2013; Phocas et al., 2016). Increasing emphasis has been placed on these new traits at the expense of production ever since, and the negative trends observed for these health and fertility traits have since then been reversed to a certain extent (Siegel et al., 2009; Kapell et al., 2012; Neeteson-van Nieuwenhoven et al., 2013; Miglior et al., 2017; Brito et al., 2021).

1.3 The desire for genetic selection for resilience

Until now, the selection on health traits has focused on specific disorders that occur often and have large economic impact (Phocas et al., 2016), such as clinical mastitis (Heringstad et al., 2000; Nielsen et al., 2000; de Haas et al., 2008; CRV, 2020c) and claw disorders (Alkhoder et al., 2010; Gernand et al., 2013; CRV, 2020d; Egger-Danner and Heringstad, 2020). However, there is desire (at least in developed countries) for less controlled, more natural animal production systems, where multiple pathogens and other environmental disturbances may act (Phocas et al., 2016). In addition, even more environmental disturbances, such as heat waves, are expected in future due to climate change (Maracchi et al., 2005; Sejian et al., 2015; Ge et al., 2016; Brito et al., 2021). Furthermore, herd sizes are increasing and more animals have to be managed per person (Fraser, 2008; ten Napel et al., 2009). Under such conditions, a more holistic approach is desired to

improve the general capacity to be healthy – to improve resilience (Phocas et al., 2016; Friggens et al., 2017). The breeding goal should thus be broadened even further with resilience traits. The following paragraphs will explain the concept of resilience in more detail, what efforts have been made into studying genetic improvement of resilience, and will then introduce new methods that could be used to genetically improve resilience.

1.4 Description of resilience and related concepts

The concept of resilience was first introduced in the field of ecology. Holling (1973) defined resilience as the ability of systems to absorb disturbances and maintain the same relationships between the components of the system. Resilience is still a hot topic in ecology, and many efforts are being made to predict so-called ‘critical transitions’ or ‘tipping points’ of ecosystems, where systems suddenly switch to a different state (Dakos et al., 2008, 2012; Scheffer et al., 2009). Through the years, other scientific disciplines have adopted the term as well, such as psychology (Masten, 2001; Rutter, 2007; Amstadter et al., 2016), disaster management (Rose, 2007; Whitson and Ramirez-Marquez, 2009), and gerontology (Gijzel et al., 2017, 2019). In livestock, the concept was introduced during the last decade, and the definition adopted in this thesis is ‘the capacity of the animal to be minimally affected by a disturbance or to quickly recover’ (Colditz and Hine, 2016; Ge et al., 2016; Berghof et al., 2019b).

In addition to the definition of resilience adopted in this thesis, many other definitions of resilience for livestock exist, some of which are broader and some more specific. A broader definition was given by Adriaens et al. (2020), who defined resilience in dairy cows as the probability to complete several lactations, by avoiding early culling by coping well with farm management conditions. Avoiding early culling is determined by the ability to be minimally affected by disturbances or to quickly recover, and by other traits such as milk yield and fertility. Other studies used the more specific definition of disease resilience, which only focuses on resilience to pathogenic or parasitic disturbances (Albers et al., 1987; Bisset and Morris, 1996). Animals can have good disease resilience and keep functioning well when faced with pathogens due to a combination of disease resistance and tolerance. Resistance is the ability to limit pathogen burden and tolerance is the ability to limit disease severity (Albers et al., 1987; Råberg et al., 2007; Knap and Doeschl-Wilson, 2020), for example through tissue damage control (Soares et al., 2014).

Before the term resilience was introduced in animal science, another closely related term was used: robustness. This term was adopted around the time that

the negative effects of selection on milk yield were recognized (Klopčič et al., 2009; Veerkamp et al., 2013). Like resilience, robustness has many definitions and some of them are more closely related with resilience than others. A definition of robustness closely linked to the definition of resilience of Adriaens et al. (2020), is the ability to carry on doing the various things an animal needs to do in the face of environmental constraints, to favor its future ability to reproduce (Friggens et al., 2017). Other studies state that robustness is different from resilience in the sense that robustness covers the ability of animals to function and maintain homeostasis in a broad range of environments, while resilience covers the ability to function in the face of short-term changes in one environment (Knap, 2005; ten Napel et al., 2009; Colditz and Hine, 2016). Although concepts such as disease resilience and robustness are not the same as the definition of resilience adopted in this thesis, they all encompass the desire for ‘trouble-free animals’. Therefore, the terms can often be used interchangeably.

1.5 Previous efforts into genetic selection for resilience or robustness

In the past 15 years, many studies addressed the need to breed for improved robustness, which is in many ways similar to improvement of resilience. The need for improved robustness was sparked by the unfavorable genetic trends for health and fertility mentioned earlier (Klopčič et al., 2009; Veerkamp et al., 2013). A book was published to summarize the state of the art knowledge on robustness in dairy cattle (Klopčič et al., 2009), and the RobustMilk project was started (Veerkamp et al., 2013). Robustness was a hot topic in pigs as well (Knap, 2005). In these studies, a number of methods to genetically improve robustness were proposed, that can be expected to improve resilience too.

The first method was to broaden breeding goals by adding additional health and fitness traits (Knap, 2005; Veerkamp et al., 2013). This method requires recording of new phenotypes on a large scale, for example through mid-infrared spectroscopy of milk (Veerkamp et al., 2013). Since the desire for improved robustness was expressed, indeed new traits have been included in genetic evaluation in certain countries, such as ketosis resistance (Vosman et al., 2015) and hoof health (Egger-Danner and Heringstad, 2020) in dairy cattle.

The second method to improve robustness, specifically for dairy cattle, was to decrease negative energy balance in the first period of lactation (Veerkamp et al., 2013). So far, specific selection against negative energy balance has not been performed. However, for example persistency of the lactation curve is genetically evaluated in the Netherlands (CRV, 2020g) and better persistency may be related

with a less severe negative energy balance (Sölkner and Fuchs, 1987; Dekkers et al., 1998). Furthermore, data is becoming available on feed intake which is used for selection for feed efficiency (Berry et al., 2014; Pryce et al., 2014; Martin et al., 2021b). Automatic recording of e.g. body condition score is an emerging area of study as well (e.g. Salau et al., 2014; Hansen et al., 2018; Song et al., 2019). These new sources of data may offer an opportunity for genetically improving energy balance (Martin et al., 2021a).

A third method, specifically for dairy cattle, was to select for more robust conformation (Hamoen et al., 2009). A cow with robust conformation is a cow with intermediate body condition score, body depth, rump width and chest width. The robustness score has been applied in The Netherlands in the overall conformation score, but was removed again due to lack of clarity of the trait for farmers (Veeteelt, 2015).

The last proposed method to improve robustness was selection for lower environmental sensitivity (Knap, 2005; Veerkamp et al., 2013). Two types of environmental sensitivity exist: macro- and micro-environmental sensitivity (for a review, see lung et al. (2020)). Macro-environmental sensitivity refers to how sensitive performance is to a measurable aspect of the environment, such as ambient temperature (Berghof et al., 2019b). Macro-environmental sensitivity can be improved by applying reaction norm models. A reaction norm model is a genetic model where the trait of interest is regressed on an environmental descriptor, such as temperature-humidity index. With this model, animals receive a breeding value for the level and the slope of the trait. A steeper slope means that the animal is more environmentally sensitive. Many studies have been performed on selection for macro-environmental sensitivity (e.g. Calus et al., 2005; Bohmanova et al., 2008; Mulder et al., 2013a; Rashidi et al., 2014; Herrero-Medrano et al., 2015; Carabaño et al., 2017; Nguyen et al., 2017b). Nevertheless, to my knowledge such a model is in practice only being applied for heat tolerance in dairy cattle in Australia (Nguyen et al., 2017b).

Micro-environmental sensitivity refers to how sensitive performance is to temporary changes within the environment, and is therefore similar to the definition of resilience used in this thesis. Studies that focused on selection for micro-environmental sensitivity used advanced statistical models on variability of available traits, within family groups or within animals. The hypothesis for family groups, is that family groups with high variability in performance within them, have high micro-environmental sensitivity (or low uniformity). The hypothesis for individual animals, is that a trait measured multiple times on the same animal is more variable for animals with high than with low micro-environmental sensitivity.

Several models have been proposed that estimate genetic parameters for the mean and the residual variance of a trait, for example the double hierarchical generalized linear model (Rönnegård et al., 2010; Felleki et al., 2012) and Bayesian methods (Sorensen and Waagepetersen, 2003). Using these models, genetic variance of residual variance has been shown both based on a single record per animal (e.g. SanCristobal-Gaudy et al., 1998; Ibáñez-Escriche et al., 2008; Mulder et al., 2009, 2013a), and based on multiple records within individual animals (Mulder et al., 2013b; Rönnegård et al., 2013; Vandenplas et al., 2013; Sell-Kubiak et al., 2015; Ehsaninia et al., 2019). Nevertheless, these methods are so far not applied in breeding programs, although uniformity of birth weight is selected for in many pig breeding programs (Damgaard et al., 2003; Sell-Kubiak et al., 2015). Reasons that double hierarchical generalized linear models and Bayesian methods are not applied in breeding programs yet, may be that the models are too computationally intensive (Felleki et al., 2012), or are too difficult to understand by users.

In summary, many methods for improving robustness through genetic selection have been proposed, but a limited number of them are so far applied in practice. In more recent years, terminology has shifted from robustness to resilience, but still the same question applies: how can we select for cows that have the general capacity to cope with disturbances?

1.6 Longitudinal sensor and automated traits offer opportunities for genetic selection for resilience

New opportunities to develop resilience phenotypes have arisen with the emergence of sensor techniques and other automated techniques, such as automatic milking systems, electronic milk recording, and automated feeders (Rutten et al., 2013; Ellen et al., 2019). Such techniques provide data that are measured very frequently on individual animals. This makes it possible to monitor performance and behavior of animals from day to day, which was not possible with older types of longitudinal data that were less frequent (e.g. test-day production records). Many traits measured by sensors and other automated techniques are sensitive to disturbances. For example, milk yield and activity in dairy cattle are sensitive to many disturbances, such as diseases and heat stress (Detilleux et al., 1994; Fourichon et al., 1999; Rajala-Schultz et al., 1999a; Kadzere et al., 2002; Edwards and Tozer, 2004; Bernabucci et al., 2010; Abeni and Galli, 2017; Carabaño et al., 2017). Similarly, activity and feed intake in pigs are sensitive to several diseases (Cornou et al., 2008; Munsterhjelm et al., 2015; van der Zande et al., 2020). Because of the vulnerability of such traits to disturbances, patterns of response and recovery can be observed in the daily data of an individual animal.

Response and recovery are the main components of the definition of resilience adopted in this thesis – the capacity to be minimally affected by disturbances, and if affected, to quickly recover (Colditz and Hine, 2016; Berghof et al., 2019b). Therefore, traits that are recorded in a frequent fashion by sensors and automated systems offer a great opportunity to quantify resilience.

Signals from longitudinal data that indicate resilience of a system have been proposed earlier in the field of ecology. These signals indicate how likely a system is to change to a different state, e.g. from healthy to diseased (Scheffer, 2009). The theory states that systems that are reaching a critical transition or tipping point become very slow in recovering from small perturbations and will show increased variance and lag-1 autocorrelation in the pattern of fluctuations of longitudinal traits measured on the system. Variance explains size of the fluctuations and autocorrelation explains similarity between subsequent time points (see Box 1.1 for a more detailed explanation). Assuming that most systems, animals included, are permanently exposed to small natural perturbations, the variance and lag-1 autocorrelation of the deviations of the system from its normal state will increase if the system is close to a critical transition. If we would translate this to animals, then non-resilient animals would show an increased autocorrelation and variance in the deviations from their baseline for traits such as milk production, activity, and growth rate (Scheffer et al., 2018). In more simple words: non-resilient animals will deviate more extremely from their baseline upon disturbances (increased variance) than resilient animals, and will recover less quickly (increased autocorrelation). The increase in variance as a sign of reduced resilience is similar to the residual variance as a measure of micro-environmental sensitivity mentioned earlier (Rönnegård et al., 2010; Mulder et al., 2013a). An additional signal of resilience of a system is the skewness of the deviations of a trait from its normal value (Guttal and Jayaprakash, 2008; Scheffer et al., 2009). As most perturbations force the level of a trait in the same direction, the distribution of the deviations is expected to be skewed in case of response to disturbances.

1.7 Gaps in knowledge

The variance, autocorrelation, and skewness of deviations of frequently measured longitudinal traits from baseline are promising resilience indicators in livestock, confirmed by the large number of studies published about these or similar resilience indicators by others throughout the course of this PhD (Elgersma et al., 2018; van Dixhoorn et al., 2018; Berghof et al., 2019a; Putz et al., 2019; Adriaens et al., 2020; Cheng et al., 2020; van der Zande et al., 2020; Kok et al.,

Box 1.1: Explanation of critical slowing down and indicators of resilience

Difference in resilience between systems can be illustrated using a ‘ball in a cup’ diagram (Figure 1.1, adapted from Scheffer et al. (2009; 2018)). The ball is the system and the cup is a steady state. An external disturbance can push the ball along the wall of the cup, and if the disturbance is big enough, it can push the ball over the edge into a different state (e.g. from healthy to ill). In a resilient system, the cup is deep and has steep walls (Figure 1.1A). When an external force pushes the ball away from the bottom of the cup, it will not easily be pushed over the edge, unless the force is extremely big. The ball will quickly roll back to the bottom because of the steep edges as well. In a non-resilient system, the cup is shallow with non-steep edges (Figure 1.1B). The ball therefore easily gets pushed over the edge, or if the disturbance is not big enough to push it over the edge, the ball will roll back to the bottom only slowly. The phenomenon that systems close to a critical transition return back to their basic state upon minor disturbances only slowly is called ‘critical slowing down’.

Critical slowing down is characterized by slower fluctuations in variables that are vulnerable to disturbances: the variables return back to baseline more slowly after minor disturbances. As the fluctuations become slower, the state of the system becomes more similar from one time point to the next, which can be observed through an increased lag-1 autocorrelation, which is the correlation between observations on subsequent time points. As the fluctuations become slower, a cumulative effect of subsequent disturbances on the variable of interest can be observed – a disturbance pushes the variable away from equilibrium already before the variable has recovered from the previous one. This way the deviations of the variable from baseline become larger, which can be observed through an increase in variance.

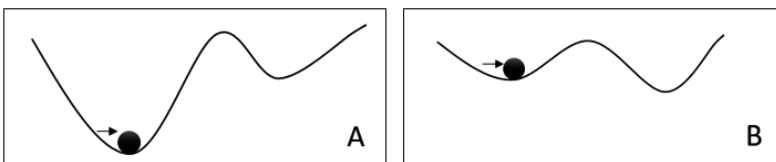


Figure 1.1 Ball in a cup diagram. The cup is the steady state, the ball is the system and the arrow is an external perturbation. A: resilient system, B: less resilient system. Figure adapted from Scheffer et al. (2009; 2018).

2021). However, the usefulness and benefits of these resilience indicators were at the start of this PhD only based on theory, and therefore needed investigation and validation with practical data. An indication that variance of longitudinal traits may be heritable was provided by studies on micro-environmental sensitivity, where genetic variation was shown for residual variance of test-day milk yield and somatic cell score (Rönnegård et al., 2013; Vandenplas et al., 2013; Ehsaninia et al., 2019). However, these studies did not have data with the same frequency as we have nowadays with sensor and automated traits. Variance of more frequently measured traits (e.g. daily) may be more informative about resilience than variance of e.g. test-day milk yield, because they are able to show complete response patterns to disturbances. The first main question that therefore remains to be answered is: are resilience indicators based on frequently measured automated traits heritable, and will selection on these traits really result in more resilient animals? Moreover, it is important to investigate if selection for resilience has economic advantages. Economic advantages are to be expected through benefits for health and longevity (Friggens et al., 2017), and favorable effects on labor requirements (Berghof et al., 2019b), but have not been tested using real data before. Furthermore, most studies focus on either genetics of resilience or phenotypic prediction of resilience on individual animals. However, herd management is expected to have a large effect on resilience as well, through effects on the number and severity of disturbances on farm and the resilience of cows to those disturbances. Herd management has so far been overlooked and therefore needs investigation. All these gaps in knowledge lead to the aim and outline of this thesis explained below.

1.8 Aim and outline of thesis

The overall aim of this thesis was to study the use of variance, autocorrelation, and skewness of daily recorded data as resilience indicators for genetic selection in dairy cattle. The structure of the research chapters of this thesis is summarized in Figure 1.2, and consists of 2 categories: (1) genetics of resilience indicators based on milk yield (Chapters 2-4) or step count data (Chapter 5), and (2) relevance of resilience indicators based on milk yield in relation to farm management (Chapters 6) and farm profit (Chapter 7). All knowledge gained in these chapters is generally discussed in Chapter 8. A more detailed description of the chapters is as follows:

In **chapter 2**, I estimate genetic variance and heritability of variance, autocorrelation, and skewness based on daily milk yield residuals from fitted lactation curves in first lactation. I investigate four different lactation curve fitting methods. Furthermore, I show genetic correlations of resilience indicators with

1 General introduction

other traits related to resilience that are currently in the breeding goal. In **chapter 3**, I extend the analysis of the most suitable resilience indicators from chapter 2 based on the most suitable lactation curve fitting method to the second and third lactation. Furthermore, I investigate if these traits are more informative about resilience when they are based on shorter periods within the lactation. In **chapter 4**, I validate if selection for the resilience indicators will result in more resilient animals that are minimally affected by disturbances and that recover quickly. Therefore, I estimate genetic correlations of the resilience indicators with traits describing response and recovery to actual disturbances. The studied disturbances are a heat wave and unknown disturbances at herd level. Furthermore, I investigate if selection for the resilience indicators based on a certain set of daughter phenotypes will result in lower realized variance and autocorrelation in other daughters in other environments at other time points by estimating genetic correlations between daughter groups. In **chapter 5**, I again perform a genetic analysis on resilience indicators, but this time the resilience indicators are based on daily step count generated by activity sensors. The rationale behind this, is that activity is more directly affected by disturbances than milk yield: often first a change in activity will be observed, followed by a decrease in milk yield. In **chapter 6**, I investigate if herd management has an effect on the resilience indicators based on milk yield, by studying if levels of the resilience indicators differ between herds and years. Furthermore, I investigate associations between the resilience indicators at herd level and other herd performance traits. In **chapter 7**, I investigate associations between the resilience indicators based on milk yield in lactation 1 and lifetime profit. Lifetime profit is expressed as the difference between all revenues and all costs generated throughout a cows' life. Finally, **chapter 8** contains a general discussion of the thesis. In this chapter, I first discuss considerations to take into account learnt in this thesis when calculating resilience indicators from longitudinal data. I finally discuss the application of the resilience indicators from this thesis in breeding programs.

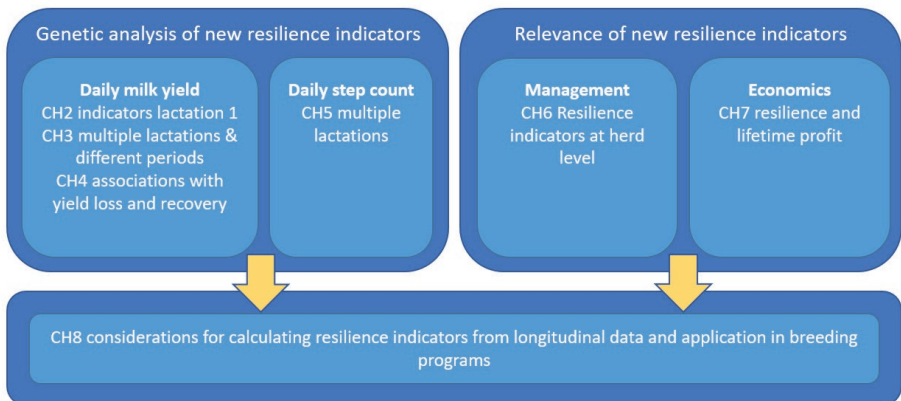


Figure 1.2 Structure of the research chapters of this thesis. CH = chapter.

2

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 or heat waves, is called resilience. To improve resilience through breeding, we need resilience indicators, which could be based on the fluctuation patterns in milk yield resulting from disturbances. The aim of this study was to explore 3 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 to 0.24), r_{auto} (0.08 to 0.10) and Skew (0.01 to 0.02), and the genetic correlations among the indicators were weak to moderate. For r_{auto} and Skew, genetic correlations with 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, lower LnVar was genetically associated with better udder health (genetic correlations from -0.22 to -0.32), better longevity (-0.28 to -0.34), less ketosis (-0.27 to -0.33), better fertility (-0.06 to -0.17), higher body condition score (-0.29 to -0.40), and greater dry matter intake (-0.53 to -0.66) at the same level of milk yield. These correlations support LnVar as an indicator of resilience. Of all 4 curve-fitting methods, LnVar based on quantile regression systematically had the strongest genetic correlations with health, longevity, and fertility traits. Thus, quantile regression is considered the best curve-fitting method. In conclusion, LnVar based on deviations from a quantile regression curve is a promising resilience indicator that can be used to breed cows that are better at coping with disturbances.

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

2.1 Introduction

Cows differ in their ability to cope with environmental disturbances such as pathogens, heat waves, and changes in feed composition and feed quantity. A cow that is unaffected by a disturbance, or that quickly returns to her normal level of functioning, is labeled resilient (Colditz and Hine, 2016; Berghof et al., 2019b). Resilience could be improved through genetic selection, but to do so we need to measure it in individual cows. Several studies have quantified responses to and recovery from an experimental disturbance in animals (Friggens et al., 2016; Revilla et al., 2019). However, such challenge experiments cannot be carried out routinely on commercial farms. Moreover, challenge experiments focus on a single type of disturbance, whereas our interest is in improving the general resilience to unknown disturbances.

Alternatively, a data-driven approach can be used. Scheffer et al. (2018) proposed methods to quantify resilience in cows using frequently measured data. These methods rely on the assumption that cows are constantly subject to unknown disturbances, which result in fluctuations in frequently measured traits. Cows with few fluctuations are less affected by disturbances than are cows with more fluctuations. Therefore, the fluctuation pattern is expected to be informative about resilience. Several resilience indicators describing fluctuations in frequently measured traits have been suggested, such as the variance of the trait, which indicates the variability of the frequently measured trait, the lag-1 autocorrelation of the trait, which indicates stretches of values above or below the expected level, and skewness of the trait, which indicates asymmetry (Scheffer et al., 2018; Berghof et al., 2019b). Until now, it has been difficult to validate resilience indicators by relating them to response to disturbances, because of the lack of data on disturbances. However, genetic analysis can be used to better understand the biology of a trait and, as such, increase our understanding of new resilience indicators, similar to validating subjectively scored traits such as body condition score (Veerkamp et al., 2002).

A trait that is frequently measured and that shows response to disturbances is milk yield. Variance of milk yield has been studied by several researchers. Elgersma et al. (2018) showed that variance of daily recorded milk yield was heritable and that cows with a lower variance had genetically better udder health, less ketosis and better longevity. Therefore, variance of daily milk yield has potential as a resilience indicator. However, Elgersma et al. (2018) did not account for the lactation curve shape, which is expected to influence the level of variance in milk yield. Other studies showed genetic variation in environmental variance in milk yield using a random regression model, which did account for lactation curve shape

(Rönnegård et al., 2013; Vandenplas et al., 2013; Ehsaninia et al., 2019). However, these authors used test-day records, which are not frequent enough to detect all fluctuations in milk yield. Overall, there is room for improvement of variance in milk yield as a resilience indicator. Furthermore, autocorrelation and skewness of daily recorded milk yield may provide additional information about resilience.

The aim of this study was to explore the use of variance, autocorrelation and skewness of deviations in daily milk yield level from a lactation curve as indicators for breeding resilient cows. We explored 4 methods to fit the lactation curve: moving average, moving median, quantile regression, and Wilmink curve. The heritabilities of all resilience indicators were estimated, as well as genetic correlations among the resilience indicators and genetic correlations among the curve fitting methods. In addition, genetic correlations between the resilience indicators and health, production, longevity, fertility, and metabolic traits were estimated.

2.2 Materials and methods

In this study, we performed a genetic analysis on 3 potential resilience indicators. The initial data contained 1,782,373,113 milk yield records on 1,120,550 cows, obtained during single milk visits to automatic milking systems (AMS) and conventional milking systems. Potential resilience indicators were calculated from these data for 198,754 first-parity Holstein Friesian cows milked by AMS (see Data Editing section). Calculation of potential resilience indicators was performed in 2 steps: (1) fitting of individual lactation curves and (2) defining resilience indicators based on deviations from lactation curves. We will first describe the 2 steps that generated the resilience indicators, followed by data editing and genetic analysis.

2.2.1 Fitting individual lactation curves

The aim of fitting individual lactation curves for each cow based on daily milk yield records was to predict the expected milk yield of a cow at each day. Ideally, a fitted lactation curve would be as close as possible to the curve that a cow would have realized in the absence of disturbances, because then deviations from the curve would contain the most information about responses to disturbances. The deviations from such a curve could thus be used to indicate resilience (see Figure 2.1 for an example of a fitted lactation curve and the deviations from that lactation curve). Fitting a lactation curve that a cow would have realized in the absence of disturbances was difficult, because information about disturbances was lacking, and disturbances may even be cow-specific and unknown. Therefore, different methods were explored for fitting the individual lactation curves using only the

daily milk yield records as input. The choice of the best curve-fitting method is, by definition, arbitrary. However, the results of this study will generate insight into which method has most potential and how sensitive genetic parameters are when changing the curve-fitting method. There are 2 generic ways of fitting a trend through a time series: nonparametric trend estimation and model-based estimation (Brockwell and Davis, 2016). Because we did not know which method would generate the best results, we decided to explore both. We used 4 methods: 2 nonparametric (moving average and moving median), and 2 model-based methods (the Wilmink lactation curve (Wilmink, 1987) and a quantile polynomial regression method). See Figure 2.2 for illustrations of the 4 lactation curve fitting methods.

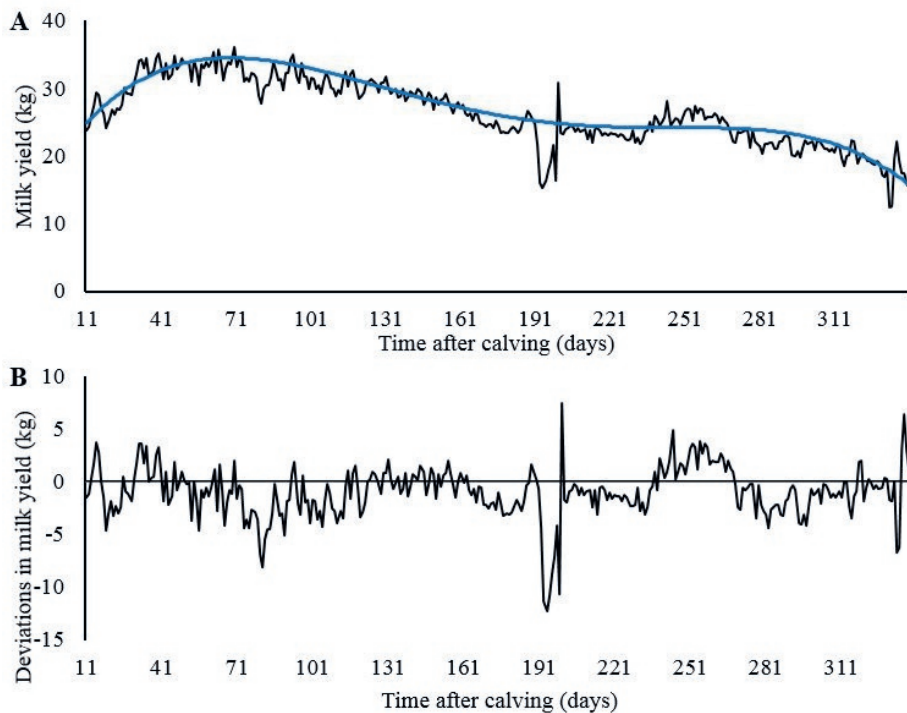


Figure 2.1 (A) Observed (black line) and predicted (blue line) daily milk yield as a function of time after calving (in days) of an example cow. (B) Deviations from predicted milk yield as a function of time after calving (in days) of the same example cow.

2 Resilience indicators based on milk yield

2.2.1.1 Nonparametric trend estimation

The first nonparametric method was a 2-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 we decided to focus on a window of 21 days. Because a moving average is relatively sensitive to drops in milk yield, we also decided to 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 mean, 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 the moving average and moving median is that they are flexible, because expected yields are dependent only on the data points that are close in time. However, the risk is that the moving average and moving median may be too flexible, which results in lost information on drops in milk yield in the deviations of the curve.

2.2.1.2 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 , β_0 is related to the level of production, β_1 describes the production decrease after the peak yield, β_2 describes the increase in milk yield at the start of the lactation, and ε is the error term. The regression coefficients were estimated for each cow using the `lm` function in R and were then 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, 2018g), 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 ε 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, 2018g). 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 the absence of disturbances. Whereas classical regression models estimate the conditional mean milk yield given certain values of DIM, quantile regression models estimate the conditional median or other quantile (Koenker, 2005). By using a quantile higher than 0.5, low milk yield values have less influence on the predicted milk yield curve than do high milk yield values. In other words, drops in milk yield have less influence on the predicted milk yield curve when using quantile regression with a quantile greater than 0.5 than when using classical linear regression, and the negative deviations from the quantile regression curve are larger. As a result, a quantile regression curve using a quantile greater than 0.5 was expected to better match the potential milk yield in absence of disturbances than was a classical linear regression curve and, thus, was expected to generate deviations that contain more information on resilience. Different quantiles higher than 0.5 were explored, but upon visual inspection of fitted curves for random cows from the data set, we decided to focus only on the 0.7 quantile. The regression coefficients of the fourth-order polynomial quantile regression model using the 0.7 quantile were estimated for each cow, using the `quantreg` package (Koenker, 2018) and the `poly` function in R. The estimated regression coefficients for each cow were then used to calculate individual expected lactation curves.

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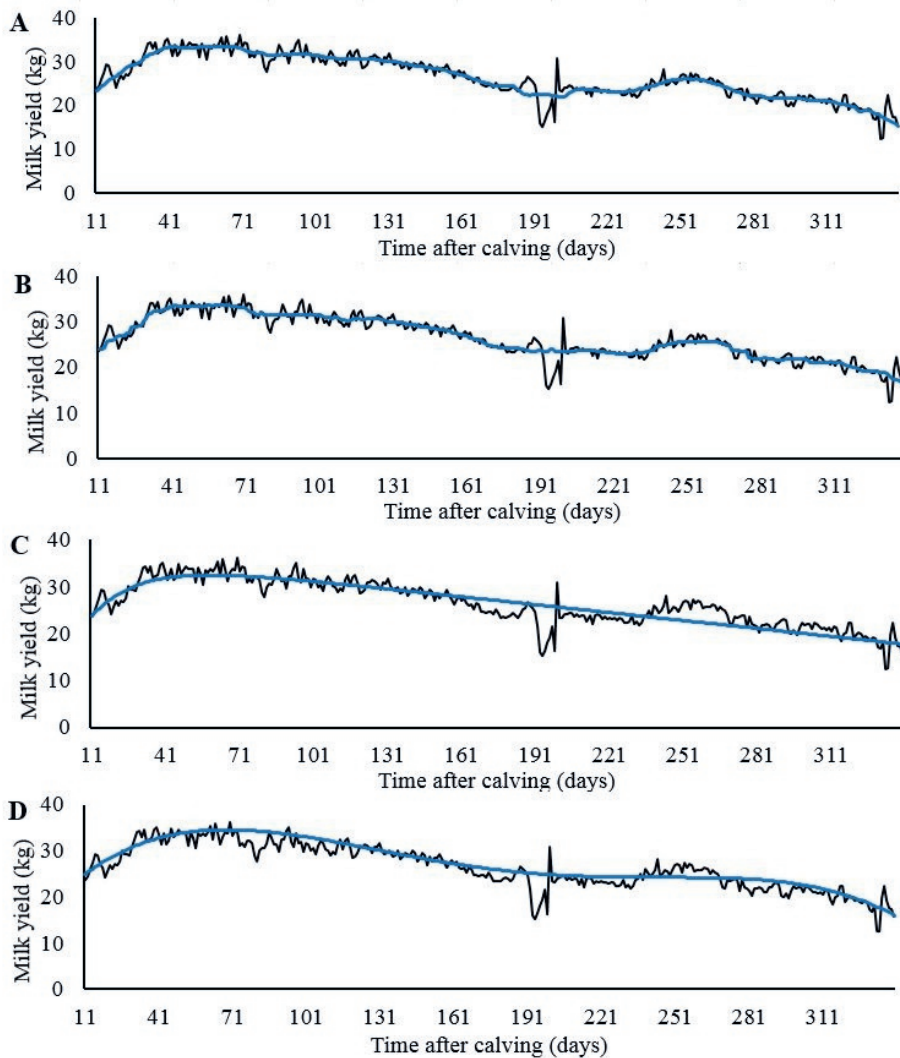


Figure 2.2 Examples of lactation curve-fitting methods for an example cow. Black lines show observed milk yield, and blue lines show predicted milk yield; (A) moving average, (B) moving median, (C) Wilmink curve, (D) quantile regression.

2.2.2 Defining resilience indicators based on deviations from lactation curves

The deviations from the fitted lactation curves ($yield - \widehat{yield}$) were expected to contain information about responses to environmental disturbances, and they were therefore used to calculate 3 potential resilience indicators: the variance, the lag-1 autocorrelation, and the skewness of the deviations. Low variance of the

deviations was expected to indicate good resilience, because resilient cows have a smaller range of deviations from their lactation curve than do less-resilient cows. A low lag-1 autocorrelation of the deviations was expected to indicate good resilience, because resilient cows have fewer and shorter stretches of negative deviations than do less-resilient cows. A skewness of the deviations close to zero was expected to indicate 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., 2019b). Because the lactation curve models had poor fit at 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 DIM of each cow were excluded from 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, which used an exponential model of the variance (SanCristobal-Gaudy et al., 1998; Hill and Mulder, 2010; Sell-Kubiak et al., 2015). From this point forward in this paper, 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 those of 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 Genetic Analysis section).

2.2.3 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 to 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 from 1,120,550 cows, recorded between 1998 and 2018. However, the resilience indicators were calculated only for first-parity Holstein Friesian cows that were milked by AMS, that were herd-book registered, that calved after 640 days of age and before the June 1, 2017, and that had no more than 5% missing daily milk yield records. Moreover,

2 Resilience indicators based on milk yield

the resilience indicators were only based on the first 350 DIM. Daily milk yield records were obtained from the records of single AMS visits by summing the milk yield of the single AMS visits per day for each cow. However, the milk yield of the first AMS visit of each day was partly assigned to the previous day, depending on the milk produced per minute since the previous AMS visit and the time between the previous AMS visit and midnight. After we had calculated the resilience indicators, resilience indicator records of individual cows were set to missing if they deviated more than 4 standard deviations (SD) from the mean of that resilience indicator. To adjust for herd, year of calving, and season of calving, herd-year-season classes were made with 4 seasons: January to March, April to June, July to September, and October to December. Herd-year-season classes with less than 5 cows were removed. Finally, 198,754 cows were used for the genetic analysis of the resilience indicators. Data editing was performed using the AWK programming language (Aho et al., 1988) and R (version 3.2.2; R Project for Statistical Computing, Vienna, Austria). All data editing steps, with information on the number of remaining records and number of cows after each editing step, are shown in Table 2.1.

2.2.4 Genetic analysis

For all resilience indicators and average daily milk yield, heritabilities and estimated breeding values (EBV) were estimated with univariate analyses, and genetic correlations among traits were estimated with bivariate analyses using ASReml 4.1 (Gilmour et al., 2015). The pedigree included 5 generations of ancestors.

2.2.4.1 Univariate analysis

Heritabilities and EBV were estimated using the following univariate linear mixed animal model:

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

where \mathbf{y} was a vector with observations of a certain resilience indicator; \mathbf{b} was a vector containing fixed effects, which were herd-year-season, age at first calving in months, and lactation length (remaining number of days after removing the first and last 10 DIM) in 7 classes, each containing a range of 40 days (50 to 90 days, 91 to 130 days, and so on); \mathbf{a} was a vector containing the additive genetic effects, $\mathbf{a} \sim N(\mathbf{0}, \mathbf{A}\sigma_a^2)$, where \mathbf{A} is the additive genetic relationship matrix and σ_a^2 is the additive genetic variance; and \mathbf{e} was a vector containing the residuals,

$\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}\sigma_e^2)$, where \mathbf{I} is the identity matrix and σ_e^2 is the residual variance. \mathbf{X} and \mathbf{Z} were incidence matrices linking the records in \mathbf{y} to the fixed effects and additive genetic effects, respectively. For the LnVar traits and RawVar a genetic coefficient of variation (**GCV**) was calculated as σ_a , because using the ln-transformation of the variance assumes an exponential model, and GCV in the exponential model for variance is equal to σ_a (see Mulder et al., 2007). For the other resilience indicators, a GCV was calculated as $\frac{\sigma_a}{\mu}$, where μ was the mean of the resilience indicator.

2.2.4.2 Bivariate analysis

Genetic correlations between the different resilience indicators, between the same resilience indicators based on different lactation curve-fitting methods, and between the resilience indicators and average daily milk yield, were estimated using the following bivariate mixed animal model:

$$\begin{bmatrix} \mathbf{y}_1 \\ \mathbf{y}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}_1 & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_2 \end{bmatrix} \begin{bmatrix} \mathbf{b}_1 \\ \mathbf{b}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{Z}_1 & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_2 \end{bmatrix} \begin{bmatrix} \mathbf{a}_1 \\ \mathbf{a}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix},$$

where \mathbf{y}_i was a vector with observations on trait i ; \mathbf{b}_i was a vector with the fixed effects for trait i , which were the same as in the univariate analysis; \mathbf{a}_i was a vector with the additive 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 incidence matrices linking the records in \mathbf{y}_i to the fixed effects and additive genetic effects, respectively. The additive genetic effects for all traits were assumed normally distributed with a mean of 0, a genetic variance of $\sigma_{a_i}^2$ for trait i , and a genetic covariance between traits of $\sigma_{a_1 a_2}$:

$\begin{bmatrix} \mathbf{a}_1 \\ \mathbf{a}_2 \end{bmatrix} \sim N\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{A} \otimes \begin{pmatrix} \sigma_{a_1}^2 & \sigma_{a_1 a_2} \\ \sigma_{a_1 a_2} & \sigma_{a_2}^2 \end{pmatrix}\right)$. The residuals were assumed to be normally

distributed as well, with a mean of 0, a residual variance of $\sigma_{e_i}^2$ for trait i , and a

residual covariance between traits of $\sigma_{e_1 e_2}$: $\begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix} \sim N\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{e_1}^2 & \sigma_{e_1 e_2} \\ \sigma_{e_1 e_2} & \sigma_{e_2}^2 \end{pmatrix}\right)$.

Because of long computing times for the bivariate analyses, the data set was randomly split into 5 subsets based on herd. The bivariate analyses were then performed on the 5 subsets and weighted means of the parameters were calculated. See Appendix for an explanation of the weighting of the parameters resulting from the bivariate analyses of the subsets.

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Table 2.1. Data editing steps and number of records, missing records, and 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 automatic milking system	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 fewer 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, 2018g)	115,747,841	12,774,619	444,281
Set milk yield greater than 100 kg 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 fewer 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 mean herd yield +/- 4 SD	378,364	0	378,364
Remove cows that calved after the June 1 st , 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 fewer than 5 cows	198,754	0	198,754

¹To fit a Wilmink curve, a sufficient number of records was needed.

2.2.4.3 Genetic correlations with health, longevity, fertility, metabolic, and production traits

Genetic correlations between the resilience indicators and several health, longevity, fertility, metabolic, and production traits were estimated using the multiple trait across country evaluation (**MACE**) procedure. The MACE procedure is used by Interbull (Interbull, 2017) to evaluate bulls in different countries for the same trait, but it can also be used to estimate genetic correlations between deregressed sire EBV of different traits (Schaeffer, 1994; Klei and Weigel, 1998; Larroque and Ducrocq, 1999). Deregressed EBV are used to make the variance of the EBV independent from their reliabilities and to take out the contribution of 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, deregressed sire EBV resulting from the univariate analyses were used as input for the MACE procedure. For the health, longevity, fertility, metabolic, and production traits, deregressed 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, 2020c), the hoof health index (CRV, 2020d), 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 3 traits, a higher value indicates better health or less ketosis. Productive longevity (CRV, 2020a) and the fertility index (CRV, 2021a), were also included, because resilient cows are expected to live longer and to be more fertile than less-resilient cows. For these 2 traits, a higher value indicates better fertility or longevity. In addition, the metabolic traits body condition score (**BCS**) (CRV, 2020h) and dry matter intake (**DMI**) (CRV, 2018b) were included because of the expected relation between resilience and the amount of resources a cow has available to respond to disturbances. For these 2 traits, higher value indicates higher BCS or greater DMI. 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, 2020g). For this trait, a higher value indicates a flatter lactation curve. Finally, the production trait milk yield (CRV, 2020g) was included to compare the average daily milk yield calculated in the current AMS dataset with the official breeding value for milk yield based on the total Dutch-Flemish cow population.

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2.2.4.4 Genetic correlations adjusted for milk yield

Considerable genetic correlations between some of the resilience indicators and average daily milk yield were observed. Therefore, partial genetic correlations between the resilience indicators and the health, longevity, fertility, and metabolic traits, adjusted for average daily milk yield ($r_{xy,z}$), were calculated as follows:

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

where x is the resilience indicator, y is the health, longevity, fertility, or metabolic trait, and z is average daily milk yield. The correlations between the resilience indicators and average daily milk yield were genetic correlations obtained from the bivariate analyses. The other correlations were genetic correlations estimated using the MACE procedure.

2.3 Results

2.3.1 Comparison of resilience indicators

The resilience indicators LnVar and RawVar had the highest heritabilities (0.20 to 0.24) and genetic coefficients 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 2.2). Although RawVar had heritability comparable 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 (Table 2.3). In addition, LnVar, r_{auto} , and Skew also 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 2.3). In summary, the genetic correlations show that RawVar, LnVar, r_{auto} , and Skew are genetically different traits.

Table 2.2 Variance components (σ_a^2 = additive genetic variance; σ_e^2 = error variance; σ_p^2 = phenotypic variance), heritabilities (h^2), and genetic coefficients of variation (GCV) from the univariate analyses of the resilience indicators (SE in parentheses).

Trait ¹	Curve ²	σ_a^2	σ_e^2	σ_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

¹LnVar = 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.

²ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

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Table 2.3 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).

Curve ¹	Resilience indicator ²			
	LnVar and r_{auto}	LnVar and Skew	r_{auto} and Skew	LnVar and 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)

¹ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

²LnVar = variance of deviations from lactation curve, r_{auto} = lag-1 autocorrelation of deviations, Skew = skewness of deviations, RawVar = variance of raw milk yield.

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

2.3.2 Comparison of lactation curve-fitting methods

The 4 lactation curve-fitting methods resulted in different means of the resilience indicators (Table 2.4). 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 were the deviations from a moving median curve. The genetic variance and heritability also differed between the curve-fitting methods, especially for Skew (Table 2.2). 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 2.5). 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 curve-fitting methods resulted in genetically similar traits, whereas for Skew the different curve-fitting methods resulted in genetically less similar traits.

Table 2.4 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

¹LnVar = 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.

²ma = moving average, mm = moving median, wilm = Wilmlink curve, quant = quantile regression.

Table 2.5 Genetic correlations between 4 lactation curve-fitting methods for each resilience indicator (SE in parentheses).

Curve ¹	Resilience indicator ²		
	LnVar	r_{auto}	Skew
ma and mm	1.00 (0.00)	0.99 (0.01)	0.95 (0.01)
ma and wilm	0.94 (0.01)	0.92 (0.01)	0.46 (0.07)
ma and quant	0.98 (0.00)	0.97 (0.00)	0.81 (0.07)
mm and wilm	0.94 (0.01)	0.90 (0.01)	0.31 (0.06)
mm and quant	0.98 (0.00)	0.95 (0.01)	0.83 (0.06)
wilm and quant	0.98 (0.00)	0.96 (0.01)	0.60 (0.03)

¹ma = moving average, mm = moving median, wilm = Wilmlink curve, quant = quantile regression.

²LnVar = variance, r_{auto} = autocorrelation, Skew = skewness.

2.3.3 Genetic correlations with health, longevity, fertility, metabolic, and production traits

We found that LnVar and RawVar were the resilience indicators with the strongest genetic correlations with the health, longevity, fertility, metabolic, and production traits (Table 2.6). Both a lower LnVar and a lower RawVar were genetically related to better udder health, better hoof health, better longevity, better fertility, higher BCS, less ketosis and lower milk yield level. However, LnVar and RawVar differed in the sign (positive or negative) of their genetic correlations with persistency and DMI: LnVar had a positive genetic correlation of only 0.08 to 0.14 with persistency, whereas RawVar had a negative genetic correlation with persistency of -0.51. With DMI, LnVar had a positive genetic correlation of 0.24 to 0.29, whereas RawVar had a negative genetic correlation with DMI of only -0.04. If we now turn to r_{auto} , we see that its genetic correlations with the health, longevity, fertility, metabolic, and production traits were generally in the same direction as for LnVar: a lower r_{auto} was genetically related to better health, fertility, and longevity, higher DMI and BCS, and lower milk yield level. However, r_{auto} had weaker genetic correlations (-0.21 to 0.20) with the health, longevity, fertility, metabolic, and production traits than did LnVar. For Skew, the genetic correlations with the health, longevity, fertility, and metabolic traits were, in general, negligible or weak (-0.25 to 0.17). A higher Skew was weakly genetically associated with more ketosis, lower BCS, and lower longevity (Table 2.6). The genetic correlations between Skew and average daily milk yield were moderate, and were negative for Skew based on a Wilmlink curve (-0.40) but positive for Skew based on the other curve-fitting methods (0.19 to 0.30).

Average daily milk yield had a strong genetic correlation (0.95) with official milk yield produced in 305 days in first lactation (Table 2.6). This strong genetic correlation indicates that the studied data set 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, DMI, and ketosis resistance were in the same direction. Interestingly, though, LnVar and average daily milk yield had opposite but weak genetic correlations with productive longevity.

To disentangle the effects 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 2.7) than the original genetic correlations had been (Table 2.6). 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 DMI were negative (-0.53 to -0.66), whereas the original genetic correlations were positive: at an equal milk yield across cows, less variable milk was genetically related to higher DMI. Skew and r_{auto} had weaker genetic correlations with average daily milk yield than did LnVar (Table 2.6). The weak genetic correlations with milk yield led to only small differences between the original and the partial genetic correlations. However, the partial genetic correlations of r_{auto} and Skew with DMI were stronger and, in most cases, had a different sign than did their original genetic correlations with DMI (Table 2.7). In summary, of the 3 resilience indicators, LnVar had the strongest genetic correlations with the health, longevity, fertility, and metabolic traits. At an equal level of milk yield across cows, lower LnVar was genetically related to better health, longevity, and fertility, and higher BCS and DMI.

Table 2.6 Genetic correlations between resilience indicators based on different lactation curve-fitting methods and average daily milk yield, and health, longevity, fertility, metabolic, and production traits, estimated using the multiple trait across country evaluation (MACE) procedure. (SE 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
	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

¹LnVar = 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.

²ma = moving average, mm = moving median, wilm = Wilink curve, quant = quantile regression.

³UH = udder health, HH = hoof health, KET = ketosis resistance in first lactation, LON = productive longevity, FER = fertility, BCS = body condition score, 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.

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

Table 2.7 Partial genetic correlations between resilience indicators based on different lactation curve-fitting methods and health, longevity, fertility, and metabolic traits, estimated using the multiple trait across country evaluation (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

¹LnVar = variance of deviations from lactation curve, RawVar = variance of raw milk yield, r_{auto} = lag-1 autocorrelation of deviations, Skew = skewness of deviations.

²ma = moving average, mm = moving median, wilm = Wilmink curve, quant = quantile regression.

³UH = udder health, HH = hoof health, KET = ketosis resistance in first lactation, LON = productive longevity, FER = fertility, BCS = body condition score, DMI = dry matter intake, PER = persistency in first lactation.

2.4 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 3 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., 2019a). 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 2 studies. In chickens, the heritability of skewness was approximately 10 times higher and heritability of variance was approximately 2 times lower than in cattle. In addition, the genetic correlations among the 3 resilience indicators differed widely between the 2 species. The main reason for the differences between the traits in the 2 studies is likely that we used deviations from individually fitted lactation curves, whereas deviations from cohort means 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, variance has. Compared with previous studies on variance in milk yield, our study provided 2 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 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 with variance in raw milk yield, as suggested by Elgersma et al. (2018). The second novelty of this study compared with 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., 2019b). 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, 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. However, we used a 2-step approach and first estimated individual lactation curves and then summarized the deviations into 1 resilience indicator per cow, on which we performed a genetic analysis. In theory, the double hierarchical generalized linear model could be applied to our daily milk yield records as well, but we would expect it to yield EBV and genetic variance in residual variance similar to those of our LnVar (Berghof et al., 2019a), 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, fluctuations in fat content may indicate resilience to ketosis or rumen acidosis, and fluctuations in somatic cell score may indicate resilience to mastitis (de Haas et al., 2008; Urioste et al., 2012). Rönnegård et al. (2013) and Vandenplas et al. (2013) showed genetic variation in variability of somatic cell score measured on test-days, and Vandenplas et al. (2013) also showed genetic variation in variability of different types of fatty acids. Furthermore, Ehsaninia et al. (2019) showed genetic variation in variability of fat and protein content measured on test-days. It would be interesting to also analyze variability of these traits using daily records and to investigate their genetic correlations with health traits. However, until now daily measurements of milk components have not been available on a large scale.

In our study, as well as in those of Rönnegård et al. (2013), Vandenplas et al. (2013), Elgersma et al. (2018), and Ehsaninia et al. (2019), the variance of (deviations in) milk yield was studied as a resilience indicator. Alternative measures could be the mean of absolute deviations or using the variance of only negative deviations. The mean of absolute deviations may give information similar to that derived from the variance, but a variance gives more weight to large deviations than to small deviations, because a variance is essentially the mean of squared deviations. Because small deviations can be due merely to noise, we expect that the variance is more powerful as a resilience indicator than the mean of absolute deviations. The use of only negative deviations to calculate the variance may seem better than also using positive deviations because disturbances cause drops in milk

yield rather than peaks. However, work on daily feed intake in turkeys has shown that variance based only on negative deviations had a considerably lower heritability than did the variance based on all deviations, although the genetic correlation between them was 0.98 (H. A. Mulder, unpublished data). Thus, we expect the variance of all deviations to be more informative about resilience than the mean of absolute deviations or the variance of only negative deviations.

All our resilience indicators were based on data from complete lactations up to 350 days in milk. However, resilience may differ between lactation stages because of differences in disease susceptibility (Ingvarsen et al., 2003). Therefore, it would be interesting to test whether resilience indicators based on data from different lactation stages are genetically different from each other and whether they differ in their genetic correlations with health, longevity, fertility, metabolic, and production traits.

2.4.1 Suitability of traits used as resilience indicators

The suitability of a resilience indicator depends on its heritability and its genetic correlations with health, longevity, fertility, metabolic, and production traits. High heritability indicates that family members are more alike than other animals, and therefore suggests that the indicator is not simply random noise. Furthermore, resilience is expected to be genetically correlated with better health, longevity, and fertility (Elgersma et al., 2018; Berghof et al., 2019b), higher DMI, higher BCS, and lower milk yield level. The expected correlations with DMI, BCS, and milk yield level can be explained by resource allocation theory. If the demand for resources for milk yield is high, fewer resources are left for coping with disturbances than when demand for resources for milk yield is low. Therefore, a high milk yield can make a cow less resilient. Alternatively, a high DMI or BCS can provide a cow with enough resources to cope with disturbances, even at a high milk yield, which makes her more resilient (Rauw, 2008). If a lower LnVar and r_{auto} indicate a better resilience, we would expect them to have negative genetic correlations with udder health, hoof health, longevity, fertility, ketosis resistance, DMI, and BCS, and positive correlations with milk yield level. If a higher (more positive) Skew indicates better resilience, we expect it to have positive genetic correlations with udder health, hoof health, longevity, fertility, ketosis resistance, DMI, and BCS, and negative correlations with milk yield level. In the following sections we will discuss which of the resilience indicators behaves most according to these expectations.

2.4.1.1 Variance

In our results, LnVar based on all curve-fitting methods had considerable heritability. In addition, a lower LnVar was genetically correlated with better health, longevity, and fertility, and higher BCS, which was as expected. These results support the hypothesis 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 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. We find 2 possible explanations for these strong genetic correlations. The first is that cows with a higher milk yield level have poorer resilience than do cows with a lower milk yield level. High-producing cows may be 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 greater tendency to take resources away from production (Rauw, 2008; Berghof et al., 2019b). 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., 2019b). 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 were in the expected direction (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 DMI and longevity were closer to our expectations of LnVar as a resilience indicator than the original genetic correlations were. The negative partial

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genetic correlation between LnVar and longevity was stronger than the original one, which was closer to our expectation, because we expected lower LnVar to be related to 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 DMI 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 higher DMI than do 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 DMI was opposite from the original positive genetic correlation that indicated that a higher LnVar was related to a higher DMI. This difference is caused by the positive genetic correlation between milk yield level and DMI: cows with genetically higher milk yields tend to eat more than less-productive cows, but they also have a higher variance in milk yield. The negative partial genetic correlations between LnVar and DMI, and the negative partial genetic correlations between LnVar and longevity, confirm that LnVar corrected for milk yield is informative about resilience.

Although most genetic correlations between LnVar and the functional traits became only slightly weaker after adjusting for milk yield level, the genetic correlations between LnVar and hoof health became negligible. Apparently, LnVar does not contain information about hoof health that is not covered by milk yield level. The negligible partial correlation is probably caused by the inability of the curve-fitting methods to capture long-term declines in milk yield that are typical for lameness (Green et al., 2002). Based on the curve fitting methods applied in this study, LnVar is therefore not suitable for long-term disturbances such as claw disorders.

In summary, LnVar contains information about health and functionality that is not covered by milk yield level. Therefore, LnVar is a promising resilience indicator and seems a good candidate to include in breeding goals. The economic value of resilience is already partly accounted for in breeding goals by health traits. However, resilience has additional economic value, because resilient cows require less time from farmers for checking and monitoring than do less-resilient cows. In addition, resilience may account for the costs of diseases that are not yet included in the breeding goal (Berghof et al., 2019b), such as ketosis and rumen acidosis in the Netherlands (CRV, 2020b). Additional research is needed to determine the correct economic value of LnVar in the breeding goal. Alternatively, a desired-gains

approach could be used (Brascamp, 1984). Such an approach should aim for a decrease in LnVar while simultaneously increasing milk yield level, health, longevity, and fertility, and decreasing DMI.

2.4.1.2 Autocorrelation

The heritability of r_{auto} was not high, but was still considerable, which suggests that r_{auto} contains information and is not just random noise. We expected that the information that r_{auto} contained would be mostly about the recovery aspect of resilience (Berghof et al., 2019b). A higher r_{auto} was expected to indicate longer stretches of negative (or positive) deviations and thus slower recovery. Because the EBV for the health traits are more informative about resistance to diseases than about recovery from diseases, the genetic correlations between r_{auto} and the disease traits may be of limited value for validating r_{auto} as an indicator of recovery time. Indeed, the genetic correlations between r_{auto} and udder health and hoof health were weak and negligible, respectively. Nevertheless, they were in the expected direction, with a lower r_{auto} indicating better health. The association between r_{auto} and udder health could be caused by the positive genetic association between mastitis resistance and recovery rate (Welderufael et al., 2018). Based on this observation, one may expect a positive genetic correlation between r_{auto} and LnVar, but we found a weak and negative genetic correlation. In summary, we cannot conclude from our results whether r_{auto} is informative about recovery time, and more research is needed. If r_{auto} turns out to contain information about recovery time that LnVar lacks, the 2 traits could be combined in a resilience index. However, as a single indicator of overall resilience, r_{auto} is less suitable than LnVar.

2.4.1.3 Skewness

Skew contained less genetic variation than LnVar and r_{auto} , indicated by the low GCV, and more noise, indicated by the low heritability. In addition, Skew had weak or unexpected genetic correlations with both LnVar and the health, longevity, fertility, and metabolic traits. For instance, a higher (closer to 0) Skew was expected to indicate a better resilience, but was weakly genetically related to shorter longevity, lower BCS, more ketosis, and higher LnVar. Therefore, Skew is not considered a good resilience indicator. The reason that Skew was unable to reflect resilience could be that this trait was too sensitive to incorrect milk yield records: a single outlier could have a large effect on Skew. We were not able to remove all outliers from the data, because to do so would be too strict: we would also remove extreme records that were informative about resilience. Because of its sensitivity to outliers, Skew is not suitable as a resilience indicator using commercial data.

2.4.2 Which curve-fitting method is best?

Because of its heritability and genetic correlations with health, longevity, fertility, metabolic, and production traits, LnVar is the most promising resilience indicator. However, we should also decide which curve-fitting method generates the best LnVar. All 4 curve-fitting methods resulted in genetically similar LnVar traits (Table 2.5), which indicates that for LnVar it is not important which curve-fitting method is used. However, we observed small differences in the genetic parameters. Moving average and moving median resulted in the highest heritability, whereas polynomial quantile regression generated the strongest genetic correlations with the health, longevity, fertility, and metabolic traits. To decide which method is best, we can calculate the indirect response in a health trait, such as udder health, that results from selection on reduced LnVar based on the 4 curve-fitting methods. If we consider genomic selection using 20,000 cows in the reference population and we assume that the number of independent chromosomal segments is 1,200, then the accuracy of a genomic EBV (Daetwyler et al., 2010) for LnVar would be approximately 0.90 based on moving average and moving median, and approximately 0.88 based on polynomial quantile regression and a Wilmlink curve. Note that this comparison is not affected by the assumption of the number of independent chromosomal segments; getting an appropriate value is an unresolved scientific issue (Brard and Ricard, 2014). Assuming the selection intensity to be 1, the genetic improvement in udder health would be 0.24, 0.23, 0.28 and 0.25 genetic SD when selection is on LnVar based on moving average, moving median, polynomial quantile regression, and Wilmlink curve, respectively. This shows that polynomial quantile regression would lead to the highest genetic improvement in udder health if selection is on LnVar. The same was observed for hoof health, ketosis, longevity, and fertility. Therefore, polynomial quantile regression is considered the best curve-fitting method among the methods studied here.

2.5 Conclusions

All potential resilience indicators explored in this study were heritable, although the heritabilities ranged from low to moderate. We found that LnVar had the highest heritability and the strongest genetic correlations with health, longevity, fertility, and metabolic traits, in the expected direction. Therefore, it has the most potential as an indicator of resilience. The genetic correlations of r_{auto} with the health, longevity, fertility, and metabolic traits were weak, but more research is needed to investigate whether r_{auto} could indicate recovery time. Skew had negligible heritability and unexpected genetic correlations with the health,

longevity, fertility, and metabolic traits. Skew is thus not considered a good indicator of resilience. The lactation curve-fitting methods on which LnVar was based resulted in genetically similar traits, but selection on LnVar based on quantile regression would consistently result in the largest correlated responses in the health, longevity, and fertility traits. Therefore, we recommend this curve-fitting method. This research is an important stepping stone to further explore the use of log-transformed variance of deviations in milk yield as an indicator that can be used to breed more resilient cows.

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2.7 Appendix

2.7.1 Bivariate analyses using subsets

Because of the long computing time, genetic correlations between the resilience indicators were estimated on subsets of the complete data. Weighted averages were subsequently estimated, which are presented in this paper. Here we provide additional information about the aggregation of the genetic correlations estimated on subsets of the data.

The complete data set was randomly split into 5 subsets based on herd. On each subset, genetic correlations between resilience indicators were estimated. Weighted averages of the genetic correlations (\bar{x}) were estimated as follows:

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

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where w_i was the number of animals in subset i and x_i was the estimated genetic correlation of subset i . Weighted standard deviations (SD) of the genetic correlations (s) were estimated thus:

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

To calculate the standard error of the weighted average genetic correlations, the weighted SD were divided by the square root of 5. In addition to the weighted genetic correlations, weighted residual and phenotypic correlations were also calculated, as shown in Appendix Table A 2.1.

Table A 2.1 Residual (above diagonal) and phenotypic correlations (below diagonal) among the resilience indicators and average daily milk yield; a dash indicates that no genetic correlation was estimated for that combination. All standard errors ≤ 0.01 .

Trait ¹	Curve ²	LnVar				RawVar				r _{auto}				Skew				AMY			
		ma	mm	wilm	quant	-	quant	wilm	mm	ma	quant	wilm	mm	ma	quant	wilm	mm	quant			
LnVar	ma	-	0.99	0.68	0.85	0.28	-	-	-0.18	-	-	-	-	-0.13	-	-	-	-	0.04		
	mm	0.99	-	0.63	0.80	0.24	-	-	-0.15	-	-	-	-0.14	-	-	-	-	-	0.04		
	wilm	0.73	0.69	-	0.79	0.46	-	-	-	-	-	0.25	-	-	-	-0.06	-	-	0.03		
	quant	0.87	0.84	0.82	-	0.37	-	-	-	-	-	-	-	-	0.12	-	-	-0.23	0.02		
RawVar	-	0.30	0.27	0.46	0.38	-	-	-	-	-	-	-	-	-	-	-	-	-	0.06		
	ma	-0.17	-	-	-	-	-	-	0.97	0.74	0.85	-	-	-0.08	-	-	-	-	0.10		
	mm	-	-0.14	-	-	-	-	-	0.97	-	0.67	0.79	-	-0.19	-	-	-	-	0.10		
	wilm	-	-	0.23	-	-	-	-	0.75	0.69	-	0.82	-	-	-	0.14	-	-	0.06		
Skew	quant	-	-	-	0.10	-	-	-	0.86	0.80	0.83	-	-	-	-	-	-	-0.09	0.06		
	ma	-0.09	-	-	-	-	-	-	-0.08	-	-	-	-	-	-	0.96	0.59	0.75	-0.04		
	mm	-	-0.09	-	-	-	-	-	-	-	-	-	-0.19	-	0.96	0.60	0.77	-0.04			
	wilm	-	-	-0.05	-	-	-	-	-	-	-	0.15	-	0.59	0.59	-	0.72	-	-0.02		
AMY	quant	-	-	-	-0.19	-	-	-	-	-	-	-	-	0.75	0.77	0.71	-	-	0.00		
	-	0.27	0.26	0.25	0.25	0.10	0.11	0.11	0.11	0.07	0.07	0.07	-0.01	-0.01	-0.05	0.01	-	-	-		

¹LnVar = 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.

²ma = moving average, mm = moving median, quant = quantile regression, wilm = wilmsink curve.

3

Genetic analysis of resilience indicators based on milk yield records in different lactations and at different lactation stages

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Abstract

Resilience is the ability of cows to cope with disturbances, such as pathogens or heat waves. To breed for improved resilience, it is important to know whether resilience genetically changes throughout life. Therefore, the aim was to perform a genetic analysis on 2 resilience indicators based on data from 3 periods of the first lactation (day 11-110, 111-210, and 211-340) and the first 3 full lactations, and to estimate genetic correlations with health traits. The resilience indicators were the natural log-transformed variance (LnVar) and lag-1 autocorrelation (r_{auto}) of daily deviations in milk yield from an expected lactation curve. Low LnVar and r_{auto} indicate low variability in daily milk yield and quick recovery, and were expected to indicate good resilience. Data of 200,084 first, 155,784 second, and 89,990 third lactations were used. Heritabilities were similar based on different lactation periods (0.12-0.15 for LnVar, 0.05-0.06 for r_{auto}). However, the heritabilities of the resilience indicators based on full first lactation were higher than those based on lactation periods (0.20 for LnVar, 0.08 for r_{auto}), due to lower residual variances. Heritabilities decreased from 0.20 in full lactation 1 to 0.19 in full lactation 3 for LnVar and from 0.08 to 0.06 for r_{auto} . For LnVar, as well as for r_{auto} , the strongest genetic correlation between lactation periods was between period 2 and 3 (0.97 for LnVar, 0.96 for r_{auto}) and the weakest between period 1 and 3 (0.81 for LnVar, 0.65 for r_{auto}). Similarly, for both traits the genetic correlation between full lactations was strongest between lactation 2 and 3 (0.99 for LnVar, 0.95 for r_{auto}), and weakest between lactation 1 and 3 (0.91 for LnVar, 0.71 for r_{auto}). For LnVar, genetic correlations with resilience-related traits, such as udder health, ketosis, and longevity, adjusted for correlations with milk yield, were almost always favorable (-0.59 to 0.02). In most cases these genetic correlations were stronger based on full lactations than on lactation periods. Genetic correlations were similar across full lactations, but the correlation with udder health increased substantially from -0.31 in lactation 1 to -0.51 in lactation 3. For r_{auto} , genetic correlations with resilience-related traits were always favorable in lactation period 1 and in most full lactations, but not in the other lactation periods. However, correlations were weak (-0.27 to 0.15). Therefore, as a resilience indicator for breeding, LnVar is preferred over r_{auto} . A multitrait index based on estimated breeding values for LnVar in lactations 1, 2, and 3 is recommended to improve resilience throughout the lifetime of a cow.

Key words: resilience, dairy cow, lactation stage, genetics

3.1 Introduction

Resilient cows are minimally affected in their functioning by environmental disturbances, such as pathogens or heat waves, or recover quickly (Colditz and Hine, 2016; Berghof et al., 2019b). A possibility to improve resilience is through genetic selection. Because resilience is not directly measurable, the use of resilience indicators has been explored (Elgersma et al., 2018; Poppe et al., 2020). These resilience indicators were derived from daily milk yield records, based on the hypothesis that milk yield of resilient cows will be minimally affected by disturbances, and if it is affected, it will quickly return to normal. Initially, the (natural log-transformed) variance of daily milk yield records was studied as a resilience indicator, where low variance was expected to indicate good resilience (Elgersma et al., 2018). However, later the variance of daily deviations from a fitted lactation curve was studied (**LnVar**), to remove effect of persistency of the lactation curve (Poppe et al., 2020). In addition, the lag-1 autocorrelation (r_{auto}), and the skewness of daily yield deviations were studied. Low r_{auto} , and a skewness around 0 were expected to indicate good resilience, because they indicate quick recovery and a symmetric distribution of milk yield deviations from an individual lactation curve due to absence of response to disturbances, respectively. Skewness was not a useful resilience indicator for breeding because of its low heritability (0.01) and unfavorable genetic correlations with some health traits. The LnVar and r_{auto} were useful because they were heritable (0.21 and 0.09), and they were favorably genetically correlated with health and longevity. Similar resilience indicators were explored for body weight deviations in layer chickens (Berghof et al., 2019a), and feed intake in pigs (Putz et al., 2019). These studies showed that the LnVar of body weight and root mean square error of feed intake were useful as resilience indicators for breeding, because of their favorable genetic correlations with health and survival traits.

The resilience indicators explored by Poppe et al. (2020) were based on all daily milk yield records up to 350 days after calving in first lactation, which allows for breeding for improved resilience in first lactation. However, traits are often not genetically the same in different lactation stages or lactations. That holds not only for milk production itself (Brotherstone et al., 2000; Weller and Ezra, 2004), but also for traits related to resilience such as liability to clinical mastitis or tolerance to heat stress. For liability to clinical mastitis, genetic correlations between different days during lactation were between -0.14 and 1 (Heringstad et al., 2004; Carlén et al., 2009; Gernand and König, 2014). In addition, genetic correlations among the first 3 lactations for incidence of clinical mastitis were between 0.42 and 0.92 (Zwald et al., 2006; Bloemhof et al., 2009; Urioste et al., 2012). For heat tolerance

of milk yield, genetic correlations among the first 3 lactations were between 0.72 and 0.79 (Aguilar et al., 2009). Based on these studies on susceptibility and tolerance to disturbances, we may hypothesize that resilience changes genetically within and between lactations.

If resilience changes genetically throughout and between lactations, breeding for the resilience indicators based on full first lactation proposed by Poppe et al. (2020) may not result in improved resilience throughout the entire lactation and throughout the entire life. Resilience indicators based on specific periods of the lactation may reflect resilience better than resilience indicators based on other periods, because vulnerability to disturbances may change throughout lactation. For example, incidence of multiple diseases is highest in early lactation (Ingvarsen et al., 2003; Gernand and König, 2014) and the effect of hot and humid weather on milk yield has been shown to be highest in mid- or late lactation (Maust et al., 1972; Aguilar et al., 2009; Santana et al., 2017). These observations suggest that fluctuations in daily milk yield at different lactation stages may be informative about different types of resilience. In addition, if the resilience indicators are genetically different traits in different lactations, an index of EBV for the resilience indicators based on different lactations may be needed to improve resilience throughout life.

The aim of this study was to estimate genetic parameters for the resilience indicators variance and autocorrelation of milk yield deviations based on 3 periods of lactation 1 and based on the first 3 full lactations, and to estimate genetic correlations among lactation periods and among lactations for these resilience indicators, and genetic correlations with health traits.

3.2 Materials and methods

In this study, we did a genetic analysis on 2 resilience indicators: the variance and lag-1 autocorrelation of milk yield deviations from individual lactation curves. The resilience indicators were based on all daily milk yield records of a cow in lactation 1, lactation 2, or lactation 3, or on daily milk yield records from 3 different periods of lactation 1. We will first describe data preparation, and we will then describe the genetic analysis.

3.2.1 Data preparation

The initial data set contained 1,782,373,113 milk yield records of 1,120,550 cows in different lactations obtained during single milkings by automatic milking systems (AMS) or conventional milking systems. The data set was obtained from Cooperation CRV and CRV BV (Arnhem, the Netherlands) and included records

between 1998 and 2018. The data, as well as data preparation, were the same as in Poppe et al. (2020), but data preparation was extended to the second and third lactations. Data preparation was performed using the AWK programming language (Aho et al., 1988) and R (R v 3.2.2; R Project for Statistical Computing, Vienna, Austria).

From the initial data set, only data from AMS and from lactation 1, 2, and 3 were extracted, and only cows were included that were herd-book registered and that were at least 87.5% Holstein Friesian. Furthermore, lactations were included only when age at calving was more than 640 days of age (lactation 1), 855 days (lactation 2), or 1,070 days (lactation 3). These numbers were based on minimum age at first calving and minimum interval between calvings used by Cooperation CRV (CRV, 2020g).

The milk yield records based on single AMS visits were first converted to daily milk yield records. Daily milk yield records after 350 days in milk (**DIM**) were removed. Then, for each cow, and for each lactation separately, a lactation curve was fitted using fourth order quantile polynomial regression, because this curve-fitting method gave the best resilience indicators among the 4 curve-fitting methods studied by Poppe et al. (2020):

$$y_t = \beta_0 + \beta_1 * t + \beta_2 * t^2 + \beta_3 * t^3 + \beta_4 * t^4 + \varepsilon,$$

where y_t is the observed milk yield on DIM t ; t^n are DIM to the power of n , where n is 1, 2, 3, or 4; β_n are regression coefficients describing the relationships between t^n and y_t ; and ε is the error term. Quantile regression with a quantile of 0.7 was used to approximate the lactation curve in absence of disturbances. Disturbances mostly cause a reduction in milk yield and therefore the fitted curve was pushed upwards to the 0.7 quantile. As a consequence, negative deviations became larger and were expected to be more informative about resilience (Poppe et al. 2020). Curves were fitted using the quantreg package (Koenker, 2018) and the poly function in R.

After fitting the individual lactation curves for each cow and each lactation, the daily deviations from the fitted lactation curve were calculated. The deviations for day 1-10 and day 341-350 were removed because of poor fit of the lactation curve model at the extremes. First lactation was then split into 3 periods of ~100 days each: day 11 to 110, 111 to 210, and 211 to 340. The last period (day 211-340) is longer, but a substantial part of the cows was dried off before day 340 (60%). To be included in the analyses, cows were required to have records available from the start of the lactation, and not more than 5% of daily deviations per lactation was

3 Resilience indicators in different lactations and lactation stages

allowed to be missing. The same standards were required for analysis of periods 2 and 3 of first lactation. For analysis of resilience indicators based on full lactations, at least 50 milk yield records were required per lactation. For analysis of resilience indicators based on the 3 lactation periods, at least 30 milk yield records were required per lactation period. As a consequence, it was possible that cows had resilience indicators based on full lactation and based on lactation period 1, but not based on lactation period 2 and 3, if a cow was, for example, culled at 70 DIM.

Natural log-transformed variance (**LnVar**) and lag-1 autocorrelation (r_{auto}) of daily milk yield deviations (the resilience indicators), were then calculated for each cow separately for lactations 1, 2, and 3, and for the 3 periods of lactation 1. Note that LnVar is different from LnVar in Elgersma et al. (2018), which was the natural log-transformed variance of raw daily milk yield instead of daily deviations from a lactation curve. Low LnVar and r_{auto} were expected to indicate good resilience, because of few fluctuations in milk yield due to disturbances. In addition to LnVar and r_{auto} , average daily milk yield (**ADMY**) was calculated for each lactation and for each period of lactation 1. Calculating ADMY allowed us to adjust genetic correlations between the resilience indicators and health, longevity, fertility, and metabolic traits for milk yield level (see Genetic Analysis section). Furthermore, results of genetic analysis of ADMY could serve as a reference of how a well-known trait changed genetically over time.

Records of LnVar, r_{auto} , and ADMY were set to missing if they deviated more than 4 standard deviations (**SD**) from the mean of that trait in that lactation or in that period of lactation 1. Finally, herd-year-season (**HYS**) of calving classes were made with 4 seasons (January-March, April-June, July-September, October-December). If a HYS class contained fewer than 5 cows in a certain lactation, the LnVar, r_{auto} , and ADMY of those cows in that lactation were removed. The final number of records for LnVar, r_{auto} , and ADMY used for analysis are shown in Table 3.1. The number of cows with resilience indicators in lactation 1 is slightly different from the number of cows with resilience indicators analyzed in Poppe et al. (2020), because of a difference in data preparation related to fitting multiple lactation curves.

Table 3.1 The number of analyzed records for the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and of ADMY (average daily milk yield, in kg), based on different periods of lactation 1 or on different full lactations.

	LnVar	r_{auto}	ADMY
Lactation period 1	202,202	202,188	202,170
Lactation period 2	194,776	194,736	194,777
Lactation period 3	187,915	187,847	187,897
Lactation 1	200,070	199,920	200,084
Lactation 2	155,723	155,610	155,784
Lactation 3	89,963	89,888	89,990

3.2.2 Genetic analysis

3.2.2.1 Estimating genetic parameters

Genetic parameters were estimated using univariate, bivariate, and trivariate models. Because of the large amount of traits and genetic parameters to be estimated, many analyses were run. Table 3.2 summarizes for each genetic parameter which analysis was used and which traits were included. The analyses were performed using ASReml 4.1 (Gilmour et al., 2015), using a pedigree including 5 generations of ancestors. The following univariate mixed animal model was used:

$$y_{ijkl} = HYS_i + CA_j + LL_k + a_l + e_{ijkl},$$

where y_{ijkl} was the observation on the analyzed trait, HYS_i was the fixed effect of herd-year-season of calving i , CA_j was the fixed effect of calving age class j , LL_k was the fixed effect of lactation length class k , a_l was the random additive genetic effect of animal l and e_{ijkl} was a random error term. The calving age classes were based on age in months. The lactation length classes were based on the remaining number of days with data after removing the first and last 10 DIM (maximum 330 days). For full lactations, 7 classes of 40 days each were used (day 50-90, 91-130, 131-170, 171-210, 211-250, 251-290, 291-330). For periods of the lactation, the same classes were used, because the total length of the lactation may be informative about the resilience in the first, second, and third period of the lactation. An additional lactation length class (30-49 days) was included for period 1 of lactation 1, containing cows that had fewer than 50 lactation days, because we required resilience indicators based on lactation periods to be based on at least 30 records instead of 50. The following assumptions were made about the vector of random genetic effects \mathbf{a} and the vector of residuals \mathbf{e} : $\mathbf{a} \sim N(\mathbf{0}, \mathbf{A}\sigma_a^2)$ and

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$\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}\sigma_e^2)$, where \mathbf{A} is the additive genetic relationship matrix and \mathbf{I} is the identity matrix, and σ_a^2 and σ_e^2 are the additive genetic variance and the residual variance.

The bivariate and trivariate models included the same fixed effects as the univariate model. The following assumptions were made about the additive genetic effects in the multivariate models:

$$\begin{bmatrix} \mathbf{a}_1 \\ \mathbf{a}_2 \end{bmatrix} \sim N \left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{A} \otimes \begin{pmatrix} \sigma_{a_1}^2 & \sigma_{a_1 a_2} \\ \sigma_{a_1 a_2} & \sigma_{a_2}^2 \end{pmatrix} \right) \quad \text{and}$$

$$\begin{bmatrix} \mathbf{a}_1 \\ \mathbf{a}_2 \\ \mathbf{a}_3 \end{bmatrix} \sim N \left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{A} \otimes \begin{pmatrix} \sigma_{a_1}^2 & \sigma_{a_1 a_2} & \sigma_{a_1 a_3} \\ \sigma_{a_1 a_2} & \sigma_{a_2}^2 & \sigma_{a_2 a_3} \\ \sigma_{a_1 a_3} & \sigma_{a_2 a_3} & \sigma_{a_3}^2 \end{pmatrix} \right),$$

where \mathbf{a}_i is the vector with additive genetic effects for trait i , $\sigma_{a_i}^2$ is the additive genetic variance of trait i , and $\sigma_{a_i a_j}$ is the genetic covariance between trait i and j . The following assumptions were made about the random effects in the multivariate models:

$$\begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix} \sim N \left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{e_1}^2 & \sigma_{e_1 e_2} \\ \sigma_{e_1 e_2} & \sigma_{e_2}^2 \end{pmatrix} \right) \quad \text{and}$$

$$\begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \\ \mathbf{e}_3 \end{bmatrix} \sim N \left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{e_1}^2 & \sigma_{e_1 e_2} & \sigma_{e_1 e_3} \\ \sigma_{e_1 e_2} & \sigma_{e_2}^2 & \sigma_{e_2 e_3} \\ \sigma_{e_1 e_3} & \sigma_{e_2 e_3} & \sigma_{e_3}^2 \end{pmatrix} \right), \text{ where } \mathbf{e}_i \text{ is the vector with residuals}$$

for trait i , $\sigma_{e_i}^2$ is the residual variance of trait i , and $\sigma_{e_i e_j}$ is the residual covariance between trait i and j . Because of long computing time, the multivariate analyses were performed on 5 random subsets each containing approximately 20% of the cows. The subsets were made based on herd, and weighted averages of the genetic correlations (\bar{x}) were estimated the same as in Poppe et al. (2020):

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

where w_i was the number of animals in subset i and x_i was the estimated genetic correlation in subset i . Weighted SD of the genetic correlations (s) were estimated as:

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

To calculate the standard error of the weighted average genetic correlations, the weighted SD were divided by the square root of 5, as in Poppe et al. (2020). For 2 trivariate analysis (among LnVar in the 3 full lactations and among r_{auto} in the 3 full lactations), one of the 5 subsets could not converge. Therefore, the weighted means of the genetic correlations from these analyses were based on 4 instead of 5 subsets (~230,000 cows with a record in at least 1 of the lactations). Similarly, weighted averages of phenotypic correlations were calculated and can be found in the Appendix.

Table 3.2 Summary of univariate and multivariate analyses used for estimating genetic parameters of 2 resilience indicators (natural log-transformed variance of deviations from a lactation curve and lag-1 autocorrelation of deviations from a lactation curve), and average daily milk yield¹.

Genetic parameters to be estimated	Analysis used
Variance components and heritabilities of each trait in each lactation period	Trivariate analysis of the same trait recorded in the 3 lactation periods
Variance components and heritabilities of each trait in each full lactation	Trivariate analysis of the same trait recorded in the 3 full lactations
Genetic correlations between full lactation 1 and the 3 lactation periods	Bivariate analysis of the same trait in full lactation 1 and in each of the 3 lactation periods
Genetic correlations between lactation periods	Trivariate analysis of the same trait recorded in the 3 lactation periods
Genetic correlations between full lactations	Trivariate analysis of the same trait recorded in the 3 full lactations
Genetic correlations among the 3 traits	Trivariate analysis of the 3 traits recorded in the same lactation period or full lactation
EBV of each trait used for MACE procedure	Univariate analyses of each trait in each lactation period and full lactation
Genetic correlations of each trait with health, longevity, fertility, and metabolic traits	MACE procedure - bivariate analysis of de-regressed EBVs of each trait in each lactation period or full lactation and health, longevity, fertility and metabolic traits

¹Trait = natural log-transformed variance of deviations from a lactation curve, lag-1 autocorrelation of deviations from a lactation curve, or average daily milk yield; MACE = multiple across-country evaluation.

3.2.2.2 *Genetic correlations with health, longevity, fertility, and metabolic traits*

Genetic correlations were estimated between the resilience indicators and udder health, hoof health, ketosis resistance, longevity, fertility, body condition score (BCS), and dry matter intake (DMI). The purpose of these genetic correlations was to determine the value of LnVar and r_{auto} based on different lactations and periods of lactation 1 as a resilience indicator. Resilience is expected to be genetically related to good health, longevity, and fertility, and with a high BCS and DMI (Elgersma et al., 2018; Poppe et al., 2020). Instead of normal bivariate analyses, the multiple across-country evaluation (MACE) procedure was used to estimate the genetic correlations. The MACE procedure estimates genetic correlations between de-regressed EBV instead of phenotypes (Schaeffer, 1994; Klei and Weigel, 1998). Thus, the MACE procedure requires only EBV and their reliabilities as input, which eliminates the need for the data and the models underlying the health, longevity, fertility, and metabolic traits. For the resilience indicators, de-regressed sire EBV from the univariate analyses were used. For the health, longevity, fertility, and metabolic traits, de-regressed sire EBV from Cooperation CRV and CRV BV from the official run of April 2019 were used. The EBV were de-regressed to make their variance independent of their reliabilities and to take out the contribution of the parents (Larroque and Ducrocq, 1999). The EBV for udder health, hoof health, fertility, and DMI were an index of EBV from lactations 1, 2, and 3 (CRV 2018b; 2020c; 2020d; 2021a; 2018b). The EBV for productive longevity were based on survival per month (CRV, 2020a). The EBV for BCS (CRV, 2020h) were based on classifier observations in lactation 1. The EBV for ketosis resistance (Vosman et al., 2015) and official 305-day milk yield (CRV, 2020g) were based on data from lactations 1, 2, and 3, and were available for the 3 lactations separately. The MACE correlations with ketosis and official 305-day milk yield were, therefore, estimated per lactation (e.g., between LnVar in lactation 2 and ketosis in lactation 2). For the aforementioned EBV, a higher value means better health, longevity, or fertility, or a higher BCS, DMI, or milk yield.

3.2.2.3 *Genetic correlations adjusted for milk yield*

Considerable genetic correlations were shown between LnVar and ADMY, both in Poppe et al. (2020) and in this study. Because ADMY was also genetically related to health-related traits, it was desired to study genetic correlations between LnVar and the health, longevity, fertility, and metabolic traits at the same level of milk yield among cows. Therefore, partial genetic correlations between the resilience

indicators and the health, longevity, fertility, and metabolic traits were calculated. The following formula was used:

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

where $r_{xy,z}$ is the partial genetic correlation between resilience indicator x and health, longevity, fertility, or metabolic trait y , adjusted for ADMY (z). Furthermore, r_{xy} is the genetic correlation between resilience indicator x and health, longevity, fertility, or metabolic trait y , r_{xz} is the genetic correlation between resilience indicator x and ADMY (z), and r_{yz} is the genetic correlation between health, longevity, fertility, or metabolic trait y and ADMY (z).

For the correlations between the resilience indicators and ADMY, genetic correlations were taken from the trivariate analyses among LnVar, r_{auto} and ADMY in each lactation period or full lactation. All other correlations were genetic correlations estimated using the MACE procedure. The same procedure was used in Poppe et al. (2020).

3.3 Results

3.3.1 Descriptive statistics of resilience indicators

The mean of LnVar decreased from 1.54 in lactation period 1 to 1.00 in lactation period 3, and the SD increased from 0.69 to 0.76 (Table 3.3). Furthermore, the mean of LnVar increased from 1.39 in lactation 1 to 1.83 in lactation 3, and the SD increased from 0.57 to 0.62. The means and SD of r_{auto} were similar in the different periods of lactation 1 and the different lactations. The means ranged from 0.52 to 0.56 in both the periods of lactation 1 and the 3 full lactations, and the SD ranged from 0.23 to 0.24 in the periods of lactation 1 and from 0.18 to 0.19 in the 3 full lactations (Table 3.3). Similar to LnVar, the mean of ADMY decreased over the 3 periods of lactation 1 (from 29.81 to 22.90 kg), and increased over lactations (from 26.60 to 33.53 kg). In summary, LnVar and ADMY on average decreased within lactation 1 and increased over lactations, whereas r_{auto} was similar within and between lactations.

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Table 3.3 Descriptive statistics of the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and of ADMY (average daily milk yield), based on different periods of lactation 1 or on different full lactations.

Trait	Moment of measurement	Mean	SD	Minimum	Maximum
LnVar	Lactation period 1	1.54	0.69	-1.21	4.28
	Lactation period 2	1.16	0.75	-1.82	4.13
	Lactation period 3	1.00	0.76	-2.01	4.01
	Lactation 1	1.39	0.57	-0.89	3.69
	Lactation 2	1.64	0.60	-0.78	4.06
	Lactation 3	1.83	0.62	-0.62	4.30
r_{auto}	Lactation period 1	0.52	0.23	-0.42	0.99
	Lactation period 2	0.54	0.24	-0.41	0.99
	Lactation period 3	0.54	0.23	-0.40	0.98
	Lactation 1	0.55	0.19	-0.22	0.98
	Lactation 2	0.56	0.18	-0.18	0.99
	Lactation 3	0.55	0.19	-0.19	0.99
ADMY	Lactation period 1	29.81	5.24	8.81	50.54
	Lactation period 2	27.18	5.60	5.00	49.13
	Lactation period 3	22.90	5.41	3.48	44.57
	Lactation 1	26.60	4.99	6.98	46.49
	Lactation 2	31.33	5.85	7.95	54.62
	Lactation 3	33.53	6.05	9.27	57.37

3.3.2 Variance components and heritabilities of the resilience indicators

Both the genetic and residual variance of LnVar increased from the first period of lactation 1 (11-110 days) to the last period (211-340 days): the genetic variance increased from 0.051 to 0.070 and the residual variance from 0.342 to 0.388 (Table 3.4). The heritability of LnVar was highest based on lactation period 3 (0.15) and lowest based on lactation period 2 (0.12). The genetic variance of LnVar was intermediate when based on the full first lactation (0.053) compared with different periods of lactation 1. However, the heritability of LnVar based on full lactation 1 (0.20) was higher than the heritabilities of LnVar based on periods of lactation 1, due to a lower residual variance. The genetic variance of LnVar based on full lactations increased from 0.053 in lactation 1 to 0.057 in lactation 3, whereas the residual variance increased from 0.21 to 0.25 (Table 3.4). The heritability decreased over lactations (0.20 to 0.19).

The genetic variance of r_{auto} increased from the first period of lactation 1 (0.0023) to the third period (0.0028). The residual variance was similar in the 3 periods of lactation 1 (0.044 to 0.046). The heritability of r_{auto} was similar in the 3 periods of lactation, ranging from 0.049 in period 1 to 0.059 in period 3. The genetic variance of r_{auto} based on full lactation 1 (0.0025) was intermediate compared with the genetic variance of r_{auto} based on the different periods of the lactation. However, the heritability of r_{auto} based on the full lactation was higher (0.084) than based on the different periods, due to a lower residual variance. The genetic variance of r_{auto} based on full lactations decreased from 0.0025 in lactation 1 to 0.0017 in lactation 3, whereas the residual variance was similar across lactations (0.026 to 0.028; Table 3.4). The heritability decreased over lactations (0.084 to 0.058).

The genetic variance of ADMY increased within lactation 1 from 5.80 in the first period to 9.37 in the last period, and the heritability increased from 0.32 to 0.45 (Table 3.4). The heritability of ADMY based on full lactation 1 (0.45) was higher than the heritability of ADMY based on lactation period 1 (0.32), but similar to the heritability of ADMY based on lactation periods 2 and 3 (0.43 and 0.45). The genetic variance of ADMY was similar across full lactations (7.96 to 9.04), and the residual variance increased over lactations (9.73 to 17.66). The heritability decreased over lactations (0.45 to 0.34). In summary, the genetic variance and heritability of LnVar and ADMY generally increased within lactation 1, whereas it remained similar for r_{auto} . However, the genetic variance and heritability decreased from lactation 1 to 3 for LnVar, r_{auto} , and ADMY.

3.3.3 Genetic correlations between lactation periods and full lactations

Strong genetic correlations were observed between different lactation periods or full lactations for LnVar, r_{auto} , and ADMY (Table 3.5 and 3.6). The genetic correlations between full lactation 1 and the different periods of lactation 1 ranged from 0.90 to 0.99 (Table 3.5). Note that these are strong because of the part-whole relationship. For each trait, the first or last period of lactation 1 had the weakest genetic correlation with the full first lactation, whereas the second period had the strongest genetic correlation with the full lactation. Within lactation 1, the genetic correlation between period 2 and 3 was strongest for all traits (0.96 to 0.97), whereas the genetic correlation between period 1 and 3 was weakest (0.65 to 0.81). For each trait, the genetic correlation between lactation 2 and 3 was strongest (0.95 to 0.99; Table 3.6), and the genetic correlation between lactation 1 and 3 was weakest (0.71 to 0.91). The lowest genetic correlation was always for

3 Resilience indicators in different lactations and lactation stages

r_{auto} , whereas the genetic correlations for LnVar and ADMY were more similar. In summary, basing a resilience indicator or ADMY on different periods of lactation 1 or on different lactations, resulted in genetically similar traits, but the genetic correlations decreased when the periods within lactation or full lactations were further apart in time.

Table 3.4 Heritability (h^2), additive genetic variance (σ_a^2) and residual variance (σ_e^2) of the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and of average daily milk yield (ADMY), based on different periods of lactation 1 or on different full lactations¹.

Trait	Moment of measurement	h^2	σ_a^2	σ_e^2
LnVar	Lactation period 1	0.13 (0.0074)	0.051 (0.0031)	0.34 (0.0025)
	Lactation period 2	0.12 (0.0065)	0.054 (0.0032)	0.40 (0.0026)
	Lactation period 3	0.15 (0.0094)	0.070 (0.0046)	0.39 (0.0035)
	Lactation 1*	0.20 (0.0040)	0.053 (0.0010)	0.21 (0.0015)
	Lactation 2*	0.18 (0.0066)	0.053 (0.0019)	0.24 (0.0019)
	Lactation 3*	0.19 (0.010)	0.057 (0.0033)	0.25 (0.0029)
	Lactation 3*	0.19 (0.010)	0.057 (0.0033)	0.25 (0.0029)
r_{auto}	Lactation period 1	0.049 (0.0027)	0.0023 (0.00012)	0.044 (0.00037)
	Lactation period 2	0.050 (0.0024)	0.0024 (0.00011)	0.046 (0.00033)
	Lactation period 3	0.059 (0.0014)	0.0028 (0.000062)	0.044 (0.00033)
	Lactation 1*	0.084 (0.0021)	0.0025 (0.000069)	0.028 (0.00017)
	Lactation 2*	0.073 (0.0062)	0.0021 (0.00017)	0.026 (0.00030)
	Lactation 3*	0.058 (0.0083)	0.0017 (0.00027)	0.028 (0.00017)
	Lactation 3*	0.058 (0.0083)	0.0017 (0.00027)	0.028 (0.00017)
ADMY	Lactation period 1	0.32 (0.0033)	5.80 (0.082)	12.50 (0.086)
	Lactation period 2	0.43 (0.0088)	9.24 (0.21)	12.38 (0.18)
	Lactation period 3	0.45 (0.012)	9.37 (0.31)	11.63 (0.19)
	Lactation 1	0.45 (0.0050)	7.96 (0.10)	9.73 (0.085)
	Lactation 2	0.37 (0.0050)	9.04 (0.13)	15.31 (0.12)
	Lactation 3	0.34 (0.0033)	9.04 (0.092)	17.66 (0.17)
	Lactation 3	0.34 (0.0033)	9.04 (0.092)	17.66 (0.17)

¹Estimates are weighted means of trivariate analyses of 5 subsets of the data; empirical SE between parentheses. * indicates weighted mean of variance components of 4 subsets of complete dataset instead of 5.

Table 3.5 Genetic correlations among periods 1, 2 and 3 of the first lactation and genetic correlations between the 3 lactation periods and the full first lactation for the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and for average daily milk yield (ADMY)¹.

	LnVar	r_{auto}	ADMY
Lactation period 1 and 2	0.88 (0.012)	0.82 (0.014)	0.90 (0.0063)
Lactation period 1 and 3	0.81 (0.017)	0.65 (0.029)	0.80 (0.012)
Lactation period 2 and 3	0.97 (0.0067)	0.96 (0.017)	0.96 (0.0024)
Lactation period 1 and full lactation 1	0.95 (0.0053)	0.91 (0.011)	0.93 (0.0037)
Lactation period 2 and full lactation 1	0.97 (0.0031)	0.98 (0.0035)	0.99 (0.00045)
Lactation period 3 and full lactation 1	0.95 (0.0063)	0.90 (0.010)	0.97 (0.0024)

¹Genetic correlations are weighted means of trivariate analyses of 5 subsets of the data; empirical SE are between parentheses.

Table 3.6 Genetic correlations between lactations 1, 2 and 3 for the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and for average daily milk yield (ADMY)¹.

	LnVar	r_{auto}	ADMY
Lactation 1 and 2	0.94 (0.0074) ¹	0.83 (0.018) ¹	0.89 (0.0065)
Lactation 1 and 3	0.91 (0.017) ¹	0.71 (0.021) ¹	0.89 (0.0063)
Lactation 2 and 3	0.99 (0.012) ¹	0.95 (0.021) ¹	0.98 (0.0020)

¹Genetic correlations are weighted means of trivariate analyses of 5 subsets of the data; empirical SE are between parentheses. LnVar and r_{auto} are weighted mean of genetic correlations of 4 subsets of complete data set instead of 5.

3.3.4 Genetic correlations among LnVar, r_{auto} , and ADMY

The genetic correlation between LnVar and r_{auto} was weak based on all 3 lactation periods and based on all full lactations (-0.13 to 0.02; Table 3.7). Therefore, LnVar and r_{auto} were genetically independent traits, irrespective of when they were measured. The genetic correlation between LnVar and ADMY was positive and strong based on all different lactation periods and based on all full lactations (0.72 to 0.81; Table 3.7), which means that cows with genetically a high milk yield tended to have a high variability in milk yield. The genetic correlations between r_{auto} and ADMY were also mostly positive (-0.04 to 0.28), but weaker than the genetic correlations between LnVar and ADMY. The genetic correlations between r_{auto} and ADMY differed considerably between different lactation periods

and different lactations. In summary, LnVar and r_{auto} were genetically independent traits based on all periods of lactation 1 and all lactations, and both traits were mostly positively correlated with ADMY, with strong genetic correlations between LnVar and ADMY.

Table 3.7 Genetic correlations among LnVar (natural log-transformed variance of deviations from a lactation curve), r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and ADMY (average daily milk yield) for periods 1, 2 and 3 of the first lactation, and for full lactations 1, 2, and 3¹.

	LnVar and r_{auto}	LnVar and ADMY	r_{auto} and ADMY
Lactation period 1	0.023 (0.031)	0.74 (0.018)	0.28 (0.033)
Lactation period 2	-0.13 (0.019)	0.79 (0.013)	-0.041 (0.011)
Lactation period 3	-0.10 (0.034)	0.80 (0.015)	0.17 (0.036)
Lactation 1	-0.016 (0.054)	0.76 (0.021)	0.15 (0.050)
Lactation 2	-0.030 (0.051)	0.81 (0.0078)	0.081 (0.036)
Lactation 3	-0.024 (0.11)	0.72 (0.025)	0.024 (0.052)

¹Genetic correlations are weighted means of trivariate analyses of 5 subsets of the data; empirical SE are between parentheses.

3.3.5 Genetic correlations with health, longevity, fertility, and metabolic traits

The LnVar based on all lactation periods and on all full lactations had negative genetic correlations (-0.04 to -0.48) with the health, longevity, fertility, and metabolic traits except DMI (Table 3.8). The genetic correlations between LnVar and DMI were positive and ranged from 0.13 to 0.35. These genetic correlations mean that low LnVar was genetically related to good health, longevity, and fertility, and a high BCS and low DMI (Table 3.8). However, LnVar had strong genetic correlations with ADMY (0.72 to 0.81; Table 3.7), and ADMY also had substantial genetic correlations with some of the health, longevity, fertility, and metabolic traits (-0.38 to 0.66; Table 3.8). The genetic correlations with ADMY were often in the same direction as the ones for LnVar. Therefore, the partial genetic correlations, adjusted for ADMY (Table 3.9) are more informative about the associations between LnVar and the health, longevity, fertility, and metabolic traits, independent of ADMY.

Table 3.8 Genetic correlations of LnVar (natural log-transformed variance of deviations from a lactation curve), r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and ADMY (average daily milk yield) based on periods 1, 2 and 3 of the first lactation and full lactations 1, 2, and 3 with health, functional, metabolic, and production traits¹.

Resilience indicator		Health, functional, and metabolic traits ²									
		UH	HH	KET	LON	FER	BCS	DMI	OMY		
LnVar	Lactation period 1	-0.30	-0.10	-0.48	-0.18	-0.36	-0.42	0.13	0.50		
	Lactation period 2	-0.28	-0.19	-0.44	-0.11	-0.36	-0.38	0.21	0.62		
	Lactation period 3	-0.21	-0.16	-0.40	-0.04	-0.35	-0.29	0.35	0.69		
	Lactation 1	-0.32	-0.14	-0.48	-0.15	-0.40	-0.41	0.23	0.64		
	Lactation 2	-0.31	-0.09	-0.41	-0.15	-0.25	-0.26	0.34	0.61		
	Lactation 3	-0.33	-0.12	-0.41	-0.17	-0.25	-0.22	0.22	0.48		
	Lactation period 1	-0.24	-0.08	-0.22	-0.06	-0.19	-0.26	-0.14	0.15		
	Lactation period 2	-0.16	-0.03	-0.07	0.02	0.04	-0.09	-0.06	-0.04		
	Lactation period 3	-0.08	0.02	-0.06	0.06	-0.01	0.01	-0.02	0.06		
r_{auto}	Lactation 1	-0.21	-0.05	-0.15	-0.03	-0.11	-0.12	-0.04	0.12		
	Lactation 2	-0.10	-0.04	-0.18	0.05	-0.08	-0.02	0.05	0.13		
	Lactation 3	-0.27	-0.01	-0.17	-0.04	-0.03	-0.03	-0.05	0.01		
	Lactation period 1	-0.23	-0.16	-0.36	-0.04	-0.34	-0.29	0.59	0.85		
	Lactation period 2	-0.15	-0.13	-0.38	0.08	-0.33	-0.19	0.63	0.93		
	Lactation period 3	-0.08	-0.12	-0.35	0.14	-0.34	-0.17	0.66	0.90		
	Lactation 1	-0.16	-0.14	-0.38	0.06	-0.35	-0.22	0.66	0.95		
	Lactation 2	-0.01	-0.10	-0.21	0.14	-0.21	-0.02	0.66	0.91		
	Lactation 3	0.04	-0.02	-0.26	0.16	-0.21	0.02	0.54	0.89		
ADMY	Lactation period 1	-0.23	-0.16	-0.36	-0.04	-0.34	-0.29	0.59	0.85		
	Lactation period 2	-0.15	-0.13	-0.38	0.08	-0.33	-0.19	0.63	0.93		
	Lactation period 3	-0.08	-0.12	-0.35	0.14	-0.34	-0.17	0.66	0.90		
	Lactation 1	-0.16	-0.14	-0.38	0.06	-0.35	-0.22	0.66	0.95		
	Lactation 2	-0.01	-0.10	-0.21	0.14	-0.21	-0.02	0.66	0.91		
	Lactation 3	0.04	-0.02	-0.26	0.16	-0.21	0.02	0.54	0.89		
	Lactation period 1	-0.23	-0.16	-0.36	-0.04	-0.34	-0.29	0.59	0.85		
	Lactation period 2	-0.15	-0.13	-0.38	0.08	-0.33	-0.19	0.63	0.93		
	Lactation period 3	-0.08	-0.12	-0.35	0.14	-0.34	-0.17	0.66	0.90		

¹Genetic correlations were estimated using the multiple across-country evaluation (MACE) procedure; SE are not calculated in the MACE procedure.

²UH = udder health; HH = hoof health; KET = ketosis resistance; LON = longevity; FER = fertility; BCS = body condition score; DMI = dry matter intake;

OMY = official milk yield in 305 days.

3 Resilience indicators in different lactations and lactation stages

Almost all partial genetic correlations between LnVar and the health, longevity, fertility, and metabolic traits, except for the correlations with DMI, were in the same direction as the original genetic correlations between LnVar and these traits (-0.51 to 0.02; Table 3.9). Most of these partial correlations were similar or weaker than the original genetic correlations. An exception is the partial genetic correlations with udder health, longevity, and BCS in lactation 2 and 3 (-0.34 to -0.51), which were considerably stronger than the original genetic correlations (-0.15 to -0.33). The partial genetic correlations suggest that among cows with genetically the same level of milk yield, the cows with a less variable milk yield (low LnVar) tended to have better health, longevity, and fertility, and a higher BCS than cows with a more variable milk yield. Strikingly, the partial genetic correlations of LnVar with DMI were negative (-0.30 to -0.59), whereas the original genetic correlations were positive, which means that among cows with genetically the same level of milk yield, the cows with less variable milk yield (low LnVar) tended to eat more than cows with more variable milk yield.

The partial genetic correlations between LnVar and the health, longevity, fertility, and metabolic traits were often comparable between the lactation periods. However, these partial correlations were weaker than or similar to the partial genetic correlations for LnVar based on full first lactation. The partial genetic correlations between LnVar and udder health and longevity were considerably stronger based on lactation 2 and 3 (-0.42 to -0.51) than based on lactation 1 (-0.30 to -0.31). In summary, at a genetically equal level of milk yield, low LnVar was genetically strongest related with health, longevity, and fertility when based on full lactations, and genetic correlations with udder health and longevity increased from lactation 1 to lactation 2 and 3.

In most lactations and lactation periods, low r_{auto} was genetically related with good udder health, hoof health, ketosis resistance, and fertility, and a high BCS and DMI. However, most correlations were weak (r_g from -0.27 to 0.06; Table 3.8). Due to the weak genetic correlations between r_{auto} and ADMY (-0.04 to 0.28; Table 3.7), the partial genetic correlations (Table 3.9) with the health, longevity, fertility, and metabolic traits were similar to the original genetic correlations. The only exceptions were the partial correlations between DMI and r_{auto} based on lactation period 1 and full lactation 1 (-0.39 and -0.19; Table 3.9), which were considerably stronger than the original correlations (-0.14 and -0.04; Table 3.8). All health, longevity, fertility, and metabolic traits had stronger genetic correlations with r_{auto} based on lactation period 1 (-0.26 to -0.06) than with r_{auto} based on full lactation 1 or based on lactation periods 2 or 3 (-0.21 to 0.06; Table 3.8). Moreover, r_{auto} based on lactation periods 2 and 3 were not favorably correlated with all health,

longevity, fertility, and metabolic traits, whereas r_{auto} based on lactation period 1 and full lactation 1 were. Furthermore, the genetic correlations between r_{auto} and the health, longevity, fertility, and metabolic traits were similar over lactations. However, the genetic correlation between r_{auto} and udder health differed substantially between lactations, with the strongest correlation for lactation 3 (-0.27) and the weakest for lactation 2 (-0.10). In summary, low r_{auto} was favorably, but mostly weakly, genetically correlated with health, longevity, and fertility based on lactation period 1 and based on most full lactations, and correlations were in most cases strongest for r_{auto} based on lactation period 1.

Table 3.9 Partial genetic correlations of the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve) based on periods 1, 2 and 3 of the first lactation and full lactation 1, 2, and 3 with health, functional, and metabolic traits adjusted for average daily milk yield¹.

		Health, functional, and metabolic traits ²						
Resilience indicator		UH	HH	KET	LON	FER	BCS	DMI
LnVar	Lactation period 1	-0.19	0.02	-0.34	-0.23	-0.17	-0.32	-0.56
	Lactation period 2	-0.26	-0.14	-0.25	-0.28	-0.17	-0.38	-0.59
	Lactation period 3	-0.23	-0.11	-0.22	-0.25	-0.14	-0.27	-0.41
	Lactation 1	-0.31	-0.05	-0.32	-0.30	-0.22	-0.38	-0.56
	Lactation 2	-0.51	-0.01	-0.43	-0.45	-0.14	-0.41	-0.44
	Lactation 3	-0.51	-0.15	-0.34	-0.42	-0.13	-0.34	-0.30
r_{auto}	Lactation part 1	-0.18	-0.03	-0.13	-0.05	-0.11	-0.19	-0.39
	Lactation part 2	-0.17	-0.04	-0.10	0.02	0.02	-0.10	-0.04
	Lactation part 3	-0.07	0.04	-0.01	0.04	0.05	0.04	-0.18
	Lactation 1	-0.19	-0.03	-0.11	-0.04	-0.06	-0.09	-0.19
	Lactation 2	-0.10	-0.03	-0.17	0.04	-0.07	-0.02	0.00
	Lactation 3	-0.27	-0.01	-0.17	-0.05	-0.03	-0.03	-0.07

¹SE are not calculated in the multiple across-country evaluation (MACE) procedure.

²UH = udder health; HH = hoof health; KET = ketosis resistance; LON = longevity; FER = fertility; BCS = body condition score; DMI = dry matter intake.

3.4 Discussion

Genetic change within and between lactations was studied for 2 resilience indicators, LnVar and r_{auto} . Low LnVar and low r_{auto} were expected to indicate good resilience, which means low vulnerability to disturbances and quick recovery (Berghof et al., 2019b; Poppe et al., 2020). Genetic correlations of the resilience

indicators between lactation periods and lactations were strong but not 1, which suggests that the resilience indicators were genetically similar but not the same traits throughout life. As expected, the estimated genetic parameters for resilience indicators based on full lactation 1 were almost the same as those in Poppe et al. (2020), because of using the same data set and model. Note that the genetic parameters for LnVar in this study were different from the genetic parameters for LnVar in Elgersma et al. (2018), which was defined differently. LnVar in Elgersma et al. (2018) was the natural log-transformed variance of raw daily milk yield instead of daily deviations, and was therefore defined the same as the raw variance in Poppe et al. (2020). However, the difference in genetic parameters between LnVar in Elgersma et al. (2018) and LnVar in the current study is probably mainly due to a difference in the model and not due to the different definition. The raw variance (Poppe et al., 2020) was analyzed with the same model as LnVar in this study and had similar genetic parameters. Nevertheless, LnVar as defined in this study is believed to be more closely related to resilience than raw variance, because it excludes the influence of the shape of the lactation curve (Poppe et al. 2020). We will first discuss genetic change of the resilience indicators between periods of the first lactation, and we will then discuss changes of the resilience indicators between lactations. Finally, we will discuss how our results can be used to improve resilience throughout life.

3.4.1 Genetic change of the resilience indicators within lactation

For both LnVar and r_{auto} , the genetic correlation between lactation period 2 and 3 (DIM 111-210 and DIM 211-340, respectively) was considerably stronger than the genetic correlations between lactation period 1 (DIM 11-110) and the other 2 periods. These correlations suggest that the resilience indicators are partly determined by different genes in early lactation than in the rest of the lactation. It is commonly observed that traits in early lactation are different than the rest of lactation, such as fat and protein yield (Jamrozik and Schaeffer, 1997), liability to clinical mastitis (Chang et al., 2004; Heringstad et al., 2004; Negussie et al., 2008), SCC and SCS (Haile-Mariam et al., 2001; Mrode and Swanson, 2003; Elsaid et al., 2011), liability to hoof problems (Alkhoder et al., 2010; Gernand et al., 2013), and traits related to energy balance (Koenen and Veerkamp, 1998; Manzanilla Pech et al., 2014; Harder et al., 2020).

An explanation for the genetic difference between the resilience indicators in early lactation and in the rest of the lactation is that increased LnVar and r_{auto} are caused by different disturbances in different periods of the lactation. Elevated

LnVar or r_{auto} due to diseases may be more abundant in the first period of the lactation than in the other periods, because incidence of multiple diseases has been shown to be highest in early lactation (Ingvarlsen et al., 2003; Gernand and König, 2014). Elevated LnVar or r_{auto} due to heat stress may be more abundant in periods 2 and 3 of the lactation than in period 1, because the effect of heat stress on milk yield has been shown to be highest in mid- or late lactation (Maust et al., 1972; Aguilar et al., 2009; Santana et al., 2017). Different genes may be involved in handling different disturbances, explaining the genetic difference between the resilience indicators in lactation period 1 and the other lactation periods. A similar explanation has been given for the genetic difference of mean SCC between early lactation and the rest of the lactation. Elevated SCC in early lactation is mainly caused by environmental pathogens that cause a spike in SCC, such as *Escherichia coli*, while elevated SCC in later lactation is mainly caused by infections that result in a more stable elevation of SCC, such as *Staphylococcus aureus* (Detilleux et al., 1997; Haile-Mariam et al., 2001; de Haas et al., 2004). In summary, the genetic difference between resilience indicators in early and later lactation may be explained by differences in vulnerability to different disturbances, which is similar to SCC.

The heritability of both LnVar and r_{auto} was comparable between lactation period 1 and 2 and increased only slightly in lactation period 3, which is different from results from literature on disease traits, SCC, and milk yield. Heritability of disease traits is often highest in early lactation compared to the remainder of the lactation (Chang et al., 2004; Heringstad et al., 2004; Gernand et al., 2013). On the contrary, heritability of mean SCC and milk yield is often lowest in early lactation due to a higher influence of environmental factors, such as diseases, resulting in a high residual variance (Haile-Mariam et al., 2001; Mrode and Swanson, 2003; Elsaid et al., 2011; Bohlouli et al., 2013). LnVar and r_{auto} showed genetic variation across the whole lactation and heritabilities were similar across lactation, which may suggest that disturbances occur and lead to genetic variation in resilience throughout the entire lactation.

The genetic correlations between lactation periods for LnVar were stronger than those for r_{auto} , and were similar to the ones for ADMY. However, because of the strong genetic correlations between LnVar and ADMY, influence of milk yield level on the genetic correlations between lactation periods for LnVar may be large. Partial genetic correlations between LnVar based on different lactation periods, adjusted for genetic correlations with ADMY based on full lactation, were 0.75 between lactation periods 1 and 2, 0.59 between lactation periods 1 and 3, and 0.92 between lactation periods 2 and 3 (data not shown). These partial correlations

are lower than the original correlations (Table 3.5), and are closer to the genetic correlations between lactation periods of r_{auto} (Table 3.5). The partial genetic correlations between LnVar based on different lactation periods and the genetic correlations between r_{auto} based on different lactation periods suggest that resilience changes more throughout lactation than milk yield.

3.4.2 Genetic change of the resilience indicators between lactations

For both LnVar and r_{auto} , the genetic correlations between lactations decreased as lactations were further apart in time, and genetic correlations were strongest between lactation 2 and 3.

It is commonly observed that genetic correlations are stronger between lactations that are closer in time than between lactations that are further apart, including correlations for milk, fat, and protein yield (Weller and Ezra, 2004), clinical mastitis (Carlén et al., 2004; Heringstad et al., 2004; Urioste et al., 2012), and SCS or SCC (Haile-Mariam et al., 2001; Carlén et al., 2004; Weller and Ezra, 2004). An explanation for the genetic difference in the resilience indicators between lactation 1 and the other lactations is that primiparous cows are different from multiparous cows in terms of nutrient partitioning and energy mobilization. Primiparous cows have to partition more of their nutrients to growth than multiparous cows, and have a lower milk yield (Wathes et al., 2007; Whittemore, 2009). Furthermore, primiparous cows mobilize less body energy than multiparous cows (Friggens et al., 2007). Therefore, different genes may be involved in partitioning energy to handling disturbances (being resilient) in first lactation than in later lactations.

The same resilience indicator recorded in different lactations could be considered a repeated trait instead of as different traits. Estimating repeatability using a repeatability model would be interesting. However, a multitrait model is preferred over a repeatability model, because a repeatability model assumes the trait to be genetically identical across lactations (Meyer and Hill, 1997), which was not true for the resilience indicators. Nevertheless, the phenotypic correlations between lactations (Appendix Table A 3.2) provide an indication of repeatability (Barker and Robertson, 1966), and suggest that r_{auto} has lower repeatability (r_p of 0.16-0.28) than LnVar (r_p of 0.29-0.36), and both have lower repeatability than ADMY (r_p of 0.53-0.57).

3.4.3 Genetic improvement of resilience to maximize trouble-free lifetime production

The below unity genetic correlations between lactation periods for LnVar and r_{auto} may suggest that genetic selection should focus on periods of the lactation that are most informative about resilience instead of on full lactation. However, for LnVar it is unlikely that a particular period of the lactation is more informative about resilience than full lactation. The partial genetic correlations between LnVar and the health traits and longevity were stronger when based on full lactation than when based on one of the lactation periods, or they were similar. Therefore, to improve resilience using LnVar, data from the full lactation is recommended to be used. However, r_{auto} was only favorably correlated with all health traits and longevity when based on lactation period 1 or full lactation and not when based on the other lactation periods. Although the genetic correlations with health traits and longevity were stronger in lactation period 1 than in the full lactation, selection on r_{auto} based on full lactation is recommended. The heritability of r_{auto} was higher based on full lactation than based on lactation period 1 and the genetic correlation between them was strong due to their part-whole relationship (0.91). Therefore, if we would assume mass selection on r_{auto} , the accuracy of direct selection on r_{auto} in lactation period 1 would be lower (0.23) than the accuracy of indirect selection on r_{auto} in lactation period 1 using r_{auto} in full lactation (0.27). Therefore, indirect selection using r_{auto} based on full lactation would be more effective than direct selection on r_{auto} based on lactation period 1.

Both LnVar and r_{auto} were genetically similar traits in different lactations, but genetic correlations deviated from unity. Therefore, to improve resilience not only in first lactation, but also later in life, records from all 3 lactations are recommended to be used. A similar recommendation has been given for other traits, such as clinical mastitis and SCC (Banos and Shook, 1990; Pösö and Mäntysaari, 1996; Carlén et al., 2004), fertility traits (Muuttoranta et al., 2019), and milk yield (Banos and Shook, 1990; Pösö and Mäntysaari, 1996). Moreover, for LnVar partial genetic correlations with the health traits were stronger in later lactations than in lactation 1. Therefore, composing a resilience index of LnVar based on not only lactation 1, but also lactation 2 and 3, is expected to increase the correlated response in the health traits, which is desired from a resilience perspective. Due to the weak genetic correlations of r_{auto} with health traits, the added value of r_{auto} as a resilience indicator is questionable and further research is needed.

In practice, the index for resilience should be incorporated into the already existing total merit index containing other important traits, such as yield, longevity,

fertility, and health traits (Berghof et al., 2019b; lung et al., 2020). Due to the favorable genetic correlations between the resilience indicators and the health, longevity, and fertility traits, inclusion of the resilience indicators will assist in genetic improvement of health, longevity, and fertility and vice versa. Furthermore, inclusion of milk yield and DMI, which were unfavorably correlated with the resilience indicators, will slow down progress in resilience (Berghof et al., 2019b; lung et al., 2020), but will make it possible to select animals that combine good resilience with good feed efficiency and high milk yield. Inclusion of the resilience indicators into the total merit index will therefore help to maximize trouble-free lifetime production.

3.5 Conclusions

For each of the 2 resilience indicators, LnVar and r_{auto} , heritabilities were similar in different periods of the lactation. Heritabilities were higher in full lactation 1, but decreased over lactations. For each of the resilience indicators, genetic correlations between different periods of lactation 1 and between different lactations were strong (0.65 to 0.99), but decreased when periods were further apart in time. These results suggest that resilience is not the same trait throughout life, but is still genetically similar. As a resilience indicator for breeding, LnVar based on full lactation is preferred over LnVar based on periods of the lactation, because of a higher heritability and stronger and favorable genetic correlations with health and longevity. R_{auto} based on period 1 of the lactation seemed to be more informative about resilience than r_{auto} based on other periods, but genetic correlations with health and longevity were still weak. Based on these results, the usefulness of r_{auto} as a resilience indicator for breeding remains to be determined. An index of EBV for LnVar based on lactations 1, 2, and 3 is recommended to optimally improve resilience throughout the first 3 lactations.

3.6 Acknowledgments

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3.7 Appendix

Table A 3.1 Phenotypic correlations among periods 1, 2 and 3 of the first lactation and phenotypic correlations between the 3 lactation periods and the full first lactation for the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and for average daily milk yield (ADMY)¹.

	LnVar	r_{auto}	ADMY
Lactation period 1 and 2	0.29 (0.0017)	0.24 (0.0017)	0.83 (0.0012)
Lactation period 1 and 3	0.21 (0.0023)	0.17 (0.0017)	0.67 (0.0021)
Lactation period 2 and 3	0.33 (0.0019)	0.29 (0.0030)	0.86 (0.0012)
Lactation period 1 and full lactation 1	0.76 (0.00098)	0.73 (0.0014)	0.89 (0.00066)
Lactation period 2 and full lactation 1	0.69 (0.0012)	0.65 (0.0021)	0.97 (0.00026)
Lactation period 3 and full lactation 1	0.64 (0.0019)	0.60 (0.0019)	0.92 (0.00076)

¹Phenotypic correlations are weighted means of trivariate analyses of 5 subsets of the data; empirical SE are between parentheses.

Table A 3.2 Phenotypic correlations between lactations 1, 2 and 3 for the resilience indicators LnVar (natural log-transformed variance of deviations from a lactation curve) and r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and for average daily milk yield (ADMY)¹.

	LnVar	r_{auto}	ADMY
Lactation 1 and 2	0.33 (0.0033) ¹	0.24 (0.0033) ¹	0.57 (0.0041)
Lactation 1 and 3	0.29 (0.0075) ¹	0.16 (0.0028) ¹	0.53 (0.0036)
Lactation 2 and 3	0.36 (0.0052) ¹	0.28 (0.0045) ¹	0.57 (0.0069)

¹Phenotypic correlations are weighted means of trivariate analyses of 5 subsets of the data; empirical SE are between parentheses. LnVar and r_{auto} = weighted mean of phenotypic correlations of 4 subsets of complete dataset instead of 5.

3 Resilience indicators in different lactations and lactation stages

Table A 3.3 Phenotypic correlations among LnVar (natural log-transformed variance of deviations from a lactation curve), r_{auto} (lag-1 autocorrelation of deviations from a lactation curve), and ADMY (average daily milk yield) for periods 1, 2, and 3 of the first lactation, and for full lactation 1, 2, and 3¹.

	LnVar and r_{auto}	LnVar and ADMY	r_{auto} and ADMY
Lactation period 1	0.11 (0.0025)	0.088 (0.0033)	0.072 (0.0041)
Lactation period 2	0.14 (0.0041)	0.16 (0.0033)	-0.0061 (0.0025)
Lactation period 3	0.11 (0.0017)	0.26 (0.0034)	0.038 (0.0020)
Lactation 1	0.10 (0.0065)	0.22 (0.034)	0.067 (0.0037)
Lactation 2	0.18 (0.0072)	0.29 (0.0034)	0.0049 (0.0048)
Lactation 3	0.24 (0.0069)	0.24 (0.0057)	-0.034 (0.0027)

¹Phenotypic correlations are weighted means of trivariate analyses of 5 subsets of the data; empirical SE are between parentheses.

4

Validation of resilience indicators by estimating genetic correlations among daughter groups and with yield responses to a heat wave and disturbances at herd level

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Abstract

Resilient cows are minimally affected in their functioning by disturbances, and if affected, they quickly recover. Previously, the variance and autocorrelation of daily deviations from a lactation curve were proposed as resilience indicators. These traits were heritable and genetically associated with good health and longevity. However, it was unknown if selection for these indicators would lead to desired changes in the phenotype. The first aim of this study was to investigate if forward prediction of the resilience indicators in another environment was possible. Therefore, the resilience indicator records were split into 2 subsets, each containing half of the daughters of each sire, split within sire into cows that calved in early year-seasons and cows that calved in more recent year-seasons. Genetic correlations between the subsets were then estimated for each resilience indicator. The second aim was to estimate genetic correlations between the resilience indicators and traits describing production responses to actual disturbances. The disturbances were a heat wave in July 2015, and yield disturbances at herd level. The latter were selected by decreases in mean yield of all primiparous cows in a herd, indicating that a disturbance occurred. The data set used for calculation of the resilience indicators and the traits describing yield responses contained 62,932,794 daily milk yield records on 199,104 primiparous cows. Genetic correlations (r_g) between recent and earlier daughter groups were 1 for both resilience indicators, which suggests that selection will result in changes in the phenotype in the next generation. Furthermore, low variance was genetically correlated with weak response in milk yield to both the heat wave and herd disturbances (r_g 0.47 to 0.97). Low autocorrelation was genetically correlated with reduced perturbation length and quick recovery after the heat wave and herd disturbances (0.28 to 0.97). These results suggest that variance and autocorrelation cover different aspects of resilience, and should be combined in a resilience index. In conclusion, genetic selection for the resilience indicators will likely result in favorable changes in the traits themselves, and in response and recovery to actual disturbances, which confirms that they are useful resilience indicators.

Key words: resilience, response, recovery, validation

4.1 Introduction

Cows are regularly subject to environmental disturbances, such as pathogens, extreme weather, and changes in feed quality. Cows that are minimally affected in their functioning by disturbances, or that quickly recover, are called resilient (Colditz and Hine, 2016; Berghof et al., 2019b). Improvement of resilience is desirable, because resilient cows require less labor and treatments and have lower production losses than nonresilient cows (Berghof et al., 2019b).

To improve resilience through genetic selection, 2 resilience indicators have been developed (Poppe et al., 2020) based on Scheffer et al. (2018). The first is the natural log-transformed variance of deviations from an expected lactation curve (**LnVar**). Low LnVar was expected to indicate good resilience based on the hypothesis that cows with stable production are less affected in their functioning by disturbances than cows with variable production. The second resilience indicator is the lag-1 autocorrelation of yield deviations (r_{auto}). Low r_{auto} was expected to indicate good resilience based on the hypothesis that cows with low similarity between subsequent deviations do not have long periods of consecutive negative deviations, and thus quickly recover from disturbances. Both resilience indicators showed genetic variation and were genetically associated with good udder health, little ketosis, and good longevity. Similar results have been shown for resilience indicators based on body weight in chickens (Berghof et al., 2019a) and feed intake in pigs (Putz et al., 2019; Cheng et al., 2020).

Although LnVar and r_{auto} are promising resilience indicators based on previous results, further validation is required. First, it should be investigated if selection for the resilience indicators based on a certain set of daughter phenotypes will result in lower realized LnVar and r_{auto} in other daughters in other environments at other time points. When the environment of selection candidates differs from the environment in which the offspring perform, especially with respect to type and amount of environmental disturbances, limited phenotypic response to selection may be observed in the presence of genotype by environment interaction (Calus, 2006; Putz et al., 2019). For LnVar and r_{auto} it is unknown if they are genetically similar across years because of possible changes in environment, and thus if selection on these traits would be effective. An option for validation of EBV is forward prediction, which is commonly used for validating genomic EBV (Mäntysaari et al., 2010), and can also be used to predict phenotypes of second-crop daughters from EBV based on first-crop daughters (Ødegård et al., 2003).

Second, it should be validated if LnVar and r_{auto} are related to strength of response and recovery to actual disturbances. The resilience indicators have only indirectly been shown to indicate resilience through genetic correlations with

4 Validation of resilience indicators

health traits and longevity, based on the hypothesis that resilient cows have fewer health problems and live longer than less resilient cows. However, health traits are mainly informative about incidence of disease, which is only one aspect of resilience and that only covers disease disturbances (Berghof et al., 2019b). Furthermore, longevity, although by some considered as a resultant of resilience, is affected largely by the culling decisions of farmers (van Pelt, 2017), which are not always related to resilience (Friggens et al., 2017). Therefore, it is important to investigate if low LnVar and r_{auto} are also genetically associated with weaker response in milk yield and quicker recovery after a variety of actual disturbances.

The first aim of this study was to perform forward prediction by estimating for both LnVar and r_{auto} the genetic correlation between recent and earlier groups of daughters of each sire from nonoverlapping herd-year-seasons. The second aim was to estimate for both LnVar and r_{auto} genetic correlations with traits describing production response to 2 disturbances selected based on available data: (1) a heat wave, and (2) an unknown disturbance at herd level.

4.2 Materials and methods

Genetic correlations between the same resilience indicators in earlier and more recent daughter groups in different herd-year-seasons of calving were estimated, as well as genetic correlations between the resilience indicators and traits describing yield responses to disturbances. The data used for these analyses will first be described. The calculation of resilience indicators and traits describing response to disturbances from these data will then be explained. Finally, the genetic analyses will be described.

4.2.1 Data

The original data set contained milk yield records obtained during single milk visits to automatic milking systems (**AMS**) and conventional milking systems. The data set was provided by Cooperation CRV and CRV BV (Arnhem, the Netherlands) and contained 1,782,373,113 milk yield records on 1,120,550 Dutch cows. From these data, only data were selected from primiparous cows that were milked by AMS during their entire lactation, that were at least 87.5% Holstein Friesian, that were herd-book registered, that calved after 640 days of age, that had at least 50 days with milk yield records, that had no more than 5% of days with missing records, and that belonged to a herd-year-season of calving (**HYS**) class with at least 5 cows. Herd-year-seasons were based on 4 seasons (January-March, April-June, July-September, October-December). Data editing was the same as in Poppe

et al. (2020), and was performed using the AWK programming language (Aho et al., 1988) and R (R v 3.2.2; R Project for Statistical Computing, Vienna, Austria).

Single milk yield records were first converted to daily records for each cow, by summing up the single milk yield records per day. The first milk yield record of each day was proportionally assigned to the current and the previous day, depending on the time between the current AMS visit and midnight and between the previous AMS visit and midnight. Milk yield records after 350 days in milk (**DIM**) were removed. In addition, daily milk yield records were removed if they deviated more than 6 standard deviations (**SD**) from a Wilmink curve fitted for individual cows (CRV, 2020g) or if they were larger than 100 kg. The limit of 6 SD appeared mild enough upon visual inspection to preserve outliers that contain information about resilience. The resulting data set contained 62,932,794 daily milk yield records on 199,104 cows in 2,733 herds. The resulting data set was used for computing (1) resilience indicators and average daily milk yield, and (2) traits describing yield response to 2 disturbances, which will be explained in the following paragraphs.

4.2.2 Computing resilience indicators

To calculate the resilience indicators, first for each cow a lactation curve was fitted to remove the effect of the shape of the lactation curve on the resilience indicators. Lactation curves were fitted using polynomial quantile regression with a quantile of 0.7, because this method yielded the best resilience indicators in Poppe et al. (2020):

$$y_t = \beta_0 + \beta_1 * t + \beta_2 * t^2 + \beta_3 * t^3 + \beta_4 * t^4 + \varepsilon,$$

where y_t is the observed milk yield on DIM t ; t^n are DIM to the power of n , where n is 1, 2, 3, or 4; β_n are regression coefficients describing the relationships between t^n and y_t ; and ε is the error term. The quantreg package (Koenker, 2018) and the poly function in R were used. Quantile regression (Koenker, 2005) with a quantile of 0.7 was used instead of classical regression to reduce the effect of decreases in milk yield due to disturbances on the expected milk yield. Consequently, the negative deviations became larger and probably more informative about resilience (Poppe et al., 2020; 2021a). After fitting the lactation curves, for each cow the deviations from her curve were calculated as $y_t - \hat{y}_t$. The resilience indicators were then computed by calculating the natural log-transformed variance (**LnVar**) and lag-1 autocorrelation (r_{auto}) of these deviations. High LnVar was expected to indicate poor resilience because decreases in milk yield due to disturbances will lead to increased variability in daily milk yield deviations. A high r_{auto} was expected

to indicate poor resilience because decreases in milk yield due to disturbances will lead to increased similarity between deviations on subsequent days, especially when recovery is slow (Scheffer et al., 2018; Berghof et al., 2019b; Poppe et al., 2020). In addition to the resilience indicators, the average daily milk yield (**ADMY**) was calculated for each cow. The average daily milk yield was needed for adjusting genetic correlations between the resilience indicators and the traits describing yield responses to disturbances for milk yield level (see “Genetic Analysis”). Records on LnVar, r_{auto} , and ADMY were removed if they deviated more than 4 SD from the mean of all lactations. The resulting data set contained 199,074 records on LnVar, 198,908 records on r_{auto} , and 199,085 records on ADMY.

4.2.3 Preparation for forward prediction

For the forward prediction, the data set containing LnVar and r_{auto} was then split into 2 subsets. Only daughters from sires with at least 10 daughters were used. From each of these sires, the daughters were sorted based on their year-season of calving. For each sire, the daughter group was then split in 2 by the midpoint of the year-seasons of calving of the daughters. As a result, each sire had a more recent and an earlier calving daughter group. Averaged over all sires, the daughters in the more recent daughter groups calved 339 days later than the daughters in the accompanying earlier daughter groups. In addition, the daughter of each sire that calved earliest, calved on average 841 days earlier than the daughter that calved most recently. The more recent calving daughter groups of all sires were placed together in subset 1, and the earlier calving daughter groups of all sires were placed together in subset 2. The resulting subsets contained cows with overlapping calving dates, because of differences in age of the sires and therefore differences in calving dates of the daughters: daughters of old and young sires with the same calving date could be placed in different daughter groups. However, the overlap is not a problem, because for the forward prediction, the interest is in similarity between the resilience indicators of the 2 subsets within sire. Finally, subset 1 contained 93,517 records on LnVar and 93,436 records on r_{auto} . Subset 2 contained 90,050 records on LnVar and 89,978 records on r_{auto} . The subsets contained daughters of 1,761 sires.

4.2.4 Computing traits describing yield response to actual disturbances

The daily milk yield records were also used to compute traits describing the responses in milk yield of cows to 2 types of disturbances. The 2 types of disturbances were a heat wave and an unknown disturbance at herd level, based

on a temporary decrease in mean herd yield. These 2 types of disturbances were selected based on availability of data on when the disturbances occurred and availability of sufficient cows with daily milk yield records. For each type of disturbance, several traits describing the response in milk yield, such as depth and length of the temporary yield decrease following the disturbance, were calculated for each cow. The determination of the 2 types of disturbances will first be described, followed by the calculation of the traits describing yield response to these disturbances (hereafter, “response traits”).

4.2.4.1 Heat wave

From the years with daily milk yield data (2011-2017), one severe heat wave was selected as a disturbance. For selecting a heat wave, mean daily temperature and mean daily relative humidity between May 2011 and September 2017 measured in a weather station in De Bilt were retrieved from the website of KNMI (KNMI, 2019). Because of the small size of the Netherlands, a heat wave detected in De Bilt was assumed to be present in the whole country. From the weather data, the temperature humidity index (THI) was calculated as (National Research Council, 1971):

$$THI = (1.8 * temperature + 32) - ((0.55 - 0.0055 * humidity) * (1.8 * temperature - 26)),$$

where *temperature* was the mean daily temperature (°C) and *humidity* was the mean daily relative humidity (%). From the weather data, 15 dates were selected with a THI of at least 72, because heat stress is assumed to start at a THI of 72 (Ravagnolo et al., 2000; Bohmanova et al., 2008). From these dates, the date was selected with the lowest mean THI across the 5 preceding days to ensure that the selected heat wave was sudden and could be considered a disturbance. This selected date was in 2011, and a limited number of cows with daily milk yield records were available at that time. Therefore, the date with the second lowest mean THI during the five preceding days was selected, which was the July 1, 2015. The THI and the mean daily milk yield of the cows in our data set in the period after this date are shown in Figure 4.1. The figure shows that the heat wave lasted 4 days and that cows on average showed a decrease in milk yield during and after the heat wave, which confirmed that the selected heat wave was suitable for studying individual responses in milk yield. The mean daily temperature during the 4-day heat wave was 25.3 °C, the minimum temperature was 15.8 °C, the maximum temperature was 33.1 °C, the mean daily relative humidity was 64.3%, the

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minimum relative humidity measured was 30%, the maximum relative humidity was 99%, and the mean THI was 73.6. From the data set with daily milk yield records, cows were selected that had records from 10 days before the heat wave until 15 days after the heat wave, which were 28,105 cows.

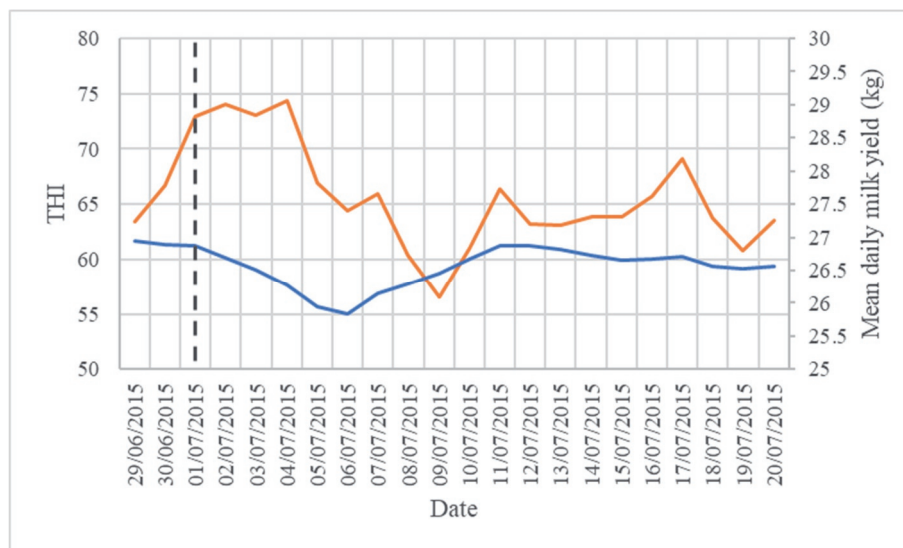


Figure 4.1 Temperature-humidity index (THI; orange) and mean daily milk yield of all cows in the data set (blue) in the period after the start of the selected heat wave (July 1, 2015; dashed line). Dates are in DD/MM/YYYY format.

4.2.4.2 Disturbance at herd level

For each herd in each year, a single date was selected where the mean milk yield of the cows temporarily decreased. In that case we can assume that a disturbance occurred at herd level, although the type of disturbance is unknown. Yield responses of individual cows to these disturbances (hereafter, “herd disturbances”) can then be compared. First, for each date in the daily milk yield data set, the mean milk yield of the cows in each herd was calculated. Then, for each herd with at least half a year of daily milk yield data, dates were selected where the mean milk yield was lower than the mean of the 5 days before and the mean of the 5 days after, and the difference was larger than 3 times the SD of the 5 days before or the 5 days after. From these preselected dates, a single disturbance date was selected for each herd and each year, with the most extreme difference in milk yield with the 5 days before. These 8,905 final single disturbance dates per herd per year in 2,622 herds were used as disturbances in the further analyses.

Figure 4.2 shows that the herd disturbances are spread evenly over all months of the year, with only somewhat increased occurrence in the summer months compared with the winter months. Therefore, the selected herd disturbances are certainly not all heat waves. For some cows, 2 herd disturbances occurred during their lactation, because their lactation was partly in 2 different years. For these cows, only the first disturbance was selected and used for calculation of the response traits. From the data set with daily milk yield records, cows were selected that had records from 10 days before the herd disturbance until 15 days after the herd disturbance, which were 129,722 cows.

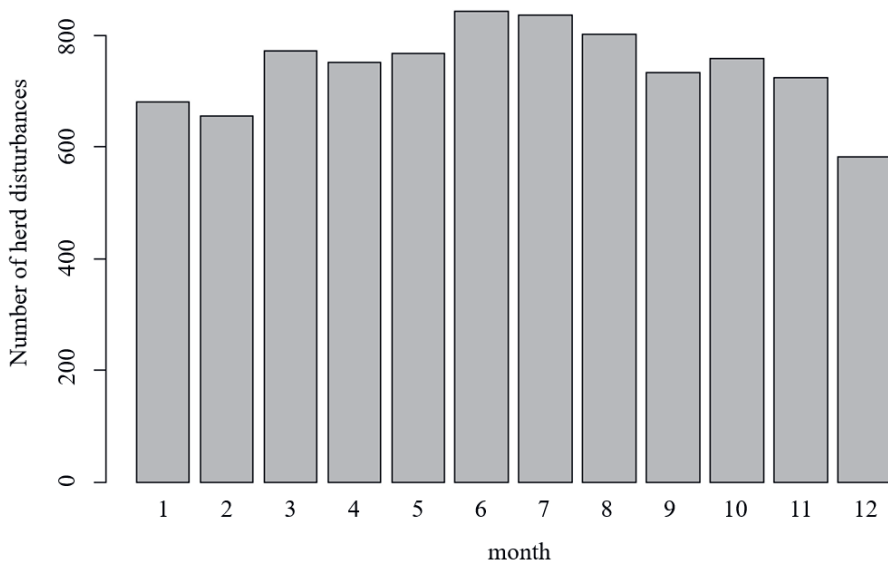


Figure 4.2 Number of herd disturbances selected in each month of the year.

4.2.4.3 Response traits

Traits that describe their response to the heat wave and the herd disturbance were computed on individual cows. These traits were the depth and length of the temporary decrease in milk yield (hereafter referred to as “decrease”), the recovery time, the total amount of yield loss during the decrease, and the mean yield loss per day during the decrease. The start and the end of the decreases of each cow were determined based on deviations from a moving median. A moving median with a window of 21 days was fitted for each cow, which means that the expected milk yield on a day was the median of the 10 days before, the 10 days after, and the day itself, as in Poppe et al. (2020). The yield decrease of a cow was

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assumed to start as soon as the milk yield decreased below the moving median at or after the start of the heat wave, and at or before the date of the herd disturbance, because the herd disturbance must have occurred at or before the date that the cows in the herd decreased their milk yield. Some of the cows (31,527) did not have a negative deviation on the herd disturbance date. These cows could be very resilient, but it is also possible that the herd disturbance did not act on them or they responded more quickly or slowly than their herd mates, causing their decrease to occur before or after the herd disturbance date. Because of the uncertainty about the exact moment of the herd disturbance and the response of these cows to the herd disturbance, it was decided to exclude them from the analyses. For the heat wave, cows that did not have a negative deviation during the heat wave were not removed, because they certainly experienced the heat wave. For both the heat wave and the herd disturbance, the decrease was assumed to end when the milk yield was at or above the moving median again.

The depth of the decrease was defined as the absolute difference between the lowest milk yield during the decrease and the milk yield at the day before the decrease. The length of the decrease was defined as the number of days between the start and end of the decrease. The recovery time was defined as the number of days between the day of the deepest yield during the decrease and the end of the decrease. The total yield loss was defined as the absolute sum of the negative deviations from the moving median during the decrease. The mean deviation per day was defined as the absolute mean of the negative deviations during the decrease. A resilient cow can be described as a cow with a shallow, short decrease with fast recovery and a small amount of yield lost in total and per day. For the heat wave, for cows that did not have a negative deviation within 4 days after the start of the heat wave, it was assumed that their milk yield did not respond to the heat wave, and the response traits were set to 0, which means their response was as resilient as possible. The boundary of 4 days was based on (Hayes et al., 2003) who showed that THI had a significant effect on milk yield up to 4 days later.

4.2.5 Genetic analyses

First, we will describe the genetic analysis that investigated whether the resilience indicators were genetically the same trait in earlier and more recent daughter groups from different herd-year-season classes. After that, we will describe the genetic analysis that investigated whether low LnVar and r_{auto} were related to shallow decreases in milk yield and quick recovery. Genetic analyses were performed using ASReml 4.1 (Gilmour et al., 2015). Variance parameters were

kept in the theoretical parameter space, which means that genetic correlations could be 1 at maximum.

4.2.5.1 Genetic correlations between earlier and more recent daughter groups

Genetic correlations were estimated between LnVar in subsets 1 and 2, and between r_{auto} in subsets 1 and 2 using a bivariate mixed sire model:

$$\begin{bmatrix} \mathbf{y}_1 \\ \mathbf{y}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}_1 & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_2 \end{bmatrix} \begin{bmatrix} \mathbf{b}_1 \\ \mathbf{b}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{Z}_1 & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_2 \end{bmatrix} \begin{bmatrix} \mathbf{s}_1 \\ \mathbf{s}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix},$$

where \mathbf{y}_i was a vector with observations on LnVar or r_{auto} in subset i ; \mathbf{b}_i was a vector with the fixed effects for LnVar or r_{auto} in subset i , which were HYS, age at first calving in months, and lactation length (remaining number of days after removing the first and last 10 DIM) in 7 classes, each containing a range of 40 days (e.g., 50-90 days, 91-130 days); \mathbf{s}_i was a vector with the additive genetic sire effects for LnVar or r_{auto} in subset i ; and \mathbf{e}_i was a vector with the residuals for LnVar or r_{auto} in subset i . \mathbf{X}_i and \mathbf{Z}_i were incidence matrices linking the records in \mathbf{y}_i to the fixed effects and additive genetic effects, respectively. The additive genetic sire effects for all traits were assumed normally distributed with a mean of zero, a genetic sire variance of $\sigma_{s_i}^2$ for trait i and a genetic covariance between traits of $\sigma_{s_1 s_2}$:

$\begin{bmatrix} \mathbf{s}_1 \\ \mathbf{s}_2 \end{bmatrix} \sim N \left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{A} \otimes \begin{pmatrix} \sigma_{s_1}^2 & \sigma_{s_1 s_2} \\ \sigma_{s_1 s_2} & \sigma_{s_2}^2 \end{pmatrix} \right)$, where \mathbf{A} is the additive genetic relationship matrix containing genetic relationships among sires. Five generations of ancestors were included. The residuals were assumed normally distributed as well, with a mean of zero, a residual variance of $\sigma_{e_i}^2$ for trait i , and a residual covariance between traits of 0: $\begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix} \sim N \left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{e_1}^2 & 0 \\ 0 & \sigma_{e_2}^2 \end{pmatrix} \right)$, where \mathbf{I} is an identity matrix.

A residual covariance of 0 was assumed because records were always on different cows. A sire model was used because the sires formed the genetic link between the 2 subsets. In addition to the genetic correlations, additive genetic variance was calculated for each trait in each subset as $\sigma_a^2 = 4\sigma_s^2$, and phenotypic variance was calculated as $\sigma_s^2 + \sigma_e^2$.

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4.2.5.2 Variance components of the response traits

Univariate mixed sire-maternal grandsire (**mgs**) models were first used to investigate if the response traits of the heat wave and the herd disturbance showed genetic variation:

$$\mathbf{y} = \mathbf{X}\mathbf{b} + (\mathbf{Z}_1\mathbf{s} + \frac{1}{2}\mathbf{Z}_2\mathbf{s}) + \mathbf{e},$$

where \mathbf{y} was a vector with observations on the response trait; \mathbf{b} was a vector with covariates and fixed effects, which were DIM at the start of the decrease, DIM², DIM³, herd-year of calving, and year-season of calving (year-season only for response traits to the herd disturbance because of significance); \mathbf{s} was a vector containing the additive genetic sire effects (linked to the phenotypes by incidence matrix \mathbf{Z}_1) overlaid by one-half of the mgs effects (linked by incidence matrix \mathbf{Z}_2), $\mathbf{s} \sim N(\mathbf{0}, \mathbf{A}\sigma_s^2)$, where σ_s^2 is the sire variance; and \mathbf{e} was a vector with the residuals, $\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}\sigma_e^2)$. The used pedigree contained 5 generations of ancestors. Additive genetic variance was calculated as: $\sigma_a^2 = 4\sigma_s^2$, and phenotypic variance was calculated as: $\sigma_p^2 = 1.25\sigma_s^2 + \sigma_e^2$.

4.2.5.3 Genetic correlations between resilience indicators, response traits, and ADMY

Genetic correlations between the resilience indicators and the response traits, among response traits, and among resilience indicators and ADMY were estimated using bivariate mixed sire-mgs models. The fixed effects were as described in the univariate analysis of the response traits, or in the bivariate analysis of the resilience indicators. The following assumptions were made about the sire effects and residuals:

$$\begin{bmatrix} \mathbf{s}_1 \\ \mathbf{s}_2 \end{bmatrix} \sim N\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{A} \otimes \begin{pmatrix} \sigma_{s_1}^2 & \sigma_{s_1 s_2} \\ \sigma_{s_1 s_2} & \sigma_{s_2}^2 \end{pmatrix}\right), \quad \begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix} \sim N\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{e_1}^2 & \sigma_{e_1 e_2} \\ \sigma_{e_1 e_2} & \sigma_{e_2}^2 \end{pmatrix}\right),$$

where $\sigma_{s_i}^2$ is the sire variance for trait i , $\sigma_{s_1 s_2}$ is the sire covariance between the traits, $\sigma_{e_i}^2$ is the residual variance for trait i , and $\sigma_{e_1 e_2}$ is the residual covariance between the traits. To ensure that there was no direct relation between the response traits and the resilience indicators within cows, for cows with data during the disturbance and therefore with a response trait to a disturbance, their record for the resilience indicators was set to missing and the residual covariance between response traits and resilience indicators was set to 0. Similarly, for the genetic correlations between the response traits to the heat wave and the same response traits to the herd disturbance, the response traits to the herd disturbance were set to missing if the herd disturbance was between June 30 and July 11, 2015 (during the studied heat wave; 44 herd disturbances). Herd-year-season of calving classes,

herd-year classes, and sires were removed that contained fewer than 5 records on the resilience indicators or the response traits. The final number of records used for estimating genetic correlations between the resilience indicators and the response traits are shown in Table 4.1.

Table 4.1 The number of records used for estimating genetic correlations between response traits and resilience indicators LnVar (natural log-transformed variance of milk yield deviations, r_{auto} (lag-1 autocorrelation of milk yield deviations), and average daily milk yield (ADMY) in kg.

Disturbance	Response trait	LnVar	r_{auto}	ADMY
Heat wave	22,282	97,349	97,235	97,388
Herd disturbance	70,584	79,280	79,169	79,294

Average daily milk yield had strong genetic correlations with both LnVar and some of the response traits. Therefore, it was difficult to determine if there was any association between LnVar and the response traits that could not be explained by ADMY. To investigate the association between LnVar and the response traits, independent of ADMY, partial genetic correlations between the resilience indicators and the response traits were computed, adjusted for genetic correlations with ADMY ($r_{xy'z}$). The following formula was used (Poppe et al., 2020):

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

where x is LnVar, y is the response trait, and z is ADMY. The genetic correlations between LnVar or ADMY and the response traits, and between LnVar and ADMY were taken from the bivariate analyses. No standard error could be computed for the partial genetic correlations.

4.3 Results

4.3.1 Forward prediction of resilience indicators

The 2 subsets with recent and earlier calving daughter groups showed similar sire and error variances and heritabilities (Table 4.2). The sire variances were 0.01 in both subsets for LnVar, and 0.0005 in both subsets for r_{auto} . The error variances were 0.24 and 0.25 for LnVar, and 0.028 in both subsets for r_{auto} . The heritabilities were 0.18 and 0.17 for LnVar, and 0.07 and 0.06 for r_{auto} . The genetic correlations between recent and earlier daughter groups were 1.00 for both LnVar and r_{auto} .

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Table 4.2 Sire variance (σ_s^2), error variance (σ_e^2), heritability (h^2), and genetic correlation (r_g) between subsets from the bivariate analysis of the resilience indicators LnVar (natural log-transformed variance of milk yield deviations) and r_{auto} (lag-1 autocorrelation of milk yield deviations) in 2 subsets of cows, one containing the daughters of each sire that calved more recently and the other containing the daughters that calved earlier¹.

Trait	Subset	σ_s^2	σ_e^2	h^2	r_g
LnVar	1	0.011 (0.00094)	0.24 (0.0013)	0.18 (0.01)	1.00 ²
	2	0.010 (0.00093)	0.25 (0.0014)	0.17 (0.01)	
r_{auto}	1	0.00053 (0.000062)	0.028 (0.00015)	0.074 (0.0084)	1.00 ²
	2	0.00045 (0.000054)	0.028 (0.00015)	0.064 (0.0076)	

¹SE in parentheses.

²SE was not estimable.

4.3.2 Descriptive statistics of response traits

Milk yield decreased on average by 2.37 kg in response to the heat wave and by 4.73 kg in response to the herd disturbance (Table 4.3). The decrease in milk yield lasted on average 2.99 days after the heat wave and 3.44 days after the herd disturbance. The time between the lowest yield and the time of recovery was on average 2.02 days after the heat wave and 2.27 days after the herd disturbance. The minimum duration of the decrease was 0 days for the heat wave, which was for cows that did not show a decrease. The minimum duration of the decrease was 1 day for the herd disturbance, because only cows were included that showed a decrease in milk yield on the date of their herd disturbance. For both the heat wave and the herd disturbance the maximum duration was 10 days. The mean deviation from the expected yield per day during the decrease was 1.41 kg after the heat wave and 2.24 kg after the herd disturbance. The total yield loss during the decrease in milk yield was on average 5.28 kg after the heat wave and 7.20 kg after the herd disturbance.

Table 4.3 Descriptive statistics of the response traits describing a temporary decrease in milk yield of individual cows in response to a heat wave and a disturbance at herd level

Disturbance	Response trait	Mean	Minimum	Maximum	SD
Heat wave	Decrease depth (kg)	2.37	-14.48	26.79	3.13
	Decrease length (days)	2.99	0	10	2.48
	Recovery time (days)	2.02	0	10	1.65
	Total yield loss (kg)	5.28	0.00	86.01	7.30
	Mean yield loss per day (kg)	1.41	0.00	20.83	1.50
Herd disturbance	Decrease depth (kg)	4.73	0.00	29.01	3.96
	Decrease length (days)	3.44	1	10	2.14
	Recovery time (days)	2.27	1	10	1.55
	Total yield loss (kg)	7.20	0.00	86.83	7.36
	Mean yield loss per day (kg)	2.24	0.00	22.41	2.28

4.3.3 Genetic variances and heritabilities of response traits and genetic correlations between them

Heritabilities of the response traits to the heat wave ranged between 0.01 for mean yield loss per day and 0.05 for total yield loss during the decrease (Table 4.4). The heritabilities and sire and error variances were all significantly different from 0. Heritabilities of the response traits to the herd disturbance ranged between 0.001 for decrease length and 0.02 for the decrease depth (Table 4.4). The heritabilities and sire and error variances were significantly different from 0, except for the sire variance and heritability of decrease length and recovery time.

All variables describing response to the heat wave were highly genetically correlated with each other, with genetic correlations from 0.77 between recovery time and mean yield loss per day, up to 1.00 between drop length and recovery time and decrease depth and recovery time (Table 4.5). The variables describing response to the herd disturbance were also positively correlated with each other, with genetic correlations ranging from 0.04 between drop length and mean yield loss per day to 1.00 between decrease depth and mean yield loss per day.

The response traits to the heat wave were in most cases positively genetically correlated with the corresponding response traits to the herd disturbance (Table 4.6). The genetic correlations ranged from -0.03 for recovery time to 0.61 for mean yield loss per day. In summary, different response traits within the same disturbance were positively, and often strongly, genetically correlated with each other, and the same response traits to different disturbances were also mostly positively genetically correlated.

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Table 4.4 Sire variance (σ_s^2), error variance (σ_e^2), and heritability (h^2) from univariate analysis of traits describing the response in milk yield to the heat wave of July 1, 2015, and to an unknown disturbance at herd level¹.

Disturbance	Response trait	σ_s^2	σ_e^2	h^2
Heat wave	Drop depth (kg)	0.034 (0.014)	8.53 (0.085)	0.016 (0.0063)
	Drop length (days)	0.036 (0.011)	5.31 (0.053)	0.027 (0.0081)
	Recovery time (days)	0.0099 (0.0038)	2.46 (0.025)	0.016 (0.0061)
	Total yield loss (kg)	0.57 (0.14)	45.17 (0.45)	0.050 (0.012)
	Mean yield loss per day (kg)	0.0060 (0.0028)	1.95 (0.020)	0.012 (0.0058)
Herd disturbance	Drop depth (kg)	0.050 (0.010)	9.87 (0.055)	0.020 (0.0040)
	Drop length (days)	0.0011 (0.0012)	4.20 (0.024)	0.0010 (0.0011)
	Recovery time (days)	0.0011 (0.00076)	2.26 (0.013)	0.0019 (0.0013)
	Total yield loss (kg)	0.13 (0.032)	42.50 (0.24)	0.012 (0.0030)
	Mean yield loss per day (kg)	0.012 (0.0028)	3.54 (0.020)	0.013 (0.0031)

¹SE in parentheses.

Table 4.5 Genetic correlations among different traits describing yield response to the same disturbance (heat wave of July 1, 2015, or an unknown disturbance at herd level)¹.

Disturbance	Response trait	Decrease length (days)	Recovery time (days)	Total yield loss (kg)	Mean yield loss per day (kg)
Heat wave	Decrease depth (kg)	0.99 (0.057)	1.00 (0.088)	0.99 (0.027)	0.99 (0.05)
	Decrease length (days)		1.00 (0.026)	0.95 (0.028)	0.85 (0.11)
	Recovery time (days)			0.93 (0.053)	0.77 (0.17)
	Total yield loss (kg)				0.95 (0.059)
Herd disturbance	Decrease depth (kg)	0.053 (0.35)	0.16 (0.26)	0.99 (0.019)	1.00 (0.025)
	Decrease length (days)		0.95 (0.22)	0.17 (0.35)	0.036 (0.37)
	Recovery time (days)			0.23 (0.26)	0.10 (0.28)
	Total yield loss (kg)				0.99 (0.035)

¹SE in parentheses.**Table 4.6** Genetic correlations (r_g) between the same traits describing yield response to two different disturbances: the heat wave of the July 1, 2015, and an unknown disturbance at herd level¹.

Item	r_g
Decrease depth (kg)	0.26 (0.20)
Decrease length (days)	0.46 (0.34)
Recovery time (days)	-0.029 (0.34)
Total yield loss (kg)	0.39 (0.16)
Mean yield loss per day (kg)	0.61 (0.20)

¹SE in parentheses.

4.3.4 Genetic correlations between resilience indicators and response traits

The genetic correlations between resilience indicators and response traits after the heat wave ranged between -0.06 and 0.71. The highest values were observed for LnVar, where correlations with decrease depth, total yield loss, and mean yield loss per day ranged between 0.39 and 0.71 (Table 4.7). These genetic correlations suggest that daughters of sires with high EBV for LnVar tended to have deeper yield

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decreases after the heat wave, a larger total yield loss, and a larger mean yield loss per day than daughters of sires with low EBV for LnVar. Genetic correlations between LnVar and decrease length and recovery time upon the heat wave were weak (0.15 and 0.07). Average daily milk yield, which had a strong genetic correlation with LnVar (0.76 in this data set, SE = 0.032), showed similar genetic correlations with the response traits of the heat wave as LnVar (0.09 to 0.59). Therefore, the partial genetic correlations between LnVar and the response traits, adjusted for genetic correlations with ADMY are needed to interpret the association between variability in milk yield and response to the heat wave, independent of milk yield level. The partial genetic correlations suggest that among cows with the same genetic milk yield level, a high LnVar was still genetically associated with large decreases in milk yield and a high mean yield loss per day, although the partial genetic correlations were weaker than the original correlations (0.21 and 0.49; Table 4.7). The partial genetic correlations between LnVar and total yield loss, decrease length and recovery time were negligible (0.00 to 0.06). Genetic correlations between r_{auto} and the response traits to the heat wave ranged from -0.05 for mean yield loss per day to 0.34 for decrease length. These genetic correlations indicate that daughters of sires with high EBV for r_{auto} tended to have deeper and longer yield decreases than daughters of sires with low EBV for r_{auto} .

In comparison with the genetic correlations after the heat wave, even larger genetic correlations were found after the herd disturbances between LnVar and decrease depth, total yield loss, and mean yield loss per day, ranging from 0.90 to 0.97 (Table 4.7). Genetic correlations between LnVar and decrease length and recovery time upon the herd disturbances remained weak (-0.001 and 0.06). Average daily milk yield again had a strong genetic correlation with LnVar (0.77 in this data set, SE = 0.030), and showed similar genetic correlations with decrease depth, total yield loss, and mean yield loss per day compared with LnVar (0.88 to 0.91), but the genetic correlations with decrease length and recovery time were slightly stronger (0.15 and 0.14). The partial genetic correlations of LnVar with depth of the decrease and total yield loss were weaker than the original correlations (0.82 and 0.74), but the partial genetic correlation with mean yield loss per day was stronger (0.99; Table 4.7). The partial genetic correlations of LnVar with decrease length and recovery time were negative but weak (-0.18 and -0.08). Genetic correlations between r_{auto} and the response traits of the herd disturbance ranged between -0.35 for mean yield loss per day and 0.97 for decrease length. These genetic correlations indicate that daughters of sires with high EBV for r_{auto} tended to have longer decreases and slower recovery, but a smaller yield loss per day than daughters of sires with low EBV for r_{auto} . The genetic correlations with

decrease depth (-0.13) and total yield loss (-0.01) were weak. In summary, daughters of sires with high EBV for LnVar seemed to have more extreme decreases in milk yield and a greater yield loss upon both the heat wave and the herd disturbance than daughters of sires with low EBV for LnVar, even when adjusted for ADMY. Daughters of sires with high EBV for r_{auto} seemed to have slower recovery from both the heat wave and the herd disturbances than daughters of sires with low EBV for r_{auto} .

Table 4.7 Genetic correlations between traits describing the response in milk yield to the heat wave of July 1, 2015, and to an unknown disturbance at herd level, and natural log-transformed variance of milk yield deviations (LnVar), lag-1 autocorrelation of milk yield deviations (r_{auto}), and average daily milk yield (ADMY)¹.

Disturbance	Response trait	LnVar	r_{auto}	ADMY	LnVar, adjusted for ADMY
Heat wave	Decrease depth (kg)	0.47 (0.14)	0.15 (0.17)	0.45 (0.15)	0.21
	Decrease length (days)	0.15 (0.14)	0.34 (0.14)	0.14 (0.13)	0.061
	Recovery time (days)	0.069 (0.16)	0.28 (0.17)	0.090 (0.16)	0.00043
	Total yield loss (kg)	0.39 (0.11)	0.22 (0.12)	0.47 (0.099)	0.060
	Mean yield loss per day (kg)	0.71 (0.15)	-0.052 (0.19)	0.59 (0.15)	0.49
Herd disturbance	Decrease depth (kg)	0.93 (0.039)	-0.13 (0.12)	0.88 (0.043)	0.82
	Decrease length (days)	-0.0011 (0.29)	0.97 (0.35)	0.15 (0.28)	-0.18
	Recovery time (days)	0.056 (0.21)	0.64 (0.19)	0.14 (0.21)	-0.080
	Total yield loss (kg)	0.90 (0.053)	-0.014 (0.13)	0.88 (0.052)	0.74
	Mean yield loss per day (kg)	0.97 (0.041)	-0.35 (0.13)	0.91 (0.049)	0.99

¹SE in parentheses. Partial correlations between LnVar and the response traits, adjusted for genetic correlations with ADMY, are also given.

4.4 Discussion

The traits LnVar and r_{auto} have been developed to assist in genetic selection for improved resilience. Low LnVar and low r_{auto} are hypothesized to indicate good resilience, because low LnVar indicates low variability in milk yield deviations from an expected curve, and low r_{auto} indicates weak similarity between subsequent milk yield deviations. Results of this study show that both LnVar and r_{auto} were genetically the same traits in a more recent and an early group of daughters of sires. This indicates that these traits are similar over time and have predictive value across herd-year-seasons. Furthermore, low LnVar was genetically correlated with good resilience measured as a weak response in milk yield to a heat wave and an unknown disturbance at herd level. Low r_{auto} was genetically correlated with quick recovery from a heat wave and herd disturbances, but with a larger production loss per day upon herd disturbances. We will first discuss in more detail the association between resilience indicators in different daughter groups. We will then discuss the association between the resilience indicators and production response to different disturbances.

The unity genetic correlations between the subsets with earlier and more recent daughters of each sire for each resilience indicator, showed that LnVar and r_{auto} were genetically the same at different time points and in different herd-year-season classes. Although a heritability estimate above zero already indicates that animals across environments have a genetic covariance, this validation is an important outcome for such an environmentally sensitive trait, because it further validates the usefulness for forward prediction under other environmental circumstances. Similar results have been found in Norwegian Red Cattle for prediction of performance for clinical mastitis of second-crop daughters using predicted transmitting abilities based on clinical mastitis records of first-crop daughters (Ødegård et al., 2003). An explanation for the unity genetic correlation of resilience indicators between the 2 daughters groups and heritability above zero, is that the range of disturbances determining LnVar and r_{auto} is probably similar between time points and between herd-year-seasons. Therefore, genetic improvement of LnVar and r_{auto} in future generations, which are expected to have a similar range of disturbances, will likely be observed upon selection.

The resilience indicators LnVar and r_{auto} were based on the theory that fluctuations in longitudinal data are informative about resilience of systems, because they describe response and recovery to small, naturally occurring disturbances (Scheffer, 2009; Scheffer et al., 2018). Previous studies, also on similar traits in pigs and poultry, have confirmed this indirectly because of favorable genetic correlations with health and longevity traits (Berghof et al., 2019a; Putz et

al., 2019; Poppe et al., 2020). However, none of these studies directly investigated if the resilience indicators were related to strength of response and recovery to actual disturbances. In this study, genetic correlations between the resilience indicators and the response traits, which were mostly moderate to strong, confirm that LnVar and r_{auto} are related to direct response of milk yield to disturbances. LnVar seems mainly informative about the extent to which production is affected by disturbances. In fact, the genetic correlations with decrease depth, total yield loss, and mean yield loss per day after the herd disturbance (Table 4.7) were close to unity and remained strong when adjusted for milk yield level. This confirms that the simple trait LnVar effectively captures the extent of response in milk yield to all kinds of disturbances. Although LnVar was not related to the length of the yield decrease and recovery time, r_{auto} showed moderate to strong genetic correlations with these traits, and therefore seems mainly informative about speed of recovery, and less to the extent of yield loss upon disturbances. Further research is needed to determine if these traits are informative about not only production response to disturbances, but also response in other elements of functioning (Colditz and Hine, 2016), such as behavior. Furthermore, genetic associations between the current resilience indicators and response to additional specific disturbances, such as mastitis as studied by I. Adriaens (KU Leuven, Geel, Belgium), I. van den Brulle (Ghent University, Merelbeke, Belgium), and B. Aernouts (KU Leuven, Geel, Belgium; unpublished data), should be studied. Moreover, it would be interesting to investigate if similar resilience indicators based on test-day milk yield data or from conventional milking systems would yield similar results. If so, the number of records on resilience indicators for genetic evaluation could be increased substantially. Nevertheless, our findings are a first important confirmation that LnVar and r_{auto} based on daily milk yield data from AMS are informative about resilience to general disturbances and a heat wave in particular.

Associations between response traits and the resilience indicators were mostly in the same direction for both the heat wave and the herd disturbance. Therefore, it is important to investigate to what extent the herd disturbances and the heat wave overlap and have the same underlying effect. Only 44 out of 8,905 herd disturbances occurred around the date of the studied heat wave, which shows that there is limited direct overlap. These 44 herd disturbances were excluded when estimating the genetic correlations between the response traits to the 2 disturbances (Table 4.6). These were different from zero, which may suggest that the remaining herd disturbances partly consist of other heat waves. Nevertheless, a substantial number of the herd disturbances occurred in winter and were thus certainly not heat waves (Figure 4.1). Therefore, a common genetic basis for

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different types of disturbances may exist, and common mechanisms may act on different disturbances in the body (Colditz and Hine, 2016). In summary, we expect the herd disturbances to represent a broad range of disturbances, heat waves being only one of them.

The resilience indicators LnVar and r_{auto} were designed without knowing if and when disturbances occurred, whereas the response traits certainly contain information about resilience. Therefore, the question may be raised if we should use the response traits directly to breed for improved resilience. However, this is not recommended for several reasons. The first reason is that the heritabilities of most response traits (0.001 to 0.05) were considerably lower than the heritabilities of LnVar and r_{auto} (0.21 and 0.08, respectively; Poppe et al., 2020). The low heritabilities of the response traits are probably due to describing response to only a single disturbance per cow. A disturbance related to a single event is more prone to random noise, and consequentially leads to increased error variance. LnVar and r_{auto} summarize response to all disturbances throughout the entire lactation or multiple lactations (Poppe et al., 2021a), which explains the higher heritability of LnVar and r_{auto} . Another disadvantage of using response traits to only a single disturbance per cow, is that for some types of disturbances or extremely severe disturbances the best approach may be to decrease milk yield severely instead of only by a little, to preserve health and resilience later in life (Friggens et al. 2017; Knap and Doeschl-Wilson, 2020). In those cases, cows may be classified as resilient if they did not show a response, but show reduced resilience in the remaining lactation or later lactations. LnVar and r_{auto} summarize response to all disturbances throughout the entire lactation or multiple lactations (Poppe et al., 2021a), and therefore generate a more complete picture of the overall resilience of the cow than response to a single disturbance. A reason not to select for the response traits to the heat wave in particular, is that in this study we were interested in breeding for general resilience to a broad range of disturbances, not only a single type of disturbance. Studying single types of disturbances is suitable for investigating physiological mechanisms underlying resilience or developing models, as performed for nutritional challenges in dairy cows (Codrea et al., 2011; Bjerre-Harpøth et al., 2012) and goats (Friggens et al., 2016), and for weaning in piglets (Revilla et al., 2019). If the desire is to select for heat tolerance, alternative approaches may be more direct (Carabaño et al., 2019). In summary, the response traits to the herd disturbance and heat wave are not the best option for breeding for general resilience themselves, but do confirm that LnVar and r_{auto} contain information about resilience.

Natural log-transformed variance has a strong positive genetic correlation with milk yield level, which was considered to be partly due to a statistical scale effect, where variance increases with the mean (Falconer and Mackay, 1996; Poppe et al., 2020). Results from this study show that not only LnVar, but also depth of the decrease, total yield loss, and average yield loss per day were unfavorably genetically correlated with ADMY. Similarly, milk yield level before a nutritional challenge has been found to be related with the strength of response in milk yield in dairy cattle (Codrea et al., 2011; Bjerre-Harpøth et al., 2012) and goats (Friggens et al., 2016). In addition, highly productive cows tend to have a stronger response in milk yield to heat stress than cows with low production (Bernabucci et al., 2010; Carabaño et al., 2019). These observations suggest that for highly productive cows, milk yield is not only more variable due to scale effect, but also for an important part due to higher vulnerability. Nevertheless, partial genetic correlations between LnVar and the response traits to the disturbances suggest that among cows with the same milk yield level, low LnVar is associated with a weaker milk yield response. This makes it possible to breed for better resilience using LnVar without comprising milk yield level. The unfavorable genetic correlation between LnVar and milk yield was lower than unity. Therefore, by including both LnVar and milk yield in the breeding goal with appropriate weights, both traits can be improved simultaneously.

Both LnVar and r_{auto} contain information about resilience, but the question remains if and how they should be applied in the breeding goal. Natural log-transformed variance clearly has an economic value because of its associations with yield loss upon disturbances. However, double-counting should be avoided when assigning an economic value based on yield loss (Berghof et al., 2019b), because yield loss to some types of disturbances, such as mastitis (Huijps et al., 2008; Halasa et al., 2009), is already accounted for by the economic values of other breeding goal traits. For r_{auto} it is less clear than for LnVar that it has an economic value, because it was not associated with total yield loss after disturbances. In addition, r_{auto} had only weak genetic correlations with health traits and longevity (Poppe et al., 2020), which suggests that r_{auto} is also not particularly informative about disease resistance and is not related to the productive lifespan of a cow. Although r_{auto} seems therefore not directly economically useful, its clear association with recovery time poses an important advantage. Quick recovery is beneficial for animal welfare (Berghof et al., 2019b), and may also lead to lower medicine use and labor requirements. As far as known, recovery from disturbances is not directly covered by current breeding indices, although we may be selecting indirectly for improved recovery rate to mastitis due to its favorable genetic correlation with SCC

(de Haas et al., 2008; Urioste et al., 2012) and mastitis susceptibility (Welderufael et al., 2017). In summary, LnVar and r_{auto} are complementary, and both are needed in the breeding goal to genetically improve all aspects of resilience.

4.5 Conclusions

This study shows that LnVar and r_{auto} were genetically very similar traits in recent and earlier daughter groups from nonoverlapping herd-year-season classes. Therefore, improvement of these traits is expected to be observed in next generations upon genetic selection. Furthermore, daughters of sires with low EBV for LnVar had weaker response in milk yield to a heat wave and disturbances at herd level than daughters of sires with high EBV. Daughters of sires with low EBV for r_{auto} had quicker recovery from disturbances than daughters of sires with high EBV. These results confirm that both LnVar and r_{auto} are informative about resilience, and they cover different aspects. Therefore, both traits should be combined in a resilience index to improve all resilience aspects simultaneously.

4.6 Acknowledgments

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5

Development of resilience indicator traits based on daily step count data for dairy cattle breeding

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Abstract

Background Resilience is the ability to be minimally affected by environmental disturbances, or to quickly recover from them. Daily activity data has potential to indicate resilience, because resilient animals are expected to keep variations due to disturbances that threat animal homeostasis, such as diseases and heat stress, at a low magnitude. The aim of this study was to use daily step count data of cows to define potential resilience indicators based on theory and literature, and then to investigate if they really can be used to genetically improve resilience by estimating their heritability and repeatability, and genetic associations with other resilience-related traits, which were health traits, longevity, fertility, and body condition score.

Results Two groups of potential resilience indicators were defined: (1) indicators describing mean step count level in different parts of the lactation for individual cows, and (2) indicators describing fluctuations in step count from individual step count curves. Heritability was highest for resilience indicators describing mean step count, ranging from 0.22 in the 2 weeks prepartum to 0.45 for the complete lactation. High mean step count was also consistently, but weakly, genetically correlated with good health, fertility, and longevity and high body condition score. Heritability of resilience indicators describing step count fluctuations ranged from 0.01 for number of step count drops to 0.15 for mean of negative residuals from individual curves. Genetic correlations with health traits, longevity, fertility, and body condition score were mostly weak, but moderate and favorable genetic correlations were shown for autocorrelation of residual steps (-0.33 to -0.44) and number of step count drops (-0.44 to -0.56) with hoof health, fertility, and body condition score. Resilience indicators that describe variability of residuals and mean of negative residuals showed strong genetic correlations with mean step count (0.86 to 0.95, absolute), which suggests that adjustment of these traits for step count level is needed. After adjustment for step count level, the trait 'mean of negative residuals' had considerable genetic correlations with hoof health, fertility, and body condition score.

Conclusions Especially the autocorrelation and the traits describing step count level and describing negative residuals from individual curves showed potential as resilience indicators, based on resilience theory, heritability, and genetic associations with health, fertility, and body condition score. Other resilience indicators were heritable as well, but had unfavorable genetic correlations with a number of health traits. This research is an important first step in the exploration of the use of activity data to breed more resilient livestock.

5.1 Background

Cows are exposed to various environmental disturbances throughout their lives, such as pathogens, heat waves, and sudden changes in feed composition. The number and severity of disturbances is expected to increase in the future. For example, due to climate change the number of extreme weather events will likely increase (Maracchi et al., 2005; Sejian et al., 2015). Therefore, it is important to improve the resilience of cows, which was defined (Colditz and Hine, 2016) as the capacity to be minimally affected by disturbances and if affected, to quickly recover. One option to improve the resilience of cows is through genetic selection (Elgersma et al., 2018; Poppe et al., 2020). The advantage of genetic selection is that it can tackle problems through prevention strategies, rather than treatment of stress or disease.

Response of cows to environmental disturbances can often be observed through temporary changes in traits such as milk yield (Fourichon et al., 1999; Rajala-Schultz et al., 1999a) and activity (Edwards and Tozer, 2004; Abeni and Galli, 2017). Therefore, patterns in longitudinal data records, such as daily production, activity, or feed intake data, contain information on their response to many kinds of naturally occurring disturbances. When such data are routinely collected, they provide the potential to derive indicators of resilience for animal breeding.

Several resilience indicators based on longitudinal data have been proposed, which were originally aimed at indicating resilience of ecosystems (Scheffer et al., 2009, 2018; Dakos et al., 2012). These resilience indicators were the variance and lag-1 autocorrelation of longitudinal traits. Variance indicates how severely a longitudinal trait fluctuates around its expected value. Resilient cows are expected not to have large fluctuations, and therefore low variance is an indicator of good resilience. Lag-1 autocorrelation indicates how dependent subsequent records are on each other and therefore how slowly the trait recovers from small natural disturbances. Resilient cows are expected to recover quickly, and therefore have low lag-1 autocorrelation.

Proposed resilience indicators based on patterns in longitudinal data have been investigated in animals. For example, variance and autocorrelation of daily milk yield data and deviations from expected yield have shown to be promising indicators to select for better resilience: they were heritable (Elgersma et al., 2018; Poppe et al., 2020) and had favorable genetic correlations with response to actual disturbances (Poppe et al., 2021c) and health and longevity traits (Elgersma et al., 2018; Poppe et al., 2020). Similar indicator traits have been successfully calculated from daily feed intake data in pigs (Putz et al., 2019; Cheng et al., 2020) and 4-weekly body weight records in layers (Berghof et al., 2019a).

In dairy cattle, development of resilience indicators for genetic selection has mainly focused on daily milk yield data. However, nowadays sensors generate daily activity data on a large scale. Activity data is expected to be more directly affected by disturbances than milk yield. Most disturbances will first result in a change in activity, followed by a change in milk yield (Edwards and Tozer, 2004). In addition, numerous studies have shown effects of diseases (Edwards and Tozer, 2004; Kamphuis et al., 2013; Thorup et al., 2015; van Dixhoorn et al., 2018) and heat stress (Cook et al., 2007; Abeni and Galli, 2017) on activity traits, such as number of steps per day, lying time, standing time, and eating time. Therefore, longitudinal activity data may provide an excellent opportunity to develop resilience indicators. The aim of this research was to develop resilience indicators based on daily step count data of dairy cows, and to estimate their heritability, repeatability, and genetic associations with health traits, longevity, fertility, and body condition score.

5.2 Methods

This study consists of two parts. The first part consists of calculation of potential resilience indicators for genetic selection based on theory, and estimation of their genetic parameters. Secondly, to assess if the potential resilience indicators indeed reflect resilience, genetic correlations with traits from current Dutch genetic evaluation that are related to resilience as well were estimated. The resilience-related traits from Dutch evaluation were udder health, hoof health, ketosis, fertility, longevity, and body condition score.

5.2.1 Data and data preparation

Most data editing was performed using Python 3.6 and 3.8.5, using the NumPy (Harris et al., 2020), Pandas (McKinney, 2010), and Statsmodels (Seabold and Perktold, 2010) packages. Data editing performed using other languages or packages are indicated in text.

Step count data were measured by Nedap Smarttag leg accelerometers (Nedap, Groenlo, the Netherlands). Part of the accelerometers measured additional traits, such as lying time and standing time. However, the number of cows with data was largest for step count, and therefore we focused on this trait. The data consisted of 9,472,978 records of daily step count, for 18,622 cows from 86 Dutch farms with automatic milking systems between July 1st 2016 and July 1st 2019. Cows were in parities 0-14, but only the cows in the first 3 parities were selected based on records of calving dates available from CRV (Arnhem, the Netherlands): 9,429 cows in parity 1, 8,608 cows in parity 2, and 6,759 cows in parity 3. Other exclusion criteria were: cows not registered in the herd-book, cows that were less than 87.5%

Holstein Friesian, cows that calved before 640, 855, or 1070 days of age for first, second, and third lactation, respectively (Poppe et al., 2021a), or cows that had a calving interval between the current and previous lactation of less than 215 days. In addition, data after 450 days in milk (**DIM**) were removed, records measured during estrus (explained later), and records with step counts lower than 200 steps per day were removed, because values below this number were likely to be errors in the device upon visual inspection (long periods of consistently the same low number of steps). The remaining number of records was 1,823,789 on 7,569 cows in parity 1, 1,735,669 on 6,840 cows in parity 2, and 1,295,398 on 5,342 cows in parity 3. The data contained 11,086 unique cows.

In addition to the step count data, other datasets were available from CRV (Arnhem, the Netherlands) to assist in data preparation. The first data set contained milk yield of cows measured during single milk visits to automatic milking systems and conventional milking systems, and this data was used to determine when cows were lactating or dry. From this data, only the data of the cows in the step count data set were selected, which were 15,955,347 records on 7,568 cows in parity 1, 18,543,964 records on 6840 cows in parity 2, and 17,487,044 records on 5,342 cows in parity 3. The second data set contained insemination records and was used as one of two ways to determine when a cow was in estrus (explained in the following paragraph). From the insemination dataset, data of cows from the step count dataset were selected, which were 35,149 records on 9,971 cows.

Part of the step count records (61%) contained a variable describing the number of seconds the accelerometer had been measuring during the day, which was usually 86,400 s (complete day). For records where the total measuring time was less than a complete day, the total number of steps was extrapolated to a complete day. For records with unknown measuring time, it was assumed that the device had been measuring the complete day. Records before or after a period of at least 7 days without records were removed, because on those days it is likely that the device did not measure the complete day. Finally, based on the step count data, days that cows were in estrus were determined. Estrus detection measurements of Nedap (Groenlo, the Netherlands) were not available to us. Therefore, a method adapted from Roelofs et al. (2005) was used as follows. If the number of steps on a day was larger than the mean of the 10 days before plus 2.5 times the standard deviation of the 10 days before, that day was determined as an estrus day. Estrus could not occur before 14 DIM or when a cow was pregnant. The timing of pregnancy was estimated based on the next calving date minus 278 days (gestation length of Holsteins according to Norman et al. (2009)). In addition to determination

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of estrus based on step count level, records were classified as estrus records if the cow was inseminated on that day according to the dataset with insemination records. Records classified as estrus records were excluded from all analyses, to avoid an effect of estrus on the resilience indicators.

5.2.2 Calculation of resilience indicators

Two types of resilience indicators were derived from the daily step count data: (1) indicators based on mean step count level, and (2) indicators based on fluctuations in step count level.

5.2.2.1 Based on mean step count level

Because of a general association of disturbances with decreased number of steps, mean step count in different parts of the lactation was calculated as a resilience indicator. To avoid differences in step count level between cows due to differences in season and pregnancy status rather than resilience, first a model was fitted to adjust the number of steps per day for these factors as follows:

$$y_{ijk} = HM_j + preg_k + e_{ijk} [1]$$

where y_{ijk} was a step count record, HM_j was herd-month j (herd 1 to 86 and month 1 to 12), $preg_k$ was pregnancy status k (not pregnant, pregnant, dry, close-up, or unknown), and e_{ijk} was the residual. A record was assigned as ‘pregnant’ if it was within 278 days before the next calving date, as “not pregnant” if the next calving date was known but the record was not within 278 days before that date, as “dry” if the record was between the last milking of the lactation and the next calving date, as “close-up” if the record was less than 14 days before the next calving date, and as “unknown” if the next calving date was unknown. The “unknown” class was included, otherwise cows that were decided to be culled after the current lactation would be excluded, which potentially excludes non-resilient cows. The residuals e_{ijk} were then used as the “corrected number of steps”. For each lactation, the mean of corrected number of steps was calculated for different stages of the lactation: (1) complete lactation: DIM 1-450, (2) early lactation: DIM 1-28, (3) later lactation: DIM 75-450, and (4) pre-partum: DIM -14 to -1. The 3 stages of lactation – early lactation, later lactation, and prepartum - were selected based on preliminary analysis which showed a sharp average decline in step count approximately in the first 4 weeks after calving and a steady step count level from ~75 DIM onwards, averaged over parities. Figure 5.1 shows the mean number of steps per day for parity 1, 2, and 3. The mean number of corrected steps of the

complete lactation and of later lactation were only calculated for cows with at least 4 weeks of data. The mean number of corrected steps of early lactation and of prepartum were only calculated for cows with at least 1 week of data and not at least 4 weeks of data, since these periods consisted of maximum 4 and 2 weeks, respectively. After calculating the resilience indicators (mean number of corrected steps in different parts of the lactation), per parity, outliers of these indicators were removed when values deviated more than 4 times the standard deviation from the mean of all lactations in that parity. The final number of records for each of the resilience indicators based on mean step count per parity are shown in Table 5.1.

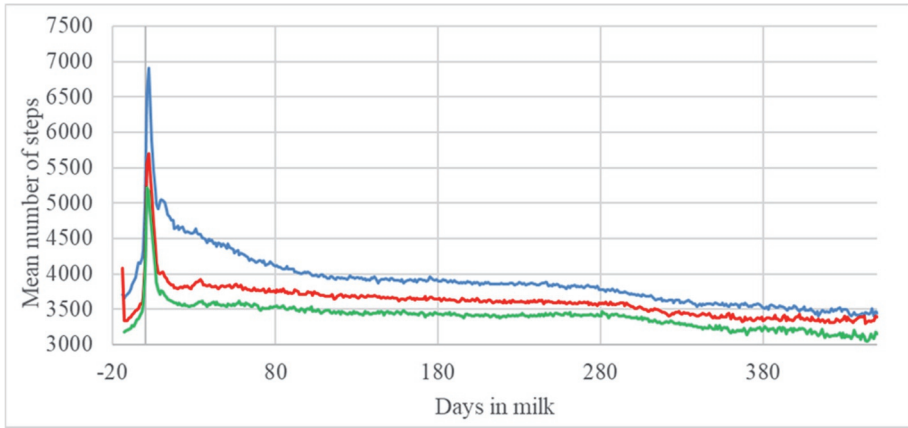


Figure 5.1 Mean number of steps per day throughout lactation for 3 parities. Blue line: parity 1; red line: parity 2; green line: parity 3.

5.2.2.2 Based on fluctuations in step count

Because disturbances may result in temporary drops in step count, additional resilience indicators were calculated based on fluctuations in step count level. To be able to study short term fluctuations independent of the long-term trend throughout lactation, first a model was fitted on each individual lactation to adjust for the long-term trend. The same model was used as in Poppe et al. (2020) for adjusting for the lactation curve shape for daily milk yield. This model is a quantile polynomial regression model with a 0.7 quantile, and it was fitted on the corrected number of steps per day from model (1) as follows:

$$y_t = \beta_0 + \beta_1 * t + \beta_2 * t^2 + \beta_3 * t^3 + \beta_4 * t^4 + \varepsilon \quad [2]$$

where y_t is the corrected number of steps from model [1] on DIM t , t^n are DIM to the power of n , where n is 1, 2, 3, or 4, β_n are regression coefficients describing

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the relationships between t^n and y_t , and ε is the error term. The quantreg package (Koenker, 2018) and the poly function in R (R version 3.5.3; R Project for Statistical Computing, Vienna, Austria) were used. Quantile regression (Koenker, 2005) with a quantile of 0.7 was used instead of classical regression to reduce the effect of drops in step count due to disturbances on the expected step count level. This generates a curve that is expected to be close to an unperturbed step count curve. After fitting the step count models, for each cow the residuals from her expected step count curve were calculated as $y_t - \hat{y}_t$. A number of resilience indicators were then calculated from the step count residuals. The first two resilience indicators were equivalent to the resilience indicators developed by Poppe et al. (2020) based on milk yield residuals: the natural log-transformed variance (**LnVar_{steps}**) and lag-1 autocorrelation (**r_{auto_steps}**) of the step count residuals. Low LnVar_{steps} and low r_{auto_steps} were expected to indicate good resilience, because of few fluctuations in step count and quick return to baseline (Scheffer et al., 2009; Dakos et al., 2012). In addition to LnVar_{steps} and r_{auto_steps}, a resilience indicator was calculated describing the mean of the negative residuals from model [2] (referred to as ‘mean of all negative residuals’). Furthermore, for each lactation the number of step count drops with at least 10 negative deviations in a row was calculated, expressed as number of drops per 100 days (referred to as ‘number of step count drops’). Finally, the mean of the negative residuals during these step count drops was calculated (referred to as ‘mean of negative residuals during step count drops’). All of the above mentioned resilience indicators were calculated only for lactations with at least 4 weeks of data. After calculating the resilience indicators, per parity, outliers were removed when values deviated more than 4 times the standard deviation from the mean of all lactations in that parity. The final number of records on the resilience indicators describing fluctuations in step count are shown in Table 5.1.

5.2.3 Analysis

5.2.3.1 Univariate genetic analysis of resilience indicators

A genetic analysis was performed on the resilience indicators using mixed animal models in ASReml 4.1 (Gilmour et al., 2015). The pedigree contained 5 generations of ancestors. The following univariate repeatability model was used:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Z_1a} + \mathbf{Z_2p} + \mathbf{e} \quad [3]$$

Where \mathbf{y} is a vector containing repeated records on the resilience indicator in parity 1, 2, and 3; \mathbf{b} is a vector containing the fixed effects for the analyzed trait, which are parity, age at calving in months nested within parity, year-season of calving nested within parity, herd-year nested within parity, and a covariate describing the first available DIM with a step count record nested within parity; \mathbf{a} is a vector containing the additive genetic effects of the cows in \mathbf{y} for the analyzed trait, $\mathbf{a} \sim N(\mathbf{0}, \mathbf{A}\sigma_a^2)$ where \mathbf{A} is the additive genetic relationship matrix and σ_a^2 is the additive genetic variance; \mathbf{p} is a vector containing the permanent environmental effects of the cows in \mathbf{y} for the analyzed trait, $\mathbf{p} \sim N(\mathbf{0}, \mathbf{I}\sigma_{pe}^2)$ where \mathbf{I} is an incidence matrix and σ_{pe}^2 is the permanent environmental variance; \mathbf{e} is a vector containing the residuals, $\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}\sigma_e^2)$ where σ_e^2 is the residual variance. \mathbf{X} , \mathbf{Z}_1 and \mathbf{Z}_2 are incidence matrices linking the phenotypic records of the analyzed resilience indicator to the fixed effects and covariates, additive genetic effects, and permanent environmental effects, respectively.

5.2.3.2 Bivariate genetic analysis of resilience indicators

Genetic correlations and permanent environmental correlations among the resilience indicators were estimated using the following bivariate repeatability model:

$$\begin{bmatrix} \mathbf{y}_1 \\ \mathbf{y}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}_1 & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_2 \end{bmatrix} \begin{bmatrix} \mathbf{b}_1 \\ \mathbf{b}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{Z}_{a1} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_{a2} \end{bmatrix} \begin{bmatrix} \mathbf{a}_1 \\ \mathbf{a}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{Z}_{p1} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_{p2} \end{bmatrix} \begin{bmatrix} \mathbf{p}_1 \\ \mathbf{p}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix} \quad [4]$$

where \mathbf{y}_i is a vector containing repeated records on a resilience indicator in parity 1, 2, and 3; \mathbf{b}_i is a vector containing the fixed effects for the trait, which are the same as in the univariate analysis; \mathbf{a}_i is a vector containing the additive genetic effects of the cows in \mathbf{y}_i ; \mathbf{p}_i is a vector containing the permanent environmental effects of the cows in \mathbf{y}_i ; \mathbf{e}_i is a vector containing the residuals. The following assumptions were made about the additive genetic effects, the permanent

environmental effects and the residuals: $\begin{bmatrix} \mathbf{a}_1 \\ \mathbf{a}_2 \end{bmatrix} \sim N\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{A} \otimes \begin{pmatrix} \sigma_{a_1}^2 & \sigma_{a_1 a_2} \\ \sigma_{a_1 a_2} & \sigma_{a_2}^2 \end{pmatrix}\right),$

$\begin{bmatrix} \mathbf{p}_1 \\ \mathbf{p}_2 \end{bmatrix} \sim N\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{pe_1}^2 & \sigma_{pe_1 pe_2} \\ \sigma_{pe_1 pe_2} & \sigma_{pe_2}^2 \end{pmatrix}\right)$ and $\begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix} \sim N\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{I} \otimes \begin{pmatrix} \sigma_{e_1}^2 & \sigma_{e_1 e_2} \\ \sigma_{e_1 e_2} & \sigma_{e_2}^2 \end{pmatrix}\right),$

where $\sigma_{a_i}^2$ is the additive genetic variance for trait i , $\sigma_{a_1 a_2}$ is the additive genetic covariance between 2 traits, $\sigma_{pe_i}^2$ is the permanent environmental variance for trait i , $\sigma_{pe_1 pe_2}$ is the permanent environmental covariance between 2 traits, and $\sigma_{e_i}^2$ is the residual variance for trait i . \mathbf{X}_1 and \mathbf{X}_2 , as well as \mathbf{Z}_{a1} and \mathbf{Z}_{a2} , and \mathbf{Z}_{p1} and \mathbf{Z}_{p2} are incidence matrices linking the phenotypic records of the 2 analyzed traits to the

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fixed effects and covariates, additive genetic effects, and permanent environmental effects, respectively. Genetic correlations (r_g) and permanent environmental correlations (r_{pe}) were calculated as $r_g = \frac{\sigma_{a_1 a_2}}{\sigma_{a_1} \sigma_{a_2}}$ and $r_{pe} = \frac{\sigma_{pe_1 pe_2}}{\sigma_{pe_1} \sigma_{pe_2}}$.

5.2.3.3 Genetic associations between resilience indicators and health traits, longevity, fertility, and body condition score

Genetic associations between the resilience indicators and several health traits, longevity, fertility, and body condition score were estimated, to investigate if the resilience indicators really contain information about resilience. Resilient cows are expected to be healthy, live long and be fertile, and have sufficient body condition to be able to cope with disturbances. Genetic correlations with these traits were estimated using the Multiple trait Across Country Evaluation (**MACE**) procedure (Interbull, 2017). The MACE procedure requires sire estimated breeding values (**EBV**) instead of phenotypes to estimate genetic correlations (Schaeffer, 1994; Klei and Weigel, 1998; Larroque and Ducrocq, 1999). Therefore, it enabled us to explore genetic associations of the resilience indicators with these traits, for which we did not have (sufficient amount of) phenotypes available in this study, while the official sire EBV are based on phenotypes from the entire Dutch-Flemish population. The sire EBV that we used were the udder health index, hoof health index, ketosis index, fertility index, productive longevity, and body condition score. The udder health index is based on clinical mastitis registrations of farmers and somatic cell count records in parities 1, 2, and 3 (CRV, 2020c). The hoof health index is based on hoof disorder registrations by professional hoof trimmers in parity 1 and in parity 2 and older, and feet and leg conformation in parity 1 (CRV, 2020d). The ketosis index is based on milk acetone level, milk β -hydroxybutyric acid level, and fat-to-protein ratio on test-days in parity 1 and 2, and parity 3 and older (Vosman et al., 2015). The fertility index is based on interval between first and last insemination and interval between calving and first insemination, measured in parity 1, 2 and 3 (CRV, 2021a). EBV for productive longevity were based on a random regression on observations for survival in month 1 to 72 after first calving (CRV, 2020a). EBV for body condition score were based on observations by professional type classifiers in parity 1 (CRV, 2020h). High values of the indices and EBV indicate good health, fertility, and longevity, and high body condition score.

As input for the MACE procedure, sire EBV from Cooperation CRV and CRV BV from the official run of December 2020 were used for the health, longevity, fertility and body condition score traits. For the resilience indicators, sire EBV resulting from the univariate analyses were used. EBV for the resilience indicators were

required to have a minimum reliability of 10% to be included in the MACE procedure, and sires were required to be born after 1985 and be officially registered as a sire for artificial insemination. For the official EBV, sires were required to have minimally 15 daughters at minimally 10 farms. Differences in reliability of EBV between sires were accounted for in the MACE procedure by de-regressing the EBV. De-regressing makes the variance of EBV independent from the reliability and takes out the contributions of the parents (Larroque and Ducrocq, 1999). The number of sires with EBV used was above 800 (and maximally 1164) for all traits except for number of step count drops (297 sires).

5.2.3.4 Partial genetic correlations

Because $\text{LnVar}_{\text{steps}}$, mean of all negative residuals, and mean of negative residuals during step count drops were strongly genetically correlated with mean number of steps, for these traits partial genetic correlations with the diseases, longevity, fertility, and body condition score were calculated. Partial genetic correlations represent the genetic association between these resilience indicators and diseases, longevity, fertility, and body condition score among cows with the same step count level. Partial genetic correlations ($r_{xy,z}$) between resilience indicators (x) and diseases, longevity, fertility, and body condition score (y), adjusted for mean number of steps in the complete lactation (z) were calculated as:

$$r_{xy,z} = \frac{r_{xy} - r_{xz}r_{yz}}{\sqrt{1-r_{xz}^2}\sqrt{1-r_{yz}^2}} \quad [5]$$

The genetic correlations between the resilience indicators and mean number of steps in complete lactation were obtained from the bivariate analyses. The other genetic correlations were estimated using the MACE procedure.

5.3 Results

5.3.1 Descriptive statistics resilience indicators

The resilience indicators describing mean step count consider step count corrected for herd-month and pregnancy stage, and are thus scaled to 0. Therefore, means of the corrected number of steps can be negative: negative values mean that the mean number of steps was lower than expected based on herd-month and pregnancy stage. Figure 5.1 provides an illustration of the raw step count values, which were between ~3,000-7,000 steps per day. The mean corrected number of

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steps was on average highest in the first 4 weeks of lactation (405.5; Table 5.1) and lowest in the 2 weeks before calving (-98.0). In other words, cows had on average 503.5 (405.5+98.0) steps per day more in the first 4 weeks after calving than in the 2 weeks before calving. The mean corrected number of steps was on average -55.89 steps per day from DIM 75 onwards and 10.90 per day across the entire lactation. The mean of all negative residuals from the lactation-specific lactation models was on average -620.3 steps. $\ln Var_{steps}$ was on average 13.2 and r_{auto_steps} was on average 0.32. On average, 1.39 step count drops occurred per 100 days, and the mean of the negative residuals during these drops was on average -685.34.

5.3.2 Genetic analysis

5.3.2.1 Heritabilities and repeatabilities

Table 5.2 shows estimates of variance components, heritabilities, and repeatabilities of all resilience indicators. Highest heritabilities and repeatabilities were observed for the traits describing means of corrected number of steps in different periods of the lactation. These heritabilities and repeatabilities ranged from 0.22 and 0.39, respectively, for the mean corrected steps prepartum, to 0.45 and 0.74, respectively, for the mean corrected steps during the complete lactation. For the other resilience indicators the heritabilities ranged from 0.01 for the number of step count drops to 0.15 for the mean of negative deviations, and the repeatabilities ranged from 0.03 to 0.37.

Table 5.1 Descriptive statistics of potential resilience indicators based on daily step count.

Resilience indicator ¹	Number of records parity 1	Number of records parity 2	Number of records parity 3	Mean	Standard deviation	Min	Max
Mean complete lactation	6,877	6,059	4,593	10.90	769.63	-2,912.94	3,518.49
Mean early lactation	3,555	4,712	3,632	405.50	1142.96	-3,913.73	5,803.58
Mean late lactation	6,452	5,567	4,122	-55.89	741.57	-3,133.34	3,143.33
Mean prepartum	2,030	4,303	3,336	-97.99	1143.46	-4,650.73	4,859.06
Mean negative residuals	6,800	6,005	4,524	-620.29	281.01	-1,876.08	-157.27
$\text{LnVar}_{\text{steps}}$	6,830	6,041	4,556	13.18	0.87	10.34	16.28
$r_{\text{auto_steps}}$	6,825	6,042	4,555	0.32	0.19	-0.43	0.89
Number of step count drops	6,826	6,042	4,556	1.39	0.70	0.00	4.11
Mean residuals during step count drops	6,816	6,023	4,534	-685.34	429.89	-2528.28	0.00

¹ $\text{LnVar}_{\text{steps}}$ = natural log-transformed variance of step residuals, $r_{\text{auto_steps}}$ = lag-1 autocorrelation of step residuals.

Table 5.2 Estimates (SE) of genetic parameters¹ from the univariate analyses of the resilience indicators based on daily step count.

Resilience indicator ²	σ_a^2	σ_{pe}^2	σ_e^2	r	h^2
Mean complete lactation	223,780 (16,406)	372,050 (8,596)	130,859 (2,287)	0.74 (0.0060)	0.45 (0.027)
Mean early lactation	261,591 (31,631)	468,060 (18,124)	503,072 (11,624)	0.48 (0.013)	0.27 (0.030)
Mean later lactation	204,592 (16,097)	349,870 (8,366)	128,566 (2,396)	0.73 (0.0060)	0.43 (0.029)
Mean prepartum	221,480 (34,552)	385,560 (20,767)	602,422 (16,203)	0.39 (0.017)	0.22 (0.033)
Mean negative residuals	4,578.21 (682.30)	11,302 (439.26)	19,678.1 (338.64)	0.37 (0.011)	0.15 (0.021)
LnVar _{steps}	0.050 (0.0078)	0.13 (0.0051)	0.24 (0.0041)	0.35 (0.012)	0.14 (0.020)
r _{auto_steps}	0.00091 (0.00025)	0.0026 (0.00030)	0.022 (0.00036)	0.11 (0.012)	0.037 (0.010)
Number of step count drops	0.005 (0.002)	0.012 (0.0050)	0.37 (0.0060)	0.033 (0.012)	0.012 (0.006)
Mean residuals during step count drops	5,205.14 (1,317.76)	18,390 (1,367.90)	84,593.5 (1,449.51)	0.18 (0.013)	0.051 (0.013)

¹ σ_a^2 = additive genetic variance, σ_{pe}^2 = permanent environmental variance, σ_e^2 = error variance, r =repeatability, h^2 =heritability.

²LnVar_{steps} = natural log-transformed variance of step residuals, r_{auto_steps} = lag-1 autocorrelation of step residuals.

5.3.2.2 Genetic and permanent environmental correlations among resilience indicators

The four traits related to mean corrected number of steps in different periods of the lactation were all strongly genetically correlated with each other (Table 5.3). The weakest genetic correlation was 0.80 between mean corrected steps prepartum and mean corrected steps in early lactation, and the strongest one was 1.00 between mean corrected steps in complete lactation and mean corrected steps in later lactation, which is a part-whole relationship. The traits describing means of corrected steps were also strongly genetically correlated with most traits describing step count fluctuations, namely $\text{LnVar}_{\text{steps}}$ (r_g 0.65 to 0.94), mean of all negative residuals (r_g -0.79 to -0.93), and mean of negative residuals during step count drops (r_g -0.85 to -0.95). These strong genetic correlations suggest that cows with high mean step count, genetically, tend to have more extreme negative deviations throughout lactation and during step count drops, and higher variability in step count than cows with low mean step count. Among the traits describing step count fluctuations, strongest genetic correlations were shown between mean of all negative residuals and $\text{LnVar}_{\text{steps}}$ (-0.93), between mean of negative residuals during step count drops and $\text{LnVar}_{\text{steps}}$ (-0.93), between $r_{\text{auto_steps}}$ and number of step count drops (0.94), and between mean of negative residuals during step count drops and mean of all negative residuals (0.96). The remaining genetic correlations were weaker, ranging from -0.73 between number of step count drops and mean of negative residuals during step count drops, to 0.48 between $\text{LnVar}_{\text{steps}}$ and number of step count drops. Most permanent environmental correlations had the same sign as the corresponding genetic correlations, but were weaker. Only the permanent environmental correlations of the number of step count drops with other traits were very different from the corresponding genetic correlations with sometimes a different sign, but with large standard errors. In summary, many resilience indicators were strongly genetically correlated among each other and genetic selection on only one of them will therefore change many others.

Table 5.3 Genetic (above diagonal) and permanent environmental (below diagonal) correlations (SE) among the resilience indicators based on daily step count¹.

	Mean complete lactation	Mean early lactation	Mean later lactation	Mean prepartum	Mean negative residuals	LnVar _{steps}	r _{auto_steps}	Number of step count drops	Mean residuals during step count drops
Mean complete lactation	x	0.96 (0.013)	1.00 (0.0005)	0.91 (0.037)	-0.93 (0.025)	0.86 (0.034)	0.25 (0.12)	0.26 (0.18)	-0.95 (0.049)
Mean early lactation	0.87 (0.023)	x	0.94 (0.019)	0.80 (0.055)	-0.88 (0.039)	0.94 (0.032)	0.25 (0.13)	0.21 (0.20)	-0.92 (0.063)
Mean later lactation	0.99 (0.0012)	0.80 (0.033)	x	0.92 (0.035)	-0.93 (0.026)	0.86 (0.036)	0.23 (0.12)	0.33 (0.18)	-0.93 (0.049)
Mean prepartum	0.73 (0.052)	0.57 (0.074)	0.70 (0.054)	x	-0.79 (0.065)	0.65 (0.084)	0.13 (0.15)	0.24 (0.22)	-0.85 (0.079)
Mean negative residuals	-0.75 (0.028)	-0.65 (0.046)	-0.76 (0.027)	-0.63 (0.073)	x	-0.93 (0.022)	-0.40 (0.13)	-0.65 (0.17)	0.96 (0.037)
LnVar _{steps}	0.67 (0.035)	0.71 (0.041)	0.64 (0.036)	0.67 (0.076)	-0.83 (0.023)	x	0.36 (0.13)	0.48 (0.18)	-0.93 (0.041)
r _{auto_steps}	0.0079 (0.090)	0.045 (0.11)	0.091 (0.089)	0.26 (0.14)	-0.14 (0.094)	0.00090 (0.10)	x	0.94 (0.14)	-0.50 (0.14)
Number of step count drops	-0.28 (0.17)	-0.20 (0.20)	-0.21 (0.17)	-0.21 (0.25)	0.24 (0.20)	-0.44 (0.25)	0.78 (0.20)	x	-0.73 (0.16)
Mean residuals during step count drops	-0.65 (0.061)	-0.69 (0.071)	-0.75 (0.052)	-0.66 (0.097)	1.00 (0.061)	-0.70 (0.057)	-0.46 (0.090)	-0.29 (0.17)	x

¹LnVar_{steps} = natural log-transformed variance of step residuals, r_{auto_steps} = lag-1 autocorrelation of step residuals.

5.3.2.3 Genetic associations with diseases, longevity, fertility, and body condition score

Most resilience indicators had weak or negligible genetic correlations with the health traits, longevity, fertility, and body condition score (Table 5.4). However, $r_{\text{auto_steps}}$ and the number of step count drops had moderate genetic correlations with hoof health, fertility, and body condition score, ranging from -0.33 to -0.44 for $r_{\text{auto_steps}}$ and from -0.44 to -0.56 for the number of step count drops. These genetic correlations mean that cows with genetically a low autocorrelation or a small number of step count drops often genetically had good hoof health and fertility, and high body condition score. Although the genetic correlations between the resilience indicators based on mean step count and the health traits, longevity, fertility, and body condition score were weak, they were all favorable (0.021 to 0.22). This means that a high step count level, especially during lactation and not before calving, was genetically related with good functionality, and particularly good hoof health, little ketosis, good longevity, and high body condition score. $\text{LnVar}_{\text{steps}}$ also had consistently positive genetic correlations with the health traits, longevity, fertility, and body condition score, which means that high $\text{LnVar}_{\text{steps}}$ was genetically associated with good health and functionality. The partial genetic correlations (Table 5.5) suggest that among cows with the same step count level, $\text{LnVar}_{\text{steps}}$ is still positively genetically associated with the other traits, but weaker. Mean of all negative residuals and mean of negative residuals during step count drops had mainly negative and weak genetic correlations with the health traits, longevity, fertility, and body condition score (Table 5.4). However, most partial genetic correlations, adjusted for correlations with mean step count (Table 5.5), were considerably larger in magnitude than the original correlations and the largest ones were positive. Especially for the genetic correlation between mean residuals during step count drops and body condition score the difference between Table 5.4 and 5.5 was large. This was due to the strong negative genetic correlation (-0.95; Table 5.3) between mean residuals during step count drops and mean step count, which means that mean of residuals during step count drops was largely determined by step count level. Mean step count itself had a positive genetic correlation with body condition score, which suppressed the genetic correlation between mean residuals during step count drops not explained by step count level and body condition score. The results from Table 5.5 suggest that among cows with the same step count level, cows with smaller negative deviations from expected step count had better health and fertility and higher body condition score than cows with larger negative deviations, genetically. In summary, genetic associations of resilience indicators with health and functionality were observed, and the

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strongest genetic correlations were shown for $r_{\text{auto_steps}}$ and number of step count drops with hoof health, fertility, and body condition score.

Table 5.4 Genetic correlations between resilience indicators based on daily step count¹ and other traits², estimated using Multiple trait Across Country Evaluation.

	UH	HH	KET	LON	FER	BCS
Mean complete lactation	0.015	0.16	0.20	0.15	0.062	0.17
Mean early lactation	0.025	0.17	0.18	0.22	0.067	0.20
Mean later lactation	0.033	0.16	0.17	0.13	0.065	0.17
Mean prepartum	0.11	0.021	0.036	0.061	0.061	0.029
Mean negative residuals	-0.047	0.021	-0.23	-0.13	0.051	-0.034
$\text{LnVar}_{\text{steps}}$	0.11	0.16	0.24	0.12	0.056	0.12
$r_{\text{auto_steps}}$	-0.16	-0.33	0.0019	0.0022	-0.44	-0.34
Number of step count drops	-0.063	-0.56	-0.24	0.16	-0.44	-0.56
Mean residuals during step count drops	-0.031	-0.044	-0.11	-0.14	0.053	0.057

¹ $\text{LnVar}_{\text{steps}}$ = natural log-transformed variance of step residuals, $r_{\text{auto_steps}}$ = lag-1 autocorrelation of step residuals.

²UH = udder health, HH = hoof health, KET = ketosis resistance, LON = longevity, FER = fertility, BCS = body condition score.

Table 5.5 Partial genetic correlations between resilience indicators based on daily step count¹ and other traits², adjusted for mean number of steps.

	UH	HH	KET	LON	FER	BCS
Mean negative residuals	-0.090	0.47	-0.12	0.026	0.30	0.34
$\text{LnVar}_{\text{steps}}$	0.19	0.04	0.14	-0.018	0.0053	-0.052
Mean residuals during step count drops	-0.054	0.35	0.26	0.0081	0.36	0.71

¹ $\text{LnVar}_{\text{steps}}$ = natural log-transformed variance of step residuals.

²UH = udder health, HH = hoof health, KET = ketosis resistance, LON = longevity, FER = fertility, BCS = body condition score.

5.4 Discussion

The goal of this study was to (1) define potential resilience indicators based on daily step count data according to theory and literature, and (2) to investigate their usefulness for genetically improving resilience by estimating heritability and genetic associations with other resilience-related traits, which were health traits, longevity, fertility, and body condition score. Traits describing the mean number of steps per day in different periods of the lactation were selected based on the assumption that resilient cows do not show many severe declines in step count (Edwards and Tozer, 2004; Abeni and Galli, 2017) and therefore have high step count level. Traits describing fluctuations in number of steps between days were selected based on the assumption that resilient cows do not show many drops and large fluctuations in step count and that they recover quickly (Scheffer et al., 2009, 2018; Berghof et al., 2019b). The resilience indicators describing mean step count had moderately high heritability, and the ones describing fluctuations in step count had lower heritability. Genetic correlations of the step count level traits with health traits, longevity, fertility, and body condition score were all favorable but weak. This means that mean step count can easily be increased through genetic selection, but will coincide with limited improvement of health, longevity, fertility, and body condition score. However, moderately strong genetic correlations with health traits, longevity, fertility, and body condition score were shown for the number of step count drops and $r_{\text{auto_steps}}$, and these correlations were favorable.

This study is one of the first to investigate heritability of step count level and other step count traits calculated from sensor data in cattle not focused on estrus or fertility. One other study that investigated heritability of activity traits outside estrus, found a much lower heritability of mean activity than we did (Schöpke and Weigel, 2014). These authors found a heritability of 0.05 and 0.03 for mean activity index based on head and neck movements, recorded in Israeli Holsteins by electronic activity neck tags in the 2 week non-estrus period before and after successful insemination, respectively. The difference in heritability with our study may be explained by difference of the activity trait (step count measured by leg accelerometers from Nedap (Groenlo, the Netherlands) versus an activity index based on head and neck movements measured by neck accelerometers from SCR (Netanya, Israel)), and study population. The difference in the length of the measurement period (up to 450 days versus 2 weeks) could also play a role, but this is likely not the main cause: our trait ‘mean step count prepartum’ was also based on 2 weeks, but its heritability was much higher (0.22). Furthermore, Schöpke and Weigel (2014) found a heritability of 0.03 for the standard deviation of daily activity, which is much lower than the heritability of the similar trait

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$\text{LnVar}_{\text{steps}}$ in this study. However, for this trait Schöpke and Weigel (2014) included measurements during estrus, while we excluded them. In addition, they took the standard deviation of the raw data, while we first adjusted for general trend across lactation. Furthermore, the difference in trait definition and study population likely play a role. Because of the moderate to moderately high heritability of traits calculated from step count data in our study, these traits offer great opportunity for genetic selection, potentially for the benefit of resilience and possibly also for other benefits.

A genetic analysis was performed in this study, while most studies on development of resilience indicators from activity data have been phenotypic (e.g. van Dixhoorn et al., 2018; van der Zande et al., 2020). However, genetic analysis poses a useful advantage over phenotypic analysis. The advantage of genetic analysis is that it is not necessary that the animal itself has enough data on response to disturbances to be able to predict its resilience to next disturbances, as is the case for phenotypic prediction. It has appeared challenging to predict resilience to a major disturbance using activity data before that disturbance (van der Zande et al., 2020). With genetic analysis, it is possible to use patterns in activity data on relatives or on animals with shared SNPs. Those animals with similar genetic background together offer data on response in activity to a wide variety of disturbances, and together give a general picture of the genetic merit for resilience. Therefore, using genetic analysis, it is possible to estimate the genetic merit for resilience of an animal without data on response to disturbances, when they have family members that do have data on response to many types of disturbances.

Step count traits are heritable and can be changed through genetic selection, but the question is if these traits can serve as a proxy to select more resilient cows. According to resilience theory, low variance and autocorrelation of longitudinal traits sensitive to disturbances indicate good resilience (Scheffer et al., 2018). Activity is indeed sensitive to disturbances (Edwards and Tozer, 2004; Liboreiro et al., 2015; Abeni and Galli, 2017), which supports the hypothesis that variance and autocorrelation of step count data contain information on resilience. Moreover, low variability of other traits sensitive to disturbances, such as milk yield (Elgersma et al., 2018; Poppe et al., 2020, 2021c), and daily feed intake in pigs (Putz et al., 2019; Cheng et al., 2020) and 4-weekly body weight records in layers (Berghof et al., 2019a) already showed to be genetically associated with good resilience. Therefore, selection for lower $\text{LnVar}_{\text{steps}}$ and $r_{\text{auto_steps}}$ is expected to result in more resilient cows. For $r_{\text{auto_steps}}$, this assumption is supported by its strong positive genetic correlation with the number of step count drops and because low values

were genetically correlated with good hoof health and fertility and high body condition score. However, for $\text{LnVar}_{\text{steps}}$ it is important to note that low values were genetically correlated with poor instead of good health, even when adjusted for step count level, although these correlations were weak. It is possible that $\text{LnVar}_{\text{steps}}$ is associated with other aspects of resilience that are not covered by the existing traits, such as strength of response to disturbances, or response to other disturbances than diseases. However, it should first be investigated if this is true, and it is important to consider that selection for lower $\text{LnVar}_{\text{steps}}$ will coincide with an undesired increase in incidence of health problems. For the trait ‘number of step count drops’ it is intuitively clear that selection for lower values will result in better resilience, and this is also supported by its moderately strong genetic correlation with hoof health, fertility and body condition score. However, because of its very low heritability and its strong genetic correlation with $r_{\text{auto_steps}}$, it is more efficient to select for $r_{\text{auto_steps}}$ rather than the number of step count drops. For the traits describing mean step count, the hypothesis was that low step count level indicates poor resilience, because most disturbances will decrease activity (Edwards and Tozer, 2004; Abeni and Galli, 2017). Indeed, low step count was genetically related with poor health, fertility, and body condition score, albeit weakly. However, it is important to consider that step count level of a cow is probably not only associated with resilience, but also with personality of the cow. Therefore, traits describing fluctuations in step count are probably more directly related with resilience than traits describing mean step count. Nevertheless, it is worthwhile to investigate the association between mean step count and resilience further, because it offers great opportunity for genetic selection because of its high heritability. For the traits describing mean of negative residuals throughout lactation and during step count drops, it was hypothesized that more extreme residuals (low values) represent poor resilience, which is rather intuitive. However, the unfavorable genetic correlations with the health traits, but favorable partial genetic correlations suggest that a statistical scale effect (Falconer and Mackay, 1996) is present, where higher mean automatically coincides with higher deviations from the mean. Therefore, these traits should be adjusted for step count level to be useful as resilience indicators. In summary, selection for $r_{\text{auto_steps}}$ and number of step count drops are likely to result in better resilience, but the other traits first need an adjustment for step count level or more research before they can be used to improve resilience.

The positive genetic correlations of $\text{LnVar}_{\text{steps}}$ with the health traits, longevity, fertility, and body condition score were surprising. They are likely not, or not entirely, due to a statistical scale effect, because although $\text{LnVar}_{\text{steps}}$ was strongly

genetically correlated with mean step count, the partial genetic correlations adjusted for mean step count were still generally positive. Another explanation is that very stable step count is not necessarily associated with good resilience, due to existence of a lower step count limit. Cows have a minimum distance to walk every day to get milked and fed. When severely challenged, for example by a claw disorder, they will likely function at this minimum activity level for a certain time period. Step count will then be very stable, but this is a sign of reduced resilience rather than good resilience. Other studies found varying phenotypic associations of variability of activity with health and resilience traits, ranging from positive (van Dixhoorn et al., 2018; Adriaens et al., 2020) to negative (Thorup et al., 2015). The association between $\text{LnVar}_{\text{steps}}$ and resilience may be curvilinear, where an optimum exists for intermediate $\text{LnVar}_{\text{steps}}$ values. A curvilinear relationship was also found between the log-transformed variance of clutch size in great tits and fitness, where intermediate variance was related to the highest fitness (Mulder et al., 2016). The existence of an optimum level of $\text{LnVar}_{\text{steps}}$ should be investigated further before it can be used as a resilience indicator.

This study provides important insights into the heritability of resilience indicators from daily step count data and associations with other traits related to resilience that are already in the breeding goal. However, the most important question to be answered before the new traits can be applied is how the new resilience indicators are associated with aspects of resilience not covered by the already existing traits, in particular strength of response to disturbances and recovery rate. Furthermore, the added value of resilience indicators based on daily step count data compared to daily milk yield data, which is more widely available, should be investigated. We hypothesize that resilience indicators based on step count data should be regarded complementary to resilience indicators based on milk yield, and not as a replacement. Sensitivity to particular disturbances is different for milk yield and step count. For example, step count seems more sensitive to locomotion problems than milk yield, while milk yield seems more sensitive to udder health problems, as suggested by the genetic correlations with claw health and udder health in this study and Poppe et al. (2020). Together, the resilience indicators based on step count data and based on milk yield data will generate a more complete picture of resilience to a wider variety of disturbances than any of them alone. In summary, more research is needed into the added value of the new resilience indicators compared to existing traits related to resilience, but this study provides an important first step for genetic selection for resilience using activity data.

5.5 Conclusions

This study investigated potential resilience indicators for genetic selection based on daily step count data. According to theory, high step count level and low magnitude of fluctuations with quick recovery are expected to be associated with good resilience. The traits autocorrelation (indicating recovery from disturbances) and number of step count drops are likely suitable as resilience indicators because their theoretical relation with resilience was supported by moderately strong genetic correlations with hoof health, fertility, and body condition score. Of these two strongly genetically correlated traits, autocorrelation was most suitable because of its higher, but still low heritability (0.04 vs. 0.01). The other resilience indicators were heritable as well, and especially mean step count had moderately high heritability (0.22-0.45). However, these heritable traits need an adjustment for step count level (mean of all negative residuals and mean of negative residuals during step count drops) or more research into the biology of the trait (natural log-transformed variance of steps and mean step count) before they can be used to improve resilience. This research is an important first step in the exploration of the use of activity data for breeding for resilience.

5.6 Acknowledgments

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6

Between-herd variation in resilience and relations to herd performance

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Abstract

Resilient cows are minimally affected in their functioning by infections and other disturbances, and recover quickly. Herd management is expected to have an effect on disturbances and the resilience of cows, and this effect was investigated in this study. Two resilience indicators were first recorded on individual cows. The effect of herd-year on these resilience indicators was then estimated and corrected for genetic and year-season effects. The 2 resilience indicators were the variance and the lag-1 autocorrelation of daily milk yield deviations from an expected lactation curve. Low variance and autocorrelation indicate that a cow does not fluctuate much around her expected milk yield and is, thus, subject to few disturbances, or little affected by disturbances (resilient). The herd-year estimates of the resilience indicators were estimated for 9,917 herd-year classes based on records of 227,655 primiparous cows from 2,644 herds. The herd-year estimates of the resilience indicators were then related to herd performance variables. Large differences in the herd-year estimates of the 2 resilience indicators (variance and autocorrelation) were observed between herd-years, indicating an effect of management on these traits. Furthermore, herd-year classes with a high variance tended to have a high proportion of cows with a rumen acidosis indication ($r = 0.31$), high SCS ($r = 0.19$), low fat content ($r = -0.18$), long calving interval ($r = 0.14$), low survival to second lactation ($r = -0.13$), large herd size ($r = 0.12$), low lactose content ($r = -0.12$), and high production ($r = 0.10$). These correlations support that herds with high variance are not resilient. The correlation between the variance and the proportion of cows with a rumen acidosis indication suggests that feed management may have an important effect on the variance. Herd-year classes with a high autocorrelation tended to have a high proportion of cows with a ketosis indication ($r = 0.14$) and a high production ($r = 0.13$), but a low somatic cell score ($r = -0.17$) and a low proportion of cows with a rumen acidosis indication ($r = -0.12$). These correlations suggest that high autocorrelation at herd level indicates either good or poor resilience, and is thus a poor resilience indicator. However, the combination of a high variance and a high autocorrelation is expected to indicate many fluctuations with slow recovery. In conclusion, herd management, in particular feed management, seems to affect herd resilience.

Key words: resilience, management, variance, automatic milking system, dairy cow

6.1 Introduction

Dairy cows have to cope with a variety of environmental disturbances, such as pathogens or extreme weather. Resilient cows are minimally affected in their functioning by such disturbances, and if they are affected, they quickly recover (Colditz and Hine, 2016; Berghof et al., 2019b). Herd management is expected to affect the resilience of cows because management is known to affect several components of resilience, such as resistance, tolerance, and recovery to and from certain infections (Deng et al., 2019). In addition, herd management is known to affect the number of environmental disturbances on a farm, such as infection pressure (Deng et al., 2019) and exposure to hot weather (Kendall et al., 2006; Fournel et al., 2017).

Recently, 2 traits were developed that indicate the resilience of individual cows. These traits were the natural log-transformed variance and lag-1 autocorrelation of daily milk yield deviations from a lactation curve (Pope et al., 2020). High variance indicates high variability in milk yield caused by disturbances, and high autocorrelation indicates slow return rate of milk yield to expected levels upon disturbances. Averaged per herd, variance and autocorrelation are expected to indicate the level of herd resilience, which is the ability of herd management to control resilience of the cows, and to control the number and severity of disturbances.

Several studies used a mixed animal model to study variation in traits between herds (Koivula et al., 2007; Caccamo et al., 2008; Stoop et al., 2008). Such models correct for genetic effects, which makes it possible to compare differences in traits between herds due to differences in management. Differences in herd estimates for the variance and autocorrelation are expected to exist, but it is still unknown how large variation between herds is, and how differences between herds are related to herd management.

The first aim of this study was, therefore, to investigate differences in herd resilience between herds, using the herd estimates of variance and autocorrelation of milk yield deviations measured on individual cows. The second aim was to explain the differences in herd resilience between herds by indicators of the herd (size) and its cow management (rumen acidosis, ketosis, somatic cell score, longevity, fertility).

6.2 Materials and methods

To address the aims of this study, for each herd included in this study the following information was needed: (1) an indication of herd resilience, (2) information about variables indicating the management and performance of the

herd. First, the calculation of the herd resilience indicators will be described. After that, the calculation of herd variables related to herd management and performance based on milk production recording data will be described. For most herds, several years of data were available. Management within herds was expected to vary between years, for example due to changes in feed management or expansion of the herd. Therefore, the data of each herd were split into herd-year classes, and the resilience indicators and herd management variables were computed for each herd-year class instead of for each herd. Data editing was performed by the AWK programming language (Aho et al., 1988) and R (version 3.4.3; R Project for Statistical Computing, Vienna, Austria).

6.2.1 Calculation of resilience indicators

Resilience indicators were first calculated for individual cows within herds using daily milk yield records obtained by automatic milking systems (AMS). These indicators were then used to compute resilience indicators at the herd-year level using mixed model equations (see equation [2]). The data used was the same as in Poppe et al. (2020), and originally contained 1,782,373,113 milk yield records on 1,120,550 cows obtained by AMS and conventional milking systems. The data were provided by Cooperation CRV (Arnhem, the Netherlands).

Data preparation started off with selecting only primiparous cows that were milked by AMS, that were at least 87.5% Holstein Friesian, that were herd-book registered, and that calved after 640 days of age and before June 1, 2017. Milk yield records obtained during single AMS visits were first converted to daily milk yield records per cow. Daily milk yield records after 350 days in milk (DIM) were excluded. The remaining milk yield records were used to model a lactation curve for each cow that reflected her expected milk yield in the absence of disturbances. Lactation curves were fitted using fourth-order polynomial quantile regression with a 0.7 quantile:

$$y_t = \beta_0 + \beta_1 * t^1 + \beta_2 * t^2 + \beta_3 * t^3 + \beta_4 * t^4 + \varepsilon \quad [1]$$

where y_t is the observed milk yield on DIM t , t^n are DIM to the power of n , where n is 1, 2, 3, or 4, β_n are regression coefficients describing the relationships between t^n and y_t , and ε is the error term. Quantile regression was used instead of classical regression, because it is better able to model a lactation curve without disturbances, which makes the negative deviations larger and more informative about resilience (Koenker, 2005; Poppe et al., 2020). The model was fitted using the quantreg package (Koenker, 2018) and the poly function in R. After fitting a

lactation curve for each cow, the deviations in milk yield were calculated as $y - \hat{y}$. The deviations on the first and last 10 days of each lactation were removed because of poor fit of the model in the beginning and end of the lactation. If a cow had at least 50 remaining daily milk yield deviations and not more than 5% was missing, these records were used to calculate the resilience indicators, which were the natural log-transformed variance (**LnVar**) and the lag-1 autocorrelation (r_{auto}) of the deviations. A low LnVar indicates that the milk yield of a cow does not fluctuate much around the expected milk yield, and thus indicates good resilience. A low r_{auto} indicates that milk yield fluctuates quickly and independent from the previous day, and thus indicates good resilience (Berghof et al., 2019b).

The data preparation until this point was the same as in Poppe et al. (2020) and resulted in 255,096 first-parity cows with an observation for LnVar and r_{auto} . The remaining 2 data preparation steps differ in the current study compared to Poppe et al. (2020) with respect to outliers and the number of cows per herd-year class. Here, records for LnVar or r_{auto} that deviated more than 4 standard deviations from the mean were removed, which were 47 LnVar records and 227 r_{auto} records. In Poppe et al. (2020), the same approach was used, but they computed each resilience indicator based on 4 different lactation curves. If one resilience indicator was an outlier based on all lactation curves, all other resilience indicators were also set to missing, resulting in removal of more records than in the current study. Finally, herd-year of calving classes were made, and classes with less than 10 cows were removed. After removal, 9,917 herd-year classes remained, including 2,644 herds from the years 2011 to 2017. These herd-year classes contained 227,615 cows with a record for LnVar and 227,453 cows with a record for r_{auto} . For a detailed description of the data preparation steps, including the number of records and cows remaining after each preparation step, see Table 1 in Poppe et al. (2020).

After calculating the LnVar and r_{auto} of individual cows, for each herd-year the level of these traits was estimated, corrected for genetic effects and general year-season effects using a mixed model. By correcting for genetic and year-season effects, differences in LnVar or r_{auto} between herds can be attributed only to herd management. The estimates of LnVar and r_{auto} per herd-year were obtained using the following mixed animal model:

$$y_{ijk} = HY_i + YS_j + a_k + e_{ijk}, [2]$$

where y_{ijk} is the LnVar or r_{auto} of cow k in herd-year class i and year-season class j , HY_i is the fixed effect of herd-year of calving i , YS_j is the fixed effect of year-season of calving j (4 seasons: January-March, April-June, July-September, October-

December), a_k is the random genetic effect of animal k , and e_{ijk} is a random error term. The following assumptions were made about the vector of random genetic effects, \mathbf{a} , and the vector of residuals, \mathbf{e} : $\mathbf{a} \sim N(\mathbf{0}, \mathbf{A}\sigma_a^2)$ and $\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}\sigma_e^2)$, where \mathbf{A} is the additive genetic relationship matrix, \mathbf{I} is the identity matrix, σ_a^2 is the additive genetic variance and σ_e^2 is the residual variance. The model was applied with ASReml 4.1 (Gilmour et al., 2015) and the pedigree included 5 generations of ancestors resulting in 758,921 animals. The estimates of LnVar and r_{auto} for each herd-year computed by the mixed model were used in our further analyses as measures of herd resilience. Herd-year classes with a high estimate for LnVar contain cows that have on average a highly variable daily milk yield, and herd-year classes with a high estimate for r_{auto} contain cows that have on average a slowly fluctuating milk yield.

6.2.2 Calculation of herd performance variables from milk production registration data

The second aim of this study was to investigate the relationships between the resilience indicators and variables indicating herd management. Variables indicating herd management were derived from milk production registration data, birth and calving dates, and information about breed and herd book status. These variables will be referred to as herd performance variables. Herd performance variables were calculated for each herd-year class that also contained cows with resilience indicators. The data set with milk production registration records included 3-, 4-, 5-, or 6-weekly records on milk yield (kg), fat percentage (%), protein percentage (%), lactose percentage (%), SCC, ureum, and a ketosis indication based on fat-protein ratio and Fourier-transform infrared measurements of milk acetone and milk β -hydroxybutyric acid (binary, only available for first 60 days after calving; Vosman et al., 2015). The original data set contained 9,272,501 records on 1,065,931 first-parity cows from 4,947 herds. However, only the 2,159,817 records on the 227,655 cows in the 9,917 herd-year classes that also had resilience indicators were used.

The herd performance variables are listed in Table 6.1. Part of the herd performance variables were based on the milk production recording data of the cows that also had a resilience indicator (that is, primiparous cows that met the inclusion requirements, such as being at least 87.5% Holstein Friesian and being herd-book registered). The other part of the herd performance variables, such as the herd size and average age, were based on pedigree data and calf dates of all cows in the herd-year, including older cows, crossbred cows, and so on. The herd performance variables that describe a mean of a trait were calculated by averaging

the trait per cow, and then taking the mean of all cows in the herd-year. The herd performance variables that describe a proportion are the number of cows with a certain condition divided by the total number of cows that calved in the herd-year.

The somatic cell score (**SCS**) was derived from somatic cell count (**SCC**) as (CRV, 2018a):

$$SCS = 1,000 + 100 * (^2\log(\frac{SCC}{1,000})). [3]$$

For the proportion of cows with 1 or more cases of elevated SCC, an SCC record was considered elevated if it was greater than 100,000 (Windig et al., 2005a; Hooijer et al., 2008). For the proportion of cows with 1 or more rumen acidosis indications, a rumen acidosis indication was given based on fat and protein content: when at least once during the lactation of a cow the fat content was lower than the protein content and at the same time lower than 4.00% (CRV, 2014), the cow received a score of 1, and otherwise 0. For the proportion of cows that survived to the second lactation, survival to second lactation was based on the second calving date: when a second calving date was known, a cow received a score of 1 and otherwise 0. If a herd-year class contained less than 10 cows with a record for a certain trait, the record for that herd-year class was set to missing. Table 6.1 shows for each herd performance variable the number of remaining herd-year classes that were used for calculation of correlations (see Analyses section). For multiple regression, only herd-year classes could be used without missing herd performance variables, which were 7,828 classes (see Analyses section).

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Table 6.1 The herd performance variables, units, the type of cows on which each herd performance variable was based, and the number of records for each herd performance variable.

Herd performance variables	Unit	Cows on which variable is based ¹	Number of herd-years with record
Mean milk yield	Kilograms	1	9,917
Mean fat content	%	1	9,914
Mean protein content	%	1	9,914
Mean lactose content	%	1	9,914
Mean ureum content	-	1	9,566
Mean somatic cell score	-	1	9,830
Mean calving interval from first to second lactation	Days	1	8,662
Mean age at first calving	Months	1	9,917
Proportion of cows with at least 1 elevated somatic cell count	-	1	9,830
Proportion of cows with at least 1 rumen acidosis indication	-	1	9,914
Proportion of cows with at least 1 ketosis indication	-	1	8,977
Proportion of cows that survived to second lactation	-	1	9,917
Mean age	Years	2	9,917
Number of cows calved	-	2	9,917
Proportion of cows that are not 100% Holstein Friesian	-	2	9,917
Proportion of cows that are herd-book registered	-	2	9,917

¹1 = primiparous cows with a resilience indicator in the herd-year class; 2 = all cows in the herd-year class.

6.2.3 Analyses

6.2.3.1 Variation in LnVar and r_{auto} between herd-years and consistency between years within herd

To investigate variation in LnVar and r_{auto} between herd-years, the standard deviation, minimum, and maximum of the herd-year estimates for LnVar and r_{auto} were computed. To investigate the association between LnVar and r_{auto} at herd-year level, Pearson correlations between the herd-year estimates of LnVar and r_{auto} were calculated. In addition, for both traits, Pearson correlations were calculated between herd-year estimates within herd between different years, to investigate how consistent LnVar and r_{auto} were within herds over years.

6.2.3.2 Associations between herd-year estimates and herd performance variables

Pearson correlations were calculated between the herd-year estimates of LnVar and r_{auto} and the herd performance variables derived from milk production recording data. In addition, a multiple linear regression with stepwise model selection was performed with the herd-year estimates of LnVar and r_{auto} as dependent variables and the herd performance variables as independent variables. Such a multiple regression yields partial effects of herd performance variables on LnVar and r_{auto} at herd-year level, conditional on the other variables involved. Stepwise model selection was performed using the StepAIC function from the MASS package (Venables and Ripley, 2002) in R. The stepwise model selection could only be performed on the 7,828 herd-years where none of the herd performance variables were missing. Multiple linear regression with stepwise model selection was performed both with mean milk yield included as a fixed independent variable, and without mean milk yield included as an independent variable, to investigate how milk yield level influences the effect of other herd performance variables on resilience. After performing stepwise model selection, the relative importance of each remaining variable was obtained using the calc.relimp function with the lmg metrics from the relaimpo package (Grömping, 2006). The lmg metric is based on sequential R^2 , but accounts for the effect of different orderings of regressors on the sequential R^2 and therefore takes the average across different orderings by permuting the order of the regressors (Grömping, 2006). The relative importance of a variable is thus in other words the average relative contribution of each variable to R^2 .

6.3 Results

6.3.1 Variation in LnVar and r_{auto} between herd-years

The LnVar and r_{auto} differed extensively between herd-year classes. The highest LnVar estimate was more than 6 times larger than the lowest LnVar estimate (Table 6.2). To illustrate this: the primiparous cows of the herd-year with the smallest LnVar had on average a standard deviation of 1.19 kg in their deviations from expected yield, whereas the primiparous cows of the herd-year with the largest LnVar had on average a standard deviation of 3.66 kg in their deviations from expected yield. The highest r_{auto} estimate was more than 4 times larger than the lowest r_{auto} estimate (Table 6.2). The first-parity cows of the herd-year class with the smallest r_{auto} had on average a correlation of 0.32 between subsequent deviations from expected yield, whereas the first-parity cows of the herd-year class with the largest r_{auto} had on average a correlation of 0.59 between subsequent deviations from expected yield. The herd-year estimates of LnVar and r_{auto} were both normally distributed upon visual inspection. At herd-year level, LnVar was negatively correlated with r_{auto} (-0.34, P-value <0.001), which means that herd-years with high LnVar tended to have low r_{auto} . Thus, if in a certain herd-year one of the indicators indicated good resilience, the other indicator tended to indicate poor resilience. In summary, herds differed extensively in the 2 resilience indicators LnVar en r_{auto} , and the 2 resilience indicators were negatively correlated at herd level.

Table 6.2 Descriptive statistics of the herd-year estimates of natural log-transformed variance of milk yield deviations (LnVar) and lag-1 autocorrelation of milk yield deviations (r_{auto}).

Herd-year estimate	Mean	Minimum	Maximum	SD
LnVar	1.339	0.381	2.557	0.269
r_{auto}	0.554	0.183	0.817	0.084

6.3.2 Consistency of LnVar and r_{auto} within herds between years

Herd-year estimates of the same herds between years were positively correlated (Table 6.3): if a herd had a high LnVar or r_{auto} in a certain year, the herd also tended to have a high LnVar or r_{auto} in other years. The correlations between years were stronger for LnVar (average: 0.58) than for r_{auto} (average: 0.53). The correlations between years decreased with the interval between years. The average correlation between herd-year estimates of subsequent years was 0.69 for

LnVar, and 0.64 for r_{auto} (Table 6.3). In summary, the resilience indicators showed consistency within herds between years.

Table 6.3 Pearson correlations of herd-year estimates between years within herds¹.

Year	Year						
	2011	2012	2013	2014	2015	2016	2017
2011		0.72	0.56	0.54	0.47	0.48	0.38
2012	0.68		0.68	0.58	0.56	0.53	0.48
2013	0.55	0.60		0.65	0.61	0.57	0.49
2014	0.56	0.52	0.63		0.66	0.60	0.52
2015	0.55	0.47	0.55	0.61		0.71	0.60
2016	0.50	0.47	0.55	0.55	0.67		0.69
2017	0.31	0.32	0.44	0.43	0.57	0.63	

¹Correlations for herd-year estimates of natural log-transformed variance of milk yield deviations are above the diagonal, and correlations for herd-year estimates of lag-1 autocorrelation of milk yield deviations are below the diagonal.

6.3.3 Association between herd-year estimates of resilience indicators and herd performance variables

The herd-year classes had a mean milk yield of 25.23 kg per day with 4.42% fat and 3.59% protein, and an SCS between 1,409 and 1,726 (Table 6.4). The correlations between LnVar and the herd performance variables ranged from -0.18 to 0.31 (Table 6.5). Herd-years with high LnVar (low resilience) tended to have high production (correlation 0.10), low fat content (-0.18), low lactose content (-0.12), high proportion of cows with a rumen acidosis indication (0.31), high SCS (0.19), high proportion of cows with an elevated SCC (0.20), long calving interval (0.14), low survival to second lactation (-0.13), large herd size (0.12), and low participation in the herd book (-0.10; $P < 0.001$). The correlations between r_{auto} and the herd performance variables ranged from -0.17 to 0.14 (Table 6.5). Herd-years with high r_{auto} (low resilience) tended to have a high production (correlation 0.13) and a high proportion of cows with a ketosis indication (0.14), but a low proportion of cows with a rumen acidosis indication (-0.12), low SCS (-0.17), and low proportion of cows with elevated SCC (-0.15; $P < 0.001$). In summary, LnVar and r_{auto} at herd-year level were correlated with several herd performance variables, and especially the correlation between the herd-year estimate of LnVar and the proportion of cows with a rumen acidosis indication was considerable (0.31).

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Table 6.4 Descriptive statistics of the herd performance variables based on milk production recording data.

Herd performance variable ¹	Mean	SD	Minimum	Maximum
Milk (kg)	25.23	2.90	13.70	37.07
Fat (%)	4.42	0.19	3.73	5.24
Protein (%)	3.59	0.11	3.17	4.05
Lactose (%)	4.64	0.05	4.41	4.81
Ureum	23.00	2.45	11.37	33.70
SCS	1,564	45.43	1,409	1,726
CIN (days)	402.10	28.23	336.50	676.70
CA (months)	25.40	1.34	21.45	34.17
PropSCC	0.67	0.17	0.08	1.00
PropACI	0.20	0.14	0.00	1.00
PropKET	0.08	0.09	0.00	0.90
PropSURV	0.85	0.13	0.00	1.00
Age (years)	4.00	0.34	1.97	5.61
Herd size	108.20	47.63	13	485
PropNonHF	0.22	0.18	0.00	1.00
PropReg	0.95	0.07	0.22	1.00

¹Milk = mean milk yield; fat = mean fat content; protein = mean protein content; lactose = mean lactose content; ureum = mean ureum content; SCS = mean somatic cell score; CIN = mean calving interval from first to second lactation; CA = mean age at first calving; PropSCC = proportion of cows with at least 1 elevated somatic cell count; PropACI = proportion of cows with at least 1 rumen acidosis indication; PropKET = proportion of cows with at least 1 ketosis indication; PropSURV = proportion of cows that survived to second lactation; age = mean age; herd size = number of cows calved; PropNonHF = proportion of cows that are not 100% Holstein Friesian; PropREG = proportion of cows that are herd-book registered.

Table 6.5 Pearson correlations of herd-year estimates of the resilience indicators natural log-transformed variance of milk yield deviations (LnVar) and lag-1 autocorrelation of milk yield deviations (r_{auto}) with the herd performance parameters.

Herd performance variable ¹	Resilience indicators			
	LnVar		r_{auto}	
	Correlation with herd performance variable	P-value	Correlation with herd performance variable	P-value
Milk (kg)	0.10	<0.001	0.13	<0.001
Fat (%)	-0.18	<0.001	0.03	0.011
Protein (%)	-0.02	0.115	-0.05	<0.001
Lactose (%)	-0.12	<0.001	0.04	<0.001
Ureum	0.01	0.372	0.02	0.024
SCS	0.19	<0.001	-0.17	<0.001
CIN (days)	0.14	<0.001	0.00	0.772
CA (months)	0.08	<0.001	0.00	0.940
PropSCC	0.20	<0.001	-0.15	<0.001
PropACI	0.31	<0.001	-0.12	<0.001
PropKET	0.03	0.009	0.14	<0.001
PropSURV	-0.13	<0.001	0.03	0.003
Age (years)	-0.05	<0.001	0.02	0.014
Herd size	0.12	<0.001	-0.08	<0.001
PropNonHF	0.01	0.225	-0.03	0.009
PropREG	-0.10	<0.001	0.05	<0.001

¹Milk = mean milk yield; fat = mean fat content; protein = mean protein content; lactose = mean lactose content; ureum = mean ureum content; SCS = mean somatic cell score; CIN = mean calving interval from first to second lactation; CA = mean age at first calving; PropSCC = proportion of cows with at least 1 elevated somatic cell count; PropACI = proportion of cows with at least 1 rumen acidosis indication; PropKET = proportion of cows with at least 1 ketosis indication; PropSURV = proportion of cows that survived to second lactation; age = mean age; herd size = number of cows calved; PropNonHF = proportion of cows that are not 100% Holstein Friesian; PropREG = proportion of cows that are herd-book registered.

6.3.4 Partial effects of the herd performance variables on LnVar and r_{auto}

The model for LnVar remaining after stepwise model selection explained 20% of the variation, and when including mean milk yield this increased to 21% (Table 6.6). All regression coefficients were in the same direction as the correlations in Table

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6.5, regardless if mean milk yield was included or not. Moreover, the relative importances of the explanatory variables were similar in the models with and without mean milk yield. The proportion of cows with a rumen acidosis indication had the highest relative importance in both the model without mean milk yield and the model with mean milk yield (0.37 and 0.40, respectively), followed by the herd size (0.12 and 0.11, respectively). Mean milk yield itself had a relative importance of 0.08. In summary, the proportion of cows with a rumen acidosis indication explained most variation in LnVar across herd-years, and the mean milk yield level had little effect on this association.

The model for r_{auto} remaining after stepwise model selection explained 8% of the variation, and when including mean milk yield this increased to 10% (Table 6.7). All regression coefficients, except the one for the proportion of non-Holstein Friesian cows, were in the same direction as the correlations in Table 6.5, regardless if mean milk yield was included or not. When including mean milk yield in the model, the relative importance of the proportion of cows with a ketosis indication decreased from 0.22 to 0.16 compared with excluding mean milk yield from the model. The relative importance of mean SCS decreased from 0.19 to 0.14. In the model without mean milk yield, the proportion of cows with a ketosis indication had the highest relative importance (0.22), whereas in the model with mean milk yield the proportion of first-parity cows with a rumen acidosis indication had the highest relative importance (0.19). Mean milk yield itself had a relative importance of 0.16. In summary, differences in r_{auto} between herd-years could be partly explained by herd performance variables obtained from milk production registration recording, and mean milk yield affected the associations between some herd performance variables and r_{auto} .

Table 6.6 Results from multiple linear regression with stepwise model selection of the herd-year estimates of natural log-transformed variance of milk yield deviations on the herd performance variables¹.

Herd performance variable ¹	Milk excluded		Milk fixed	
	Regression coefficient	Relative importance	Regression coefficient	Relative importance
Milk (kg)	-		1.16E-04	0.08
Fat (%)	-1.20E-05	0.11	-	-
Protein (%)	-	-	-8.13E-06	0.00
Lactose (%)	-7.24E-05	0.07	-7.98E-05	0.07
Ureum	-	-	-	-
SCS	4.58E-04	0.09	5.29E-04	0.09
CIN (days)	6.55E-04	0.04	6.42E-04	0.04
CA (months)	7.36E-03	0.01	8.56E-03	0.01
PropACI	4.93E-01	0.37	5.14E-01	0.40
PropKET	1.33E-01	0.01	5.45E-02	0.00
PropSURV	-2.06E-01	0.04	-2.18E-01	0.04
PropSCC	1.99E-01	0.10	2.20E-01	0.11
Age (years)	-5.31E-02	0.02	-3.79E-02	0.01
Herd size	8.98E-04	0.12	8.52E-04	0.11
PropNonHF	-	-	-	-
PropREG	-2.62E-01	0.03	-3.11E-01	0.03
Adjusted R ²		0.20		0.21

¹Regression coefficients and relative importances are shown for the herd performance variables remaining in the model after stepwise model selection, both when mean milk yield based on milk production recording (Milk) was excluded as an independent variable, and when Milk was included as an independent variable. Adjusted coefficients of determination (R²) of the models are shown in the bottom row.

²Milk = mean milk yield; fat = mean fat content; protein = mean protein content; lactose = mean lactose content; ureum = mean ureum content; SCS = mean somatic cell score; CIN = mean calving interval from first to second lactation; CA = mean age at first calving; PropSCC = proportion of cows with at least 1 elevated somatic cell count; PropACI = proportion of cows with at least 1 rumen acidosis indication; PropKET = proportion of cows with at least 1 ketosis indication; PropSURV = proportion of cows that survived to second lactation; age = mean age; herd size = number of cows calved; PropNonHF = proportion of cows that are not 100% Holstein Friesian; PropREG = proportion of cows that are herd-book registered.

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Table 6.7 Results from multiple linear regression with stepwise model selection of the herd-year estimates of lag-1 autocorrelation of milk yield deviations on the herd performance variables¹.

Herd performance variable ¹	Milk excluded		Milk fixed	
	Regression coefficient	Relative importance	Regression coefficient	Relative importance
Milk (kg)	-	-	4.68E-05	0.16
Fat (%)	-2.83E-06	0.02	-	-
Protein (%)	-	-	-1.40E-06	0.02
Lactose (%)	5.61E-06	0.01	-	-
Ureum	6.54E-04	0.00	8.76E-04	0.00
SCS	-2.37E-04	0.19	-2.14E-04	0.14
CIn (days)	1.47E-04	0.02	1.45E-04	0.02
CA (months)	1.58E-03	0.01	1.64E-03	0.01
PropACI	-8.19E-02	0.18	-8.53E-02	0.19
PropKET	1.26E-01	0.22	9.90E-02	0.16
PropSURV	3.46E-02	0.03	2.68E-02	0.02
PropSCC	-3.16E-02	0.14	-2.21E-02	0.10
Age (years)	-	-	8.57E-03	0.01
Herd size	-1.76E-04	0.14	-1.98E-04	0.14
PropNonHF	1.58E-02	0.00	2.71E-02	0.01
PropREG	6.39E-02	0.02	6.41E-02	0.02
Adjusted R ²	0.08		0.10	

¹Regression coefficients and relative importances are shown for the herd performance variables remaining in the model after stepwise model selection, both when the herd performance variable mean milk yield based on milk production recording (milk) was excluded as an independent variable, and when milk was included as an independent variable. Adjusted coefficients of determination (R^2) of the models are shown in the bottom row.

²Milk = mean milk yield; fat = mean fat content; protein = mean protein content; lactose = mean lactose content; ureum = mean ureum content; SCS = mean somatic cell score; CIN = mean calving interval from first to second lactation; CA = mean age at first calving; PropSCC = proportion of cows with at least 1 elevated somatic cell count; PropACI = proportion of cows with at least 1 rumen acidosis indication; PropKET = proportion of cows with at least 1 ketosis indication; PropSURV = proportion of cows that survived to second lactation; age = mean age; herd size = number of cows calved; PropNonHF = proportion of cows that are not 100% Holstein Friesian; PropREG = proportion of cows that are herd-book registered.

6.4 Discussion

This study investigated herd differences between 2 resilience indicators, LnVar and r_{auto} , measured on individual cows. Low LnVar of a cow indicates that milk yield does not fluctuate a lot from day to day, and low r_{auto} indicates that milk yield of a cow recovers upon a disturbance quickly rather than slowly. Therefore, low LnVar and r_{auto} were expected to indicate cows with good resilience (Berghof et al., 2019b). Because herd-years with low herd-year estimates for the resilience indicators had low LnVar and r_{auto} among cows, low herd-year estimates were expected to indicate good herd resilience. This study showed that herd-year estimates of LnVar and r_{auto} differed between herd-years. Because the variation between herds was corrected for genetic effects and general year-season effects, this indicates that herd management affects LnVar and r_{auto} . Other studies also found variation in herd estimates resulting from genetic analyses, especially for production traits and SCS (Koivula et al., 2007; Caccamo et al., 2008; Stoop et al., 2008). This study also showed that herds with high LnVar tended to have worse health and a lower survival than herds with low LnVar. These associations confirm the importance of herd LnVar as an indicator of herd resilience. However, the associations between r_{auto} and herd performance variables were ambiguous, which may indicate that r_{auto} at herd level is less directly associated with health-related traits and therefore might be perceived as not being a good indicator of resilience. In the following paragraphs, we will first discuss the meaning of herd resilience, we will then discuss the associations of LnVar and r_{auto} with the herd performance indicators in more detail, and finally we will discuss potential application for improvement of herd management.

Throughout the paper, we have considered LnVar and r_{auto} at herd level as indicators of herd resilience. It is, however, important to discuss that herd resilience consists of 2 aspects, which could not be disentangled in our study. The first aspect of herd resilience is the control of number and severity of disturbances in the herd. With respect to this aspect, herds are resilient if management reduces exposure of cows to disturbances. For example, hygiene practices can reduce exposure to pathogens (Deng et al., 2019), and roof insulation can reduce exposure to extreme weather (Fournel et al., 2017). The second aspect of herd resilience is the ability of cows in a herd to cope with disturbances. With respect to this aspect, herds are resilient if management reduces vulnerability of cows to disturbances. For example, feeding an adequate amount of vitamins and minerals can reduce vulnerability to mastitis pathogens (Heinrichs et al., 2009). The resilience indicators in this study capture both aspects of herd resilience simultaneously, and in the case of high LnVar or r_{auto} it is unknown whether it is the result of a high number of

6 Differences in resilience between herds

disturbances or the lack of ability of the cows to respond to disturbances, or a combination of the 2 aspects. Although it is unknown from our resilience indicators which aspect leads to poor herd resilience, high LnVar and r_{auto} can still provide a sign that management may need improvement.

Herd resilience is expected to be affected by multiple factors and is not a direct measure of health, survival, or fertility. Nevertheless, herds with a high LnVar among cows tended to have a high proportion of cows with a rumen acidosis indication, high SCS, a high proportion of cows with elevated SCC, low survival to second lactation, long calving interval, a high proportion of cows with a ketosis indication and high age at first calving. These relations suggest that high LnVar is also indicative of the health, survival, and fertility status of the herd. It is not surprising that LnVar is indicative of health traits, because rumen acidosis (Krause and Oetzel, 2006; Enemark, 2008; Humer et al., 2018), mastitis (Rajala-Schultz et al., 1999b; Gröhn et al., 2004; Halasa et al., 2009), and ketosis (Rajala-Schultz et al., 1999a) can all lead to drops in milk yield in individual cows. A high number of cows with drops in yield in a herd will lead to increased mean LnVar at the herd level as well. In addition, the effect of health problems on LnVar in individual cows will likely be reinforced by the increased vulnerability to other disturbances once a cow has a health problem, such as subclinical ketosis (Raboisson et al., 2014). Furthermore, if high LnVar indicates reduced health, and we assume that reduced health is related to low survival (Beaudeau et al., 1995; Neerhof et al., 2000) and poor fertility (Fourichon et al., 2000; Wolfenson et al., 2015), then high LnVar is also expected to be related to low survival and fertility as we observed. In addition, there may be management practices, such as feeding frequency (DeVries, 2019), that underlie both LnVar and health and fertility traits. Although correlations between the herd performance variables and LnVar were in the expected direction, most of them were weak. However, strong correlations were not expected because LnVar indicates general resilience that is affected by many factors (Putz et al., 2019; Poppe et al., 2020). If the correlation with, for example, SCC, would be strong, LnVar would be a mastitis indicator rather than a general resilience indicator. The fact that all correlations with health and survival traits were favorable, without any exception, is an important confirmation that LnVar indicates general herd resilience.

The positive association between LnVar and the proportion of cows with a rumen acidosis indication was by far the most important one. This association may suggest that management practices that lead to rumen acidosis, such as feeding too many rapidly fermentable carbohydrates (Krause and Oetzel, 2006; Enemark, 2008; Humer et al., 2018), are important factors contributing to an increased

LnVar. This association is as expected because a decreased rumen pH can result in a reduction in feed intake, followed by an increase in feed intake (Humer et al., 2018). This fluctuating feed intake pattern can lead to a variable milk yield (increased LnVar). However, in this study, we used an indicator of rumen acidosis based on an inverted fat-protein ratio, which is not the same as true rumen acidosis. Not only intake of large amounts of rapidly fermentable carbohydrates, but also grazing can increase the probability of an inverted fat-protein ratio (Elgersma et al., 2004; Couvreur et al., 2006). Yet, grazing does not necessarily deprive health (Dijkstra et al., 2020). Grazing is also likely to lead to a higher LnVar than TMR due to variations in grass quality, which may explain the positive association between LnVar and the proportion of cows with a rumen acidosis indication. Because of the expected association between LnVar and the application of grazing, as well as application of different grazing strategies within and between herds, it is important to properly account for grazing in future research, especially in the relationship between LnVar and the rumen acidosis indication.

A positive correlation was observed between LnVar and mean milk yield, which was in accordance to some hypotheses, but in contrast to others. To start with the contrasting one, we may hypothesize that a high mean milk yield is related to low LnVar (negative association) because environments that lead to high milk yield have been shown to be related to good udder health (Haile-Mariam et al., 2003; Montaldo et al., 2010) and few drops in milk yield (Windig et al., 2005b). However, a hypothesis that is in accordance with our results, is that LnVar and mean milk yield are positively associated because of scaling. From a statistical perspective, an increase in mean of a trait leads to a proportional increase in variance (Falconer and Mackay, 1996). However, scaling cannot be the only reason for the positive association between LnVar and milk yield because herds with high LnVar also tended to have a higher coefficient of variation (SD/mean) than herds with a low LnVar (data not shown). From a feeding perspective, we may also hypothesize a positive association between LnVar and mean milk yield. Feeding large proportions of rapidly fermentable carbohydrates results in a high milk yield, but also increases the risk of rumen acidosis (Krause and Oetzel, 2006; Enemark, 2008; Humer et al., 2018), which was indicated to be related to high LnVar. The observed positive correlation between LnVar and mean milk yield is probably a result of all 3 hypotheses and therefore also not very strong.

Previous studies have suggested that high r_{auto} indicates reduced resilience (Scheffer, 2009; Berghof et al., 2019b; Poppe et al., 2020). The positive association between r_{auto} and the proportion of cows with a ketosis indication suggests that high r_{auto} among cows indicates reduced herd resilience: ketosis reduces milk yield

(Rajala-Schultz et al., 1999a; Raboisson et al., 2014), and reduces resilience to further disturbances (Raboisson et al., 2014). However, herds with high r_{auto} among their cows also tended to have low SCS, low incidence of cows with an elevated SCC, low proportion of cows with a rumen acidosis indication, and high survival. These associations indicate that a low instead of a high r_{auto} is a sign of decreased resilience. Moreover, r_{auto} and LnVar were negatively correlated (-0.34) at herd level, whereas a positive association was expected if high r_{auto} indicated poor resilience. An explanation for the finding that poor resilience could be indicated by both high and low r_{auto} , could be that drops with slow recovery lead to increased r_{auto} , while deep drops that immediately recover lead to low r_{auto} . Both types of drops are signs of poor resilience, but lead to opposing r_{auto} .

Because of the ambiguous correlations of r_{auto} with the herd performance variables, r_{auto} by itself is not a good indicator of resilience at the herd level. However, in combination with increased LnVar, the herd-year estimates of r_{auto} may provide information about recovery. If a herd has both a high LnVar and a high r_{auto} , drops in milk yield occur and the recovery is slow. If a herd has a high LnVar but a low r_{auto} , drops occur but recovery is fast. Therefore, resilience may be more severely affected in herds with high LnVar and high r_{auto} than in herds with high LnVar but low r_{auto} . In summary, r_{auto} is by itself not a good resilience indicator, but an index of LnVar and r_{auto} may be a better indicator of resilience at herd level than LnVar alone.

The question still remains how the index of LnVar and r_{auto} should be used as a management tool, given that AMS systems provide warning tools related to drops in milk yield as well. The most important application is the tactical and strategic benchmarking of the resilience of a herd relative to other herds and relative to the previous year. This benchmarking may assist farmers in making tactical or strategic decisions, such as changing the feeding regimen. Warnings provided by AMS have a different purpose than the resilience indicators because they act on the operational level rather than the tactical or strategic level. A warning is given when milk yield of individual cows drop or if the average herd yield drops, and action is expected immediately upon a warning. However, these warnings do not inform farmers if they have a lot of individual or herd drops in milk yield compared with other farms or compared with previous years, which the resilience indicators do. In summary, warnings provided by AMS are useful for operational management, whereas the herd resilience indicators are useful for tactical or strategic management.

Herd-year estimates of LnVar, perhaps in combination with r_{auto} , can inform about resilience level, but they do not indicate how herd resilience can be improved. The information from milk production recording, such as SCC, can

provide clues, but many more factors are related to herd resilience (e.g., protection from weather influences, nutrition, cow density) that are not covered by milk production recording, as the low R^2 of our regression models showed. Therefore, there is probably not a single solution to improve resilience, and the optimal solutions will likely differ between farms. Using their own expert knowledge of their farm, farmers can deduce which of their management practices likely contribute to decreased resilience. In some cases data from milk production recording and the AMS may help. Farmers can then decide if and how they will adjust management to improve resilience. In this sense, improving herd resilience is no different from improving other multifactorial traits, such as herd milk yield. There are also multiple methods to increase milk yield level; the optimal method will differ between farms, and some farmers accept a low milk yield level whereas others want to increase it. In summary, resilience of a farm could be a measure of the management quality and the general level of control at the farm, and provide information additional to the existing data on health and productivity level.

This study investigated herd estimates of resilience indicators based on AMS data on a yearly basis. However, herd estimates of the resilience indicators could potentially also be calculated for farms with a conventional milking system with electronic milk meters, although this should be studied first. In addition, the herd resilience indicators could be even more useful when calculated for shorter periods, because this would show effects of herd management adjustments on herd resilience more quickly. Such an approach has been taken for monthly herd estimates of production traits and SCS by Koivula et al. (2007) and Caccamo et al. (2008). The resilience indicators could for example be provided on a monthly basis together with the milk production recording data. In some cases the data of the resilience indicators and the milk production recording data may support each other, for example if herd resilience decreased and SCC increased compared with the previous month. In other cases, the resilience indicators may warn of resilience problems, while no problems are suggested (yet) by the milk production recording data. This would be an important benefit of the resilience indicators compared with already existing tools because they allow farmers to detect decreasing resilience and intervene before any real health problems arise.

6.5 Conclusions

This study showed that LnVar and r_{auto} , which were supposed to indicate resilience, varied widely between herd-year classes. Moreover, the differences between herd-year classes were related to several herd performance variables obtained from milk production recording. The associations with the herd

performance variables demonstrated that low LnVar indicates good resilience at herd level, and suggest that resilience can be improved through management. The ambiguous findings for r_{auto} suggest that this variable is less suitable as a resilience indicator at herd level than LnVar. However, for herds with high LnVar, r_{auto} may indicate rate of recovery. In conclusion, differences in resilience indicators between herds exist, and these differences can be partly explained by herd management.

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7

Associations between resilience indicators based on daily milk yield in first lactation and lifetime profitability

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Abstract

Resilience is the ability of cows to be minimally affected by environmental disturbances, such as pathogens or heat waves, or to quickly recover. Obvious advantages of resilience are good animal welfare and easy and pleasant management for farmers. Furthermore, economic effects are expected, but these remain to be determined. The goal of this study was to investigate the association between resilience and lifetime gross margin, using indicators of resilience calculated from fluctuations in daily milk yield. Resilience indicators and lifetime gross margin were calculated for 1,337 cows from 21 herds. These cows were not alive anymore and therefore had complete lifetime data available. The resilience indicators were the natural log-transformed variance (LnVar) and the lag-1 autocorrelation (r_{auto}) of daily milk yield deviations from cow-specific lactation curves in parity 1. Good resilience is indicated by low LnVar (small yield response to disturbances) and low r_{auto} (quick yield recovery to baseline). Lifetime gross margin was calculated as the sum of all revenues minus the sum of all costs throughout life. Included revenues were from milk, calf value, and slaughter of the cow. Included costs were from feed, rearing, insemination, management around calving, health and other treatments, and destruction in case of death on farm. The statistical effect of each resilience indicator on lifetime gross margin, and also on the underlying revenues and costs was investigated using ANCOVA models. Mean yield in first lactation, herd, and year of birth were included as covariates and factors. LnVar had a significantly negative effect on lifetime gross margin, which means that cows with stable milk yield (low LnVar, good resilience) in parity 1 generated on average a higher lifetime gross margin than cows that had the same milk yield level but with more fluctuations. The effect on lifetime gross margin could be mainly attributed to higher lifetime milk revenues for cows with low LnVar, due to a longer lifespan and higher levels of milk components. Unlike LnVar, r_{auto} was not significantly associated with lifetime gross margin or any of the underlying lifetime costs and revenues. However, it was significantly associated with yearly treatment costs, which is important for ease of management. In conclusion, the importance of resilience for total profit generated by a cow at the end of life was confirmed by the significant association of LnVar with lifetime gross margin, and the economic advantage can be mainly ascribed to benefits of long lifespan and high milk components.

Key words: resilience, lifetime gross margin, economics, profitability

7.1 Introduction

The production environment of cows is changing, with an increasing number of cows per labor unit and more environmental disturbances, e.g. due to climate change. In these changing environments it is important that cows can cope with environmental disturbances well, and are therefore easy to manage (Berghof et al., 2019b). The ability to be minimally affected by disturbances, and if affected, to quickly recover, is called resilience (Colditz and Hine, 2016).

Resilience of cows and other animals, and especially quantification of resilience, has been studied extensively in recent years (e.g. van Dixhoorn et al., 2018; Putz et al., 2019; Poppe et al., 2020; van der Zande et al., 2020). Many studies quantified resilience using indicators based on fluctuations in longitudinal traits. The theory behind the use of fluctuations in longitudinal traits is that many longitudinal traits are sensitive to environmental disturbances. Therefore, the fluctuation pattern of such longitudinal traits is indicative of the resilience of an animal (Scheffer et al., 2018). Examples of resilience indicators based on longitudinal traits in dairy cattle are the variance and the lag-1 autocorrelation of milk yield (Elgersma et al., 2018; Poppe et al., 2020) and activity (van Dixhoorn et al., 2018). Here, low variance and autocorrelation indicate a stable pattern over time and thus good resilience. Such resilience indicators are useful to distinguish resilient from less resilient animals. Some of these studies have investigated the use of resilience indicators in genetic selection (Elgersma et al., 2018; Poppe et al., 2020). The natural log-transformed variance and lag-1 autocorrelation of daily deviations from expected milk yield were heritable, and genetically associated with sensitivity of milk yield to disturbances and recovery time (Poppe et al., 2021c), and with health traits and longevity (Poppe et al., 2020, 2021a).

Being resilient has obvious advantages for cow welfare and job satisfaction of the farmer. However, effects on cow profitability are expected as well (Berghof et al., 2019b; Knap and Doeschl-Wilson, 2020). Positive effects of resilience on profitability are expected through a smaller yield loss upon environmental disturbances (Poppe et al., 2021c) and fewer labor costs due to fewer health problems and fewer cows with alerts generated by automated systems (Berghof et al., 2019b). Positive effects are also expected through favorable associations with health, longevity, and fertility. These traits all have an impact on cow profitability, for example through decreasing treatment costs with fewer diseases (Huijps et al., 2008; Bruijnis et al., 2010), dilution of rearing costs per kg of milk with increasing productive life (Rendel and Robertson, 1950; Grandl et al., 2019), and decreasing insemination costs and increasing number of productive days in peak lactation with improved fertility (Inchaisri et al., 2010).

Negative effects of resilience on profitability are expected as well, because of a trade-off between resilience and feed efficiency, where resilient cows need more feed to produce a certain amount of milk than less resilient cows (Friggens et al., 2017; Poppe et al., 2020; Martin et al., 2021b). However, feed efficiency is often considered only on lactation level. It is important to recognize that through a positive effect of resilience on longevity the association between resilience and feed efficiency may actually be favorable because of more milk produced per cow, which dilutes feed costs during rearing. It is therefore important to take costs and revenues throughout the whole lifetime into account and not only throughout the first lactations.

Nowadays, more and more information that can help to determine costs and revenues throughout life is becoming routinely available on commercial dairy farms. For example, with electronic milk recording on many farms, milk yield data is available on a more frequent basis than before with test-day milk yield. This daily data makes it possible to determine the exact lifetime production, including all drops in milk yield due to poor resilience, instead of having to rely on an estimation based on test-day records (e.g. Strandberg, 1992; Mulder and Jansen, 2001; Pérez-Cabal and Alenda, 2003). Earlier, this type of information was mainly available on research farms. Research farms still do have an advantage over commercial farms in that they often measure feed intake (e.g. Simm et al., 1994; Hüttmann et al., 2009), while commercial farms do not. Still, the advantage of commercial farms is that data is available on more cows, and cows are not subjected to experiments. We believe that the amount and frequency of data on commercial farms that is available nowadays provides a good opportunity to investigate the association between resilience and lifetime profitability.

In summary, many associations between resilience and costs and revenues contributing to profitability are expected, but it is still unclear what the overall effect of resilience on lifetime profit is. Investigating the effect of resilience indicators on lifetime profitability can build further support why resilience is important. Therefore, the aim of this study was to investigate the association of resilience indicators measured in first parity (natural log-transformed variance and lag-1 autocorrelation of daily deviations from expected milk yield; Poppe et al., 2020) with the lifetime gross margin of cows, expressed as the sum of all revenues throughout life minus the sum of all costs throughout life.

7.2 Materials and methods

In this study, the association between resilience indicators measured in first parity and lifetime gross margin was investigated. The data and data processing will

first be explained, followed by the analysis. Data processing and analyses were performed using the NumPy (Harris et al., 2020), Pandas (McKinney, 2010), and Statsmodels (Seabold and Perktold, 2010) packages from Python 3.6 and 3.8.5, the AWK programming language (Aho et al., 1988), and R (R v 3.2.2; R Project for Statistical Computing, Vienna, Austria).

7.2.1 Data

Four data sets were used to calculate resilience indicators and lifetime gross margin for individual cows. All data sets were obtained from Cooperation CRV (Arnhem, The Netherlands). The first data set contained milk yield records obtained during single milk visits to automatic milking systems (AMS) and conventional milking systems. This data set contained 2,763,357,043 milk visit records on 1,528,030 cows in 5,799 herds, from January 14, 1998, to September 4, 2020. The second data set was obtained during official milk production registration, which takes place every 3 to 6 weeks depending on herd, and included records on fat, protein, and lactose content of the milk. This data set contained 39,239,081 records on 1,499,375 cows in 5,786 herds, from January 4, 1991, to August 27, 2020. The third data set contained registrations of inseminations, and contained 11,044,353 records on 1,506,583 cows in 15,846 herds, from February 14, 1990, to August 28, 2020. The fourth data set contained records of health disorders registered by farmers, and by the claw health program DigiKlauw (Digiklauw, 2021). The data set contained 4,186,231 records on 893,260 cows in 9,200 herds, from May 23, 2010, to September 5, 2020. A total of 4,701 herds had records in all 4 data sets, but with varying degrees of data quantity and quality. For the purpose of this study, complete data throughout the entire life of as many cows as possible were needed to be able to calculate profit generated over the entire lifetime. Therefore, strict requirements were set on data quantity and quality in the selection of herds.

7.2.2 Selection of herds

From all available herds, herds were selected that had data in all 4 data sets from before 2012 until at least the 1st of January 2020, and cows should be milked the entire period by AMS. Furthermore, herds were required to have continuous registration of milk yield in the AMS: not more than 5% of dates in the timeframe of a herd were allowed to have no milk yield records. Furthermore, only herds were selected where artificial inseminations were performed by AI technicians and not by farmers to assure appropriate quality of insemination registrations. Furthermore, herds were required to have registrations of each of the following

common diseases: claw disorders, mastitis, and uterus related disorders. Finally, 21 herds met all criteria. For these 21 herds, 13,896,163 AMS milk visit records on 6,164 cows were available, 175,976 milk production registration records on 6,049 cows, 46,556 insemination records on 6,150 cows, and 47,071 disease diagnosis records on 5,215 cows.

7.2.3 Selection of cows

Because the aim was to calculate realized lifetime gross margin of cows, within the selected herds, cows were selected that were not alive anymore and had continuous AMS visit data in the same herd from first parity until the date of death (39% of all cows in the herds). Death dates and death code (slaughter or dead on farm) were available from Cooperation CRV (Arnhem, the Netherlands). Additionally, to reduce skewness in the data because cows born more recently are automatically cows that were culled early, cows were required to have had the opportunity to reach a productive life of 3 years in the data sets (82% of remaining cows). To clarify, cows were allowed to be culled before they reached a productive life of 3 years, but time between first calving of a cow and last available milk record from the whole herd should be at least 3 years. No restriction was set on the maximum age, and the oldest cow in the data set was culled at 10.7 years of age. Furthermore, cows were required to be at least 87.5% Holstein Friesian (76% of remaining cows), and to have calved for the first time after 640 days of age (99% of remaining cows). To be able to calculate resilience indicators following the same rules as in Poppe et al. (2020), the first milk yield record in first lactation was required to be within 2 weeks after calving, and at least 50 milk yield records were required until 350 days in milk, excluding the first and last 10 DIM. Finally, at least 5 cows were required to be born within the same herd in the same year, to be able to include a contemporary group effect in the analyses. Herd-birthyear groups with less than 5 cows were removed (7% of remaining cows). Finally, 1,337 cows were suitable for analysis, with 3,500,720 AMS records, 38,160 milk production registration records, 11,247 insemination records, and 13,145 disease records.

7.2.4 Data preparation

The AMS milk visit records were first converted to daily milk yield records. Within cow, all milk yield records within a day were summed to get the total daily milk yield, but the first milking of the day was partly assigned to the previous day, depending on the proportion of time since the last milking on the previous day that was before midnight. This resulted in 1,283,463 daily milk yield records. Outlying daily milk yield records were removed if they deviated positively from an

individually fitted Wilmink curve (Wilmink, 1987), and the deviation was larger than 6 times the standard deviation of the deviation of all cows in the same parity, year of calving, and day of lactation (CRV, 2020g). Because still some high milk yield records were present that were deemed outliers based on visual inspection, milk yield records larger than 90 kg were removed as well. In total, 770 daily milk yield records were removed, resulting in 1,282,693 final daily milk yield records.

7.2.5 Calculation of resilience indicators

For all cows, resilience indicators were calculated based on daily milk yield data in first parity, using the same method as Poppe et al. (2020). First, potential daily milk yield until DIM 350 in absence of environmental disturbances was estimated using polynomial quantile regression on the 0.7 quantile:

$$y_t = \beta_0 + \beta_1 * t + \beta_2 * t^2 + \beta_3 * t^3 + \beta_4 * t^4 + \varepsilon,$$

where y_t is the observed milk yield on DIM t , t^n are DIM to the power of n , where n is 1, 2, 3, or 4, β_n are regression coefficients describing the relationships between t^n and y_t , and ε is the error term. The quantreg package (Koenker, 2018) and the poly function in R were used. The 0.7 quantile causes the expected milk yield to be less influenced by low milk yield records than by high records, resulting in a lactation curve that is closer to what is expected in absence of disturbances. Deviations from the regression curve were calculated as $y_t - \hat{y}_t$, and they represent the short term fluctuation pattern in milk yield due to disturbances. The resilience indicators were then calculated on all deviations until 350 DIM per cow, excluding the first and last 10 deviations. The resilience indicators were the natural log-transformed variance (**LnVar**) and the lag-1 autocorrelation (r_{auto}) of the daily deviations. In addition to the resilience indicators, also the average daily milk yield until 350 DIM in parity 1 (**ADMY**) was calculated for each cow. The ADMY was needed to investigate relationships between the resilience indicators and lifetime gross margin, independent of milk yield level, because especially LnVar, but also r_{auto} are positively associated (genetically and at herd level) with ADMY (Poppe et al., 2020, 2021a; b). In this paper, also positive correlations were observed with ADMY (0.23 for LnVar, 0.14 for r_{auto}).

7.2.6 Calculation of lifetime gross margin

To get insight in the lifetime profitability, we calculated the lifetime gross margin (**LGM**), as the sum of all revenues minus the sum of all costs during the lifetime of a cow:

$$LGM = (revenues_{milk} + revenues_{calves} + revenues_{slaughter}) - (costs_{feed} + costs_{rearing} + costs_{insemination} + costs_{calves} + costs_{treatments} + costs_{destruction}).$$

All revenues and costs taken into account in this study will be explained below.

7.2.6.1 Lifetime revenues

The first source of lifetime revenues of each cow consisted of the sum of all revenues from milk, depending on the amount of milk, fat, protein, and lactose produced. The amount of milk produced on each day for each cow was obtained from the AMS daily milk yield dataset. Missing records during lactation were linearly interpolated with the interpolate method in Python. Daily fat, protein, and lactose content were linearly interpolated within lactation from the 3 to 6-weekly fat, protein, and lactose content measurement in the milk production registration dataset. The records before the first milk production registration within cow were assigned the fat, protein, and lactose content of the first milk production registration. The same accounts for the records after the last milk production registration, but these were assigned the fat, protein, and lactose content of the last registration. For lactations without fat, protein, and lactose records (when cow was culled before the first milk production registration in the last lactation; 2.9% of all lactations), their fat, protein, and lactose content were assumed to be equal to the mean of all fat, protein, and lactose records in their herd in the same parity at the same date. If there were no cows with data in the same herd, parity, and date, the mean of all cows in the same herd at the same date were taken. The total milk yield, fat yield, protein yield, and lactose yield in kg produced throughout life were then calculated, and the lifetime milk revenues were calculated as:

$$Revenues_{milk} = P_{milk} * Milk + P_{fat} * Fat + P_{protein} * Protein + P_{lactose} * Lactose$$

where P_{milk} , P_{fat} , $P_{protein}$, and $P_{lactose}$ were the prices of milk and milk contents (Table 7.1), and *Milk*, *Fat*, *Protein*, and *Lactose*, were the total amount of milk, fat, protein, and lactose calculated for the entire life (kg).

The second source of lifetime revenues were value of all calves born from a cow. The total value of calves born per cow was calculated by multiplying the total number of calves born by the price of a calf sold at 2 weeks of age (Table 7.1).

The third source of lifetime revenues were sale of the cow at the end of life. It was assumed that cows were sold for slaughter price (Table 7.1). For cows that

were euthanized according to the dataset with diagnoses and treatments, or that died on farm, the slaughter price was set to €0. Costs for euthanization and destruction will be described under ‘lifetime costs’.

Table 7.1 Prices used for calculation of costs and revenues.

Parameter	Value	Unit	Source
Milk	-0.0067	€/kg	FrieslandCampina (2015-2020)
Protein	5.5084	€/kg	FrieslandCampina (2015-2020)
Fat	2.7542	€/kg	FrieslandCampina (2015-2020)
Lactose	0.5508	€/kg	FrieslandCampina (2015-2020)
Feed costs	0.1619	€/kVEM	Steenefeld et al., 2020
Slaughter price cow	665	€/cow	Blanken et al., 2020
Insemination costs	31.75	€/insemination	Blanken et al., 2020
Calf price	75	€/calf	Steenefeld et al., 2020
Calf management costs	180	€/calving	Steenefeld et al., 2020
Collect and destruction costs	61.80	€/cow	Rendac, 2020

7.2.6.2 Lifetime costs

For lifetime costs, only those costs were taken into account that were expected to vary with varying resilience measures. The first source of lifetime costs are feed costs. Feed costs were estimated based on energy requirements using the VEM system (Dutch net energy system for lactation; CVB, 2016). Daily VEM requirements depended on milk yield, maintenance requirements, gestation stage, and growth. Daily VEM requirements for milk yield and maintenance were calculated as (CVB, 2016):

$$VEM = (42.4 * BW^{0.75} + (442 * FPCM)) * (1 + (FPCM - 15) * 0.00165)$$

where *BW* is body weight (kg) and *FPCM* is fat-protein corrected milk. Because no records on body weight were available, it was assumed that body weight was 540 kg at the start of lactation 1, 595 at the start of lactation 2, and 650 at the start of lactation 3 (CVB, 2016), and body weight increased linearly in between (Kok et al., 2017). Daily fat-protein corrected milk yield (*FPCM*), was calculated for each cow as follows (Blanken et al., 2020):

$$FPCM = (0.337 + 0.116 * fat + 0.06 * protein) * milk$$

where *fat* and *protein* were fat and protein content (%) and *milk* was amount of milk (kg). In addition to the daily VEM requirements for milk yield and

maintenance, extra daily VEM requirements for gestation were 450, 850, 1500, and 2700 VEM per day in the 6th, 7th, 8th, and 9th month of pregnancy, respectively (CVB, 2016). Extra daily VEM requirements for growth were 660 VEM per day for cows in first parity and 330 VEM per day for cows in second parity (CVB, 2016). The total lifetime VEM requirement of each cow was then calculated by summing all daily VEM requirements throughout life. The lifetime feed costs were then calculated by multiplying lifetime VEM requirement by the VEM price (Table 7.1).

The second source of lifetime costs was the rearing cost, which depends on the length of the rearing period, represented by the age at first calving. An age at first calving of 25 months was taken as a baseline, where the rearing cost was assumed to be €1567 (Mohd Nor et al., 2012). For each cow a cost was extracted or added when the age at first calving was earlier or later than 25 months. The amount of money extracted or added was €2.19 per day, based on Mohd Nor et al. (2012), who estimated the difference in costs between a heifer calving at 24 and 30 months of age to be €400.

The third source of lifetime costs were insemination costs. Lifetime insemination costs of each cow were obtained by multiplying the number of inseminations in the inseminations dataset with the price of an insemination by an AI technician plus average semen price (Table 7.1). Registered natural matings (3%) were treated as artificial inseminations as well for simplicity. Inseminations before first calving were not included in the number of inseminations, because of missing records for substantial part of youngstock.

The fourth source of lifetime costs were costs of birth of a calf and keeping it until 2 weeks of age (Table 7.1), multiplied by the number of calvings from a cow.

The fifth source of lifetime costs were total treatments costs, consisting of disease costs and costs of euthanasia. Only diseases that occurred at least 40 times in the dataset (13 diseases) were included to avoid a too broad range of diseases. Diseases with a lower occurrence (33 diseases) were rather incidental and most occurred less than 10 times or were not related to resilience (for example a bruise or a sharp object in the rumen). The costs of the selected diseases were added up for each cow throughout the entire life. The costs of each treatment, including labor, were obtained from a veterinarian and are summarized in Table 7.2. The costs of claw disorders are summarized in Table 7.3. For treatments with antibiotics, the price of discarded milk was included in the total treatment costs. Price of discarded milk was calculated using the amount of milk, fat, protein, and lactose produced during the treatment period and waiting period after treatment (Table 7.2) multiplied by the milk price formula shown earlier.

The last source of lifetime costs were destruction and collection costs, which were assigned to cows that were euthanized and/or died on farm (Table 7.1), and otherwise set to €0.

7.2.7 Analyses

The association between the resilience indicators and LGM was investigated using analysis of covariance, with herd, year of birth, the interaction between herd and year of birth, and ADMY as covariates. Herd and year of birth were included to adjust for effects on LGM of common management effects in contemporary groups and difference in opportunity period for cows born in recent years compared to less recent years. ADMY was included to adjust for milk yield level, which was positively correlated with especially LnVar (0.23), but also r_{auto} (0.14). To obtain a better understanding of the association between the resilience indicators and LGM, the analysis was repeated for all revenues and costs contributing to LGM, and also for all underlying traits such as herd life, number of inseminations, and number of diseases. Furthermore, the same analysis was performed on LGM, revenues, costs, and underlying traits expressed per year of productive life. Profit, revenues, costs, and underlying traits per productive year (y_{yearly}) were calculated as:

$$y_{\text{yearly}} = \frac{y}{PL} * 365$$

where y is LGM, revenues, costs, or an underlying trait and PL is productive life (d), expressed as the time between first calving and culling date. If the productive life was less than 365 d, the correction was not applied and y_{yearly} was assumed to be y (Pérez-Cabal and Alenda, 2003).

Table 7.2 Costs of diseases and other treatments, provided by veterinarian¹.

Disorder / treatment	Medicine price (€/complete treatment)	Labor costs veterinarian + call-out fee (€/complete treatment)	Labor time farmer (min./complete treatment)	Labor costs farmer (€/complete treatment) ²	Total costs (€/complete treatment)	Treatment duration (d)	Waiting time (d)
Uterus prolapse	15	185	90	27	227	1	5
Abnormal vaginal discharge	12	-	15	4.5	16.5	1	0
Uterus infection	24	-	15	4.5	28.5	3	5
Retained placenta	9	-	15	4.5	13.5	1	4
Swollen hock	25	-	30	9	34	3	4
Joint infection	12	-	30	9	21	3	4
Ketosis	65	85	30	9	159	1	3
Displaced abomasum	60	147	90	27	234	3	2
Pneumonia	30	-	30	9	39	3	5
Clinical mastitis	85	-	60	18	103	6	4
Milk fever	32	-	180	54	86	4	0
Cystic ovaries	17	-	10	3	20	1	0
Inactive ovaries	17	48	10	3	68	1	0
Euthanasia	20	60	20	6	86	1	-

¹Dierenartsenpraktijk Mid-Fryslân, Akkrum.²Assuming an hourly rate of 18€/hour and an estimate of the time spent by the farmer based upon authors' expertise and consultation of farmers.

Table 7.3 Costs of claw disorders, provided by Edwardes, F. (Wageningen University and Research, Wageningen, the Netherlands, personal communication).

Disorder	Medicine costs (€/ treatment)	Labor costs farmer (€/complete treatment) ¹	Costs claw trimmer (€/complete treatment) ²	Labor costs veterinarian + call-out fee (€/complete treatment)	Total costs (€/complete treatment)	Treatment duration (d)	Waiting time (d)
Panaritium	13	1.5	7.75	-	22.25	1	5
Interdigital dermatitis	0.6	1.5	7.75	-	9.85	1	0
Digital dermatitis	2.61	1.5	7.75	-	11.35	1	1
Sole heamorrhage	8.10	1.5	7.75	-	17.35	1	0
Interdigital hyperplasia	42.88	12	-	215	269.88	1	0
White line defect	8.10	1.5	7.75	-	17.35	1	0
Toe necrosis	42.88	12	-	215	269.88	1	0
Laminitis	-	1.5	7.75	-	9.25	1	0

¹Assuming an hourly rate of 18€/hour and an estimate of the time spent by the farmer based upon authors' expertise²Blanken et al., 2020.

7.3 Results

7.3.1 Descriptive statistics

Table 7.4 shows the descriptive statistics of the resilience indicators and mean milk yield in lactation 1 and of the variables that are used to calculate lifetime costs and revenues. Cows gave on average 25 kg of milk per day in lactation 1 with an LnVar of 1.34 and an r_{auto} of 0.55. Cows on average had a lifespan of 1,849 days (~5 years), of which 1,074 days (~3 years) belonged to the productive life (after first calving). On average, cows had 3 calves throughout their lives, and their first calf was on average born at 775 days of age (25.4 months). The lifetime production of cows was on average 27,227 kg of milk, with 1,190 kg fat, 974 kg protein, and 1,249 kg lactose. Cows produced on average 8,659 kg of milk per year with 378 kg fat, 309 kg protein and 398 kg lactose. Total feed requirements throughout productive life were on average 19,000 kVEM, and feed requirements per productive year were 6,086 kVEM. On average, 112 kg of milk were discarded throughout life upon treatments with antibiotics, with 4.9 kg fat, 3.9 kg protein, and 5.1 kg lactose. Cows had on average 6.5 inseminations throughout their productive life, and 2.2 inseminations per productive year. On average, 2.5 disease events occurred in total per cow, and 0.8 disease events occurred per productive year. Of all cows, 84% were slaughtered and 0.8% were euthanized. Of course this data excludes animals that were sold to other farms.

Table 7.5 shows the descriptive statistics of the number of disease events per disease. Claw disorders occurred most often, with on average 1.4 cases throughout life, ranging from 0 to even 45 cases throughout life. Clinical mastitis was the disease with the second highest occurrence, with on average 0.39 cases throughout life, ranging from 0 to 11 cases in total. Abomasal displacement was the disease that occurred least often, with on average 0.01 occurrences throughout life.

Table 7.4 Descriptive statistics of variables describing resilience (natural log-transformed variance: LnVar; lag-1 autocorrelation: r_{auto}) and average daily milk yield (ADMY) in lactation 1, lifetime traits, and traits expressed per productive year of life used to investigate associations between resilience and lifetime profit.

Trait	mean	min	max	std
LnVar	1.34	-0.97	4.12	0.66
r_{auto}	0.55	-0.24	0.92	0.19
ADMY	24.98	10.82	40.66	4.74
Herd life (d)	1,849.12	783	3,923	591.82
Productive life (d)	1,074.32	70	3,093	588.82
Number of parities	3.08	1	9	1.51
Age at first calving (d)	774.80	640	1,726	80.85
Lifetime milk yield (kg)	27,227.05	799.31	89,079.11	16,476.08
Lifetime fat yield (kg)	1,190.37	33.99	3,867.28	715.48
Lifetime protein yield (kg)	973.68	29.64	3,094.12	586.82
Lifetime lactose yield (kg)	1,248.53	34.08	4,173.726	750.27
Lifetime VEM requirement ¹	19,000,362	775,861	56,089,558	11,038,919
Lifetime discarded milk (kg)	112.27	0	2,079.41	243.47
Lifetime discarded fat (kg)	4.94	0	94.78	10.76
Lifetime discarded protein (kg)	3.93	0	68.47	8.54
Lifetime discarded lactose (kg)	5.09	0	98.14	10.99
Lifetime number of inseminations	6.46	0	34	4.43
Lifetime number of disease events	2.54	0	47	4.76
Euthanasia (1/0)	0.008	0	1	0.09
Dead on farm (1/0)	0.16	0	1	0.37
Milk yield per productive year (kg)	8,659.46	799.31	13,238.32	2,051.37
Fat yield per productive year (kg)	378.38	33.99	570.49	85.23
Protein yield per productive year (kg)	309.42	29.64	480.15	71.86
Lactose yield per productive year (kg)	398.33	34.08	620.75	94.03
VEM requirement per productive year	6,085,562	775,861	8,399,331	1,203,239
Number of inseminations per productive year	2.17	0	12.11	1.23
Number of disease events per productive year	0.77	0	8	1.23

¹VEM requirement: energy requirement using the Dutch net energy system for lactation (CVB, 2016).

7 Resilience and lifetime profitability

Table 7.5 Descriptive statistics about the number of times diseases occurred during the life of a cow.

	mean	min	max	std
Uterus prolapse	0.027	0	6	0.272
Vaginal discharge	0.063	0	5	0.351
Uterus infection	0.117	0	7	0.488
Retained placenta	0.032	0	3	0.211
Hock absces	0.027	0	5	0.224
Joint infection	0.027	0	4	0.227
Ketosis	0.013	0	2	0.128
Abomasal displacement	0.010	0	4	0.154
Pneumonia	0.022	0	6	0.278
Clinical mastitis	0.392	0	11	1.103
Milk fever	0.064	0	3	0.314
Cystic ovaries	0.142	0	7	0.542
Inactive ovaries	0.187	0	7	0.599
Claw disorder	1.412	0	45	3.974

Table 7.6 shows the descriptive statistics of the profit, revenues, and costs per cow throughout lifetime and expressed per productive year. On average, cows generated €4,340 profit (not including fixed costs) throughout life, ranging from €-1,956 up to €16,716. Cows generated on average €1,221 per productive year, ranging from €-1956 to €2,506. The highest revenues were the milk revenues, which were on average €9,147 throughout the entire lifetime and €2,908 per productive year. The highest costs were the feed costs, which were on average €3,076 throughout the entire lifetime and €985 per productive year. The lowest costs were destruction costs, which were on average €10 per cow. Total treatment costs, consisting of medicine costs, labor costs of veterinarian and farmer, and discarded milk, were the second lowest costs, with on average €157 throughout life and €48 per productive year. Large variation in disease costs existed, ranging from €0 up to €3,581 per cow in her lifetime and €751 per productive year.

Table 7.6 Descriptive statistics of gross margin, revenues, and costs, expressed per lifetime and per year of productive life.

	Lifetime				Per year of productive life			
	mean	min	max	std	mean	min	max	std
Gross margin	4,340.48	-1,956.19	16,715.63	3,386.00	1,220.89	-1,956.19	2,505.99	680.81
Milk revenues	9,147.17	270.31	27,855.54	5,492.11	2,907.92	270.31	4,409.65	659.40
Calving revenues	231.23	75	675	113.17	79.84	30.32	150	16.52
Slaughter revenues	558.06	0	665	244.38	258.24	0	665	200.71
Feed costs	3,076.16	125.61	9,080.899	1,787.20	985.25	125.61	1,359.85	194.80
Calving costs	554.94	180	1,620	271.60	191.60	72.76	360	39.65
Rearing costs	1,592.85	1,297.63	3,675.97	177.06	727.40	189.03	3,675.97	448.26
Insemination costs	205.03	0	1,079.50	140.56	68.91	0	384.32	39.02
Total treatment costs	157.06	0	3,580.56	315.26	47.78	0	751.22	86.59
Destruction costs	9.94	0	61.80	22.71	4.15	0	61.80	11.35

7.3.2 Associations between resilience indicators and profit, revenues, and costs, and underlying traits

Associations between the resilience indicators and the traits in Table 7.7, 7.8, 7.9, and 7.10 are corrected for a number of covariates and factors, and should be interpreted as associations that would be observed among cows born in the same year on the same farm with the same ADMY in lactation 1. The regression coefficients of ADMY are included in the tables as well, but will not be discussed. The estimates for each herd and birth year are not shown.

7.3.2.1 LnVar

LnVar had significant negative associations with LGM, lifetime milk revenues, lifetime calving revenues, lifetime feed costs, lifetime calving costs, and lifetime insemination costs (Table 7.7). The regression coefficients show that cows with low LnVar (good resilience) had higher LGM, higher milk revenues, and higher calving revenues, but also higher feed costs, calving costs and insemination costs, than cows with the same ADMY but high LnVar. To illustrate the size of the regression coefficients: if LnVar decreased with 1 standard deviation (resilience improved) while ADMY remained the same, LGM increased with €282.47. The significant effect of LnVar was largest on profit, milk revenues and feed costs, and lowest on insemination costs and calving revenues.

Expressed per year of productive life, the profit, milk revenues, slaughter revenues, feed costs, and rearing costs, were all significantly associated with LnVar. The regression coefficients show that cows with low LnVar (good resilience) had higher profit per year, and also higher milk revenues and feed costs per year than cows with the same ADMY but high LnVar. In addition, cows with low LnVar had lower slaughter revenues, but also lower rearing costs per year of productive life. To illustrate the size of the regression coefficients: if LnVar decreased with 1 standard deviation (resilience improved) while ADMY remained the same, profit per year increased with €66.50. The significant effect of LnVar in absolute terms was largest on profit and milk revenues, and lowest on feed costs.

LnVar was significantly associated with most traits underlying the costs and revenues (Table 7.8). The regression coefficients show that cows with low LnVar (good resilience) had a longer lifespan and productive life, a higher number of parities, a higher lifetime milk, fat, protein, and lactose yield, higher lifetime feed requirements, and higher total number of inseminations than cows with the same ADMY but high LnVar. Cows with low LnVar also had higher feed requirements per year and higher fat and protein yield per productive year, but not a higher milk yield per productive year than cows with high LnVar. LnVar did not have a

significant association with the number of disease events per productive year. However, when looking at diseases separately, LnVar was significantly and positively associated with number of cases of clinical mastitis and pneumonia per productive year, but negatively associated with number of cases of ketosis per productive year (Table 7.9).

Table 7.7 Intercept, regression coefficients (β) and P-values of regression coefficients from the Analysis of Covariance models explaining gross margin, revenues, and costs across lifetime and per year of productive life from average daily milk yield (ADMY) and the resilience indicator natural log-transformed variance of milk yield deviations (LnVar).

Trait	Lifetime						Per year of productive life					
	Intercept	β ADMY	P-value ADMY	β LnVar	P-value LnVar	Intercept	β ADMY	P-value ADMY	β LnVar	P-value LnVar	Intercept	β ADMY
Gross margin	1,484.32	201.45	0.00	-427.98	0.008	-117.68	68.60	0.00	-100.76	0.001	68.60	-100.76
Milk revenues	5,074.94	323.45	0.00	-694.13	0.007	998.42	87.20	0.00	-67.78	0.012	998.42	-67.78
Calving revenues	228.32	2.76	0.00	-17.27	0.002	77.98	-0.47	0.00	-0.073	0.93	77.98	-0.073
Slaughter revenues	481.79	-5.30	0.002	-1.62	0.90	312.85	-11.33	0.00	25.93	0.008	312.85	-11.33
Feed costs	2,008.76	97.67	0.00	-228.08	0.007	463.01	24.27	0.00	-19.05	0.022	463.01	24.27
Calving costs	547.96	6.63	0.00	-41.45	0.002	187.15	-1.13	0.00	-0.18	0.93	187.15	-1.13
Rearing costs	1,740.48	4.04	0.00	-2.83	0.73	850.79	-18.54	0.00	71.99	0.001	850.79	-18.54
Insemination costs	84.37	6.02	0.00	-14.28	0.036	25.69	1.17	0.00	0.40	0.84	25.69	1.17
Total treatment costs	-97.88	4.61	0.017	1.46	0.92	-21.76	0.77	0.15	5.15	0.20	-21.76	0.77
Destruction costs	17.03	0.49	0.002	0.15	0.90	2.05	0.27	0.001	0.53	0.37	2.05	0.27

7.3.2.2 r_{auto}

No significant associations were shown between r_{auto} and LGM, revenues, or costs (Table 7.10). However, expressed per year of productive life, the milk revenues, slaughter revenues, feed costs, total treatment costs, and destruction costs were significantly associated with r_{auto} . The regression coefficients show that cows with low r_{auto} (good resilience) had lower milk revenues, feed costs, total treatment costs and destruction costs per year and higher slaughter revenues per year than cows with the same ADMY but high r_{auto} . To illustrate the size of the regression coefficients: if r_{auto} decreased with 1 standard deviation (resilience improved) while ADMY remained the same, milk revenues per year decreased with €49.00 and treatment costs per year decreased with €5.69. The significant effect of r_{auto} was largest on yearly milk revenues and lowest on destruction costs.

Low r_{auto} (good resilience) was significantly associated with low milk, fat, protein, and lactose yield per productive year and low feed requirements per productive year, and with few disease events per productive year (Table 7.8). However, when looking at diseases separately per year of productive life, r_{auto} was not significantly associated with any of the diseases (Table 7.9).

Table 7.8 Intercept, regression coefficients (β) and P-values of regression coefficients from the Analysis of Covariance models explaining traits across lifetime and per year of productive life from average daily milk yield (ADMY) and the resilience indicator natural log-transformed variance ($\ln Var$) or lag-1 autocorrelation of milk yield deviations (r_{auto}).

Trait	$\ln Var$			r_{auto}		
	Intercept	β ADMY	P-value ADMY	β $\ln Var$	P-value $\ln Var$	P-value r_{auto}
Herd life (d)	1,928.99	23.11	0.00	-84.44	0.002	93.83
Productive life (d)	1,086.77	21.27	0.00	-83.15	0.003	107.13
Number of parities	3.04	0.037	0.00	-0.23	0.002	0.22
Age at first calving (d)	842.22	1.84	0.00	-1.29	0.73	-13.30
Lifetime milk yield (kg)	10,981.55	1,086.19	0.00	-1,754.24	0.022	2,418.30
Lifetime fat yield (kg)	711.91	38.96	0.00	-93.89	0.006	109.77
Lifetime protein yield (kg)	526.99	35.57	0.00	-72.57	0.009	86.46
Lifetime lactose yield (kg)	517.22	49.89	0.00	-86.36	0.013	108.22
Lifetime VEM requirement	12,407.43	603,295.20	0.00	-1,408,776	0.007	1,803,747
Lifetime discarded milk (kg)	-110.84	5.22	0.001	1.65	0.89	62.29
Lifetime discarded fat (kg)	-4.01	0.19	0.004	-0.008	0.99	2.95
Lifetime discarded protein (kg)	-3.60	0.17	0.001	0.055	0.89	2.17
Lifetime discarded lactose (kg)	-5.03	0.24	0.001	0.063	0.90	2.83
Lifetime number of inseminations	2.66	0.19	0.00	-0.45	0.036	-0.058

Trait	LnVar		r _{auto}					P-		P-value		P-	
	Intercept	β ADMY	β LnVar	β ADMY	Intercept	β ADMY	β LnVar	LnVar	value	ADMY	β r _{auto}	value	r _{auto}
Lifetime number of disease events	-2.17	0.11	-0.02	0.00	-2.51	0.10	0.91	0.91	0.00	0.00	0.71	0.20	0.20
Milk yield per productive year (kg)	1,646.46	301.72	-95.87	0.00	1,271.98	294.61	0.21	0.21	0.00	0.00	743.92	0.001	0.001
Fat yield per productive year (kg)	151.03	10.20	-9.67	0.00	131.69	9.66	0.009	0.009	0.00	0.00	35.49	0.002	0.002
Protein yield per productive year (kg)	99.93	9.71	-6.94	0.00	85.54	9.32	0.017	0.017	0.00	0.00	26.58	0.003	0.003
Lactose yield per productive year (kg)	78.11	13.86	-6.42	0.00	60.43	13.46	0.07	0.07	0.00	0.00	33.95	0.002	0.002
VEM requirement per productive year	2,859,825	149,874.20	-117,675	0.00	2,562,163	142,692.80	0.02	0.02	0.00	0.00	565,690.60	0.00	0.00
Number of inseminations per productive year	0.81	0.037	0.013	0.00	0.76	0.037	0.84	0.84	0.00	0.00	0.12	0.54	0.54
Number of disease events per productive year	-0.52	0.024	0.028	0.00	-0.65	0.023	0.53	0.53	0.00	0.00	0.30	0.03	0.03

Table 7.9 Intercept, regression coefficients (β) and P-values of regression coefficients from the Analysis of Covariance models explaining number of disease events per year of productive life from average daily milk yield (ADMY) and the resilience indicator natural log-transformed variance (LnVar) or lag-1 autocorrelation of milk yield deviations (r_{auto}).

Disease	LnVar			r_{auto}			P -value r_{auto}			
	Intercept	β ADMY	P -value ADMY	β LnVar	P -value LnVar	Intercept		β ADMY	P -value ADMY	β r_{auto}
Uterus prolapse	-0.005	0.0004	0.34	-0.0032	0.33	-0.0007	0.0003	0.42	-0.011	0.26
Vaginal discharge	-0.035	0.0016	0.022	0.0016	0.77	-0.025	0.0017	0.009	-0.021	0.19
Uterus infection	0.030	-0.0011	0.59	-0.0061	0.70	0.027	-0.0013	0.49	0.0026	0.96
Retained placenta	-0.015	0.0009	0.062	-0.0027	0.45	-0.012	0.0008	0.070	-0.0099	0.36
Hock abces	-0.043	0.0017	0.039	0.0069	0.28	-0.044	0.0020	0.014	0.0047	0.81
Joint infection	-0.0084	0.0004	0.27	-0.0005	0.86	-0.010	0.0004	0.29	0.0035	0.70
Ketosis	-0.0029	0.0003	0.089	-0.0035	0.016	-0.0027	0.0002	0.28	-0.0026	0.56
Abomasal displacement	-0.0056	0.0003	0.43	-0.0011	0.72	-0.0054	0.0003	0.47	-0.0010	0.92
Pneumonia	0.0016	-0.0007	0.37	0.013	0.045	-0.0098	-0.0004	0.62	0.032	0.092
Clinical mastitis	0.025	-0.0037	0.15	0.047	0.015	-0.0066	-0.0023	0.36	0.097	0.10
Milk fever	-0.016	0.0011	0.18	-0.0059	0.32	-0.020	0.0008	0.29	0.0063	0.73
Cystic ovaries	-0.039	0.0026	0.014	-0.014	0.088	-0.037	0.0021	0.038	-0.012	0.61

Table 7.10 Intercept, regression coefficients (β) and P-values of regression coefficients from the Analysis of Covariance models explaining gross margin, revenues, and costs across lifetime and per year of productive life from average daily milk yield (ADMY) and the resilience indicator lag-1 autocorrelation of milk yield deviations (r_{auto}).

Trait	Lifetime					Per year of productive life					P-value	
	Intercept	β ADMY	P-value	β r_{auto}	P-value	Intercept	β ADMY	P-value	β r_{auto}	P-value		
Gross margin	1,172.26	182.64	0.00	404.77	0.41	-221.41	63.89	0.00	160.22	0.091		
Milk revenues	4,491.64	292.22	0.00	822.006	0.30	858.65	83.37	0.00	257.90	0.002		
Calving revenues	215.60	2.00	0.004	16.603	0.33	78.00	-0.47	0.00	-0.093	0.97		
Slaughter revenues	506.91	-5.12	0.001	-54.888	0.16	358.70	-9.94	0.00	-82.30	0.006		
Feed costs	1,806.88	87.32	0.00	292.027	0.26	414.81	23.10	0.00	91.59	0.00		
Calving costs	517.43	4.81	0.004	39.846	0.33	187.20	-1.14	0.00	-0.22	0.97		
Rearing costs	1,753.24	4.05	0.00	-29.116	0.25	924.53	-15.17	0.00	-113.66	0.094		
Insemination costs	81.11	5.46	0.00	-1.835	0.93	24.11	1.17	0.00	3.66	0.54		
Total treatment costs	-131.47	4.35	0.019	72.93	0.10	-34.23	0.84	0.098	29.94	0.014		
Destruction costs	14.69	0.48	0.001	5.101	0.16	0.34	0.27	0.00	4.00	0.027		

7.4 Discussion

Resilience is the ability to be minimally affected by disturbances and to quickly recover from them. The desire for resilient cows is growing due to an increase in environmental disturbances, a decrease in labor availability per individual cow, and a decrease in opportunities to use antibiotics to treat cows. Although from this angle the advantages of resilience seem obvious, the economic impact of resilience is not clear yet. The aim of this study was to investigate the association between resilience and LGM, using the resilience indicators LnVar and r_{auto} based on daily milk yield proposed by Poppe et al. (2020). Low values of LnVar and r_{auto} indicate good resilience because of limited deviations in milk yield from baseline due to disturbances, and quick recovery to the baseline (Scheffer et al., 2018; Berghof et al., 2019b; Poppe et al., 2020). LnVar was significantly associated with LGM in the expected direction, but r_{auto} was not, also not when expressed per year of productive life. Associations between resilience and LGM thus only seem to exist for the resilience indicator LnVar, although r_{auto} did have a significant association with total yearly treatment costs.

For this study, we had detailed data on milk yield, inseminations, and treatments throughout the entire lifetime of many cows available. This made it possible to quantify many real-life lifetime costs and revenues for individual cows and relate them to the resilience indicators. This approach is different from other studies that investigated the economics of resilience, which completely relied on theory-based simulation models (Berghof et al., 2019b; Knap and Doeschl-Wilson, 2020). Even though we relied to a larger extent on real data, we did have to make large assumptions on feed intake and body weight, because we had no data on these traits. Feed intake was calculated as a function of milk yield and body weight (which was assumed the same between cows), which neglects possible differences in feed required for maintenance between cows. Because resilient cows likely use more feed for maintenance (Poppe et al., 2020; Martin et al., 2021b), and feed is the largest contributor to costs (Table 7.6), results may change when real feed intake data and body weight would be used. Furthermore, slaughter price was assumed to be the same for all cows. However, as there is likely an association between resilience and body condition (Poppe et al., 2020), slaughter weight and therefore slaughter price may be associated with resilience. As such, repeating this analysis on farms with many years of feed intake and body weight data, in addition to milk yield, inseminations and treatment data, would be of great value. Such commercial farms may not be available, but research farms may offer a solution. For example, Simm et al. (1994) had detailed feed intake, milk yield, health, and insemination data available from a research farm and therefore were able to

calculate realized profit. Nevertheless, the data used in this study still gave us novel insights into the association between resilience and at least a number of revenues and costs, while taking into account differences in lifespan.

For this study 21 farms were selected based on having an AMS for many years and having treatment registrations. Before interpreting the results, it is important to evaluate if these farms are representative for the average Dutch situation. The selected herds may differ from the average Dutch situation because most Dutch farms do not have AMS (Stichting KOM, 2021), and have incomplete treatment registrations. Nevertheless, when the requirement on the treatment registrations was lifted and the analyses were repeated (64 farms with 4,606 cows then met all requirements), regression coefficients were similar to what we found in this study (data not shown). This observation suggests that the requirement on treatment registrations does not create bias. Moreover, the lifetime figures of the cows in our study were close to the mean lifetime figures across the Netherlands (Table 7.11). In summary, our data seems representative for the Dutch situation, but the applicability of our results for farms with milking parlors remains to be tested.

Table 7.11 Comparison between mean lifetime figures in this study and mean lifetime figures of the Netherlands.

	This study, birthyear <2011 ^a	Dutch situation (2016-2020) ^b
Herd life	2,099.3	2,076.2
Productive life	1,311.8	1,256.4
Number of parities	3.6	3.5
Age at first calving	787.5	781.2
Lifetime milk yield	33,318.7	31,341.6
Lifetime fat yield	1,450.1	1,363.8
Lifetime protein yield	1,188.4	1,110.4

^aOnly cows born before 2011 were included (at least the opportunity to become 10 years old), because cows born in recent years showed an overrepresentation of cows that were culled early and therefore had low lifetime figures.

^b(CRV, 2021b).

A significant negative association was observed between LnVar and LGM, which means that cows with stable milk yield in lactation 1 generated a higher LGM than cows that had the same milk yield level, but with more fluctuations. The association between LnVar and LGM can mainly be explained by the association with lifetime milk revenues (Table 7.7). The negative association between LnVar and milk revenues seems to have two reasons. The first reason is the negative association of LnVar with productive life, which led to a longer lifespan and therefore higher

lifetime milk yield for cows with low than with high LnVar (Table 7.8). A decrease of 1 standard deviation LnVar while keeping ADMY the same would coincide with an increase of productive life of 55 days and an increase in lifetime milk yield of 1,158 kg. The association of LnVar with productive life is also the reason for the significant associations with lifetime insemination costs and lifetime calving costs and revenues - the association was not significant anymore when these variables were expressed per year. The association of LnVar with productive life is in line with the negative genetic correlation between LnVar and longevity (Poppe et al., 2020, 2021a) and the negative association between mean LnVar within herd and proportion of cows in a herd that survived to second lactation (Poppe et al., 2021b). The association is also in line with the expectation that animals that have good resilience or robustness have long productive life (Friggens et al., 2017). However, Adriaens et al. (2020) found that cows with variable milk yield in lactation 1 had a higher resilience rank (which was largely determined by lifespan) than cows with stable milk yield. The difference with our study may be because of a difference in definition between productive life and resilience rank or because Adriaens et al. (2020) did not adjust for ADMY, while we did. The second reason for the negative association between LnVar and milk revenues is that low LnVar was associated with high fat and protein yield per year of productive life. If LnVar would decrease with 1 standard deviation, the amount of fat produced per year would increase with 6.38kg and the amount of protein with 4.58kg. Assuming that the total amount of milk produced per productive year would stay the same, this means an absolute increase of fat and protein content of 0.07% and 0.06%, respectively. In summary, the favorable effect of having a stable milk yield, which represents good resilience, on LGM is mainly due to increased lifespan and higher milk components.

The r_{auto} was not significantly associated with LGM or any of the underlying lifetime costs or revenues. However, we did see a significant positive association with yearly treatment costs, which suggests that having low r_{auto} (good resilience) is at least important for having low yearly costs associated with diseases. This observation confirms the claim that easy management and low labor and treatment costs due to few health problems are important advantages of resilience (Elgersma et al., 2018; Berghof et al., 2019b). However, when looking at separate diseases, r_{auto} was not significantly associated with any of them. The largest coefficients were positive though, so apparently the summed costs of these diseases were sufficient to make the association with total treatment costs significant. Although the effect of r_{auto} on yearly total treatment costs was significant and favorable, an unfavorable significant association was found with yearly milk revenues, which was surprising. Low r_{auto} (good resilience) was

associated with low yearly milk revenues, due to low yearly milk yield. As the regression coefficients were corrected for milk yield level in lactation 1, no difference in yearly milk yield was expected between cows with low and cows with high r_{auto} . Possibly, cows with high r_{auto} had a higher milk yield in later lactations than cows with low r_{auto} . Nevertheless, when looking across the total life of cows, having low or high r_{auto} does not seem to have an economic benefit.

Unlike r_{auto} , LnVar was not significantly associated with yearly treatment costs. This was surprising because better health is one of the most often mentioned advantages of resilience (Elgersma et al., 2018; Berghof et al., 2019b). Two explanations can be given for the insignificant effect of LnVar on yearly treatment costs. The first explanation is that LnVar was favorably associated with some diseases (clinical mastitis, pneumonia; Table 7.9), but unfavorably with others (ketosis; Table 7.9), which levels out the economic effects. The significant association with clinical mastitis is in line with Kok et al. (2021). The second explanation for the insignificant effect is that farmers likely did not register all (minor) health problems that required attention. Labor costs due to unregistered disturbances could be dealt with like in Berghof et al. (2019b). Those authors assumed that cows require labor if their milk yield drops below a certain value, and labor costs automatically rise with increasing LnVar. However, the assumption that drops in milk yield require labor has not been tested yet and therefore was not applied here. Nevertheless, the significant associations with some individual diseases suggest that LnVar may still be important for easy management.

Even though significant effects of LnVar and r_{auto} on yearly treatment costs or individual diseases were found, treatment costs were minor compared to other costs and revenues. Total lifetime treatments costs only accounted for 2.8% of all variable lifetime costs (Table 7.6). Similarly, health costs only accounted for 4% of total costs in Simm et al. (1994). Therefore, the economic importance of treatments seems limited. However, it is important to acknowledge that the significant associations with individual diseases can still be important to a farmer. In this study, a standard labor price of €18/hour was used, but an hour of labor may be worth much more to a farmer in case of unanticipated extra labor due to health problems. Huijps et al. (2008) showed that some farmers valued their hourly rate as high as €200 in case of mastitis. Indeed, when we used a labor price that was 10 times higher than the original labor price (€180/hour), total treatment costs were relatively larger compared to other costs and revenues. Now, total treatment costs were only 29 times as small (€313 average) as total revenues from milk. In addition, with a labor price of €180/hour, the effect of r_{auto} on total treatment costs per productive year was 1.8 times as strong ($\beta=54.18$) as previously in Table 7.10

($\beta=29.94$). This illustrates that good health through good resilience is economically important for a farmer, as long as he or she values their time high enough.

7.5 Conclusions

The association between two resilience indicators (log-transformed variance and lag 1-autocorrelation of daily milk yield deviations) and lifetime gross margin was investigated using data obtained throughout the entire lifetime of cows. The variance had a significantly negative effect on lifetime gross margin, which means that cows with stable milk yield in parity 1 generated on average a higher lifetime gross margin than cows with the same milk yield level in parity 1 but with more fluctuations. Unlike the variance, autocorrelation was not significantly associated with lifetime gross margin. However, it was significantly associated with yearly treatment costs, which is important for ease of management. In summary, the importance of resilience for total gross margin generated by a cow at the end of life was confirmed by the significant association of LnVar with lifetime gross margin.

7.6 Acknowledgments

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8

General discussion

8.1 Introduction

Resilience is the ability of a cow to be minimally affected by disturbances, and if affected, to quickly recover from them (Colditz and Hine, 2016). It is important for cows to be resilient because of societal concerns about animal welfare (Ge et al., 2016; Clay et al., 2020), desire of farmers to work with problem-free cows (Elgersma et al., 2018; Berghof et al., 2019b; Egger-Danner and Heringstad, 2020), and an increasing amount of environmental disturbances due to climate change (Maracchi et al., 2005; Sejian et al., 2015; Ge et al., 2016; Brito et al., 2021). Resilience can be improved through genetic selection, where the genetically most resilient animals are selected as parents for the next generation.

In the past decades, improvements of health and functionality have been made already by broadening the traditionally production focused breeding goal with health, fertility, and longevity traits (Miglior et al., 2017). Now, it is time to broaden the breeding goal even more by adding resilience. Unlike the current health traits, resilience covers vulnerability to many types of disturbances, and not only diseases. Examples are extreme weather and social stress. Moreover, resilience covers the incidence of disturbances, as well as magnitude of impact and rate of recovery, while health traits cover only incidence. Hence, resilience contains new information that is not represented yet by current breeding goal traits.

Resilience, sometimes termed robustness (Chapter 1), is a broad and complex trait and it is impossible to capture it in one trait (Friggens et al., 2017). Therefore, it is necessary to develop multiple traits that indicate how resilient a cow is: 'resilience indicators'. In this thesis I developed and studied resilience indicators for dairy cattle based on patterns in two longitudinal traits, daily milk yield and daily step count. These traits are available on many cows, and it is expected that differences in response and recovery to disturbances between cows can be observed in the data patterns from day to day (Scheffer et al., 2009, 2018).

Major part of this thesis focuses on resilience indicators that were proposed by Scheffer et al. (2009), and that were originally used to quantify resilience of ecosystems. These resilience indicators were the variance, lag-1 autocorrelation and skewness of longitudinal traits. Furthermore, some additional resilience indicators were investigated based on the daily step count data. These were the mean, number of drops and mean of negative deviations from expected step count. These traits were included only for step count, because similar traits had been studied already or are even well-known (mean milk yield) based on milk yield (Miglior et al., 2017; Elgersma et al., 2018). I investigated if the original proposed resilience indicators by Scheffer et al. (2009) and the additional resilience indicators were heritable, if selection on them will result in improved resilience, if they can be

used to indicate resilience of the herd rather than the individual animal, and if they are related to cow profitability.

The general discussion consists of two sections. In the first section, I focus on the calculation of the resilience indicators proposed by Scheffer et al. (2009) on animal data, and what lessons can be learnt from this thesis and other literature for future applications. In the second section I discuss the applicability of the resilience indicators from this thesis in a breeding program.

8.2 Application of indicators of resilience based on ‘critical slowing down’-theory to data from cows and other animals

Within the field of ecology, much work has been performed on quantifying resilience of living systems (Scheffer, 2009; Scheffer et al., 2009, 2012; Dakos et al., 2015). Resilience is here the proximity of the system to a ‘tipping point’, which is a point where the system abruptly shifts to an alternative state. For example, a lake ecosystem can suddenly shift from a clear to a turbid state. Tipping points can be observed in the system ‘animal’ as well, when an animal suddenly shifts from a healthy to a diseased or stressed state, or more drastically, from alive to dead.

To quantify the proximity of a system to a tipping point, or in other words, the resilience of the system, a number of resilience indicators have been suggested (Scheffer et al., 2009; Dakos et al., 2012). These resilience indicators (also called early warning signals) are based on the mathematical properties that a broad range of systems have when approaching a tipping point. Systems then become increasingly slow in recovering from small naturally occurring disturbances, which is termed ‘critical slowing down’. Critical slowing down can be observed through increasing lag-1 autocorrelation and variance of fluctuations in the system state variables, and lag-1 autocorrelation and variance can thus serve as resilience indicators. Lag-1 autocorrelation is the correlation of a time series with itself shifted 1 time point. Autocorrelation increases because with slower recovery, the state of the system becomes more and more like its past state (Scheffer et al., 2009). Variance increases, because new disturbances occur already before the system is recovered from the previous disturbance. These new disturbances cause the system to shift away further from the baseline, increasing the variance (Scheffer et al., 2009). In addition to autocorrelation and variance, the skewness of longitudinal system state variables has been proposed as an indicator of resilience. Skewness is expected to increase in proximity of a tipping point, because most disturbances force the system state in one direction, and the system stays in that direction for a longer time (Guttal and Jayaprakash, 2008; Scheffer et al., 2009). In

summary, increased variance, autocorrelation and skewness of a longitudinal system state variable can indicate the resilience of the system.

For several systems, these resilience indicators have already been shown to work as an early warning signal for a critical transition. For example, the climate showed critical slowing down in the form of increased autocorrelation before abrupt change to a different state (Dakos et al., 2008), a lake with few bass showed increased autocorrelation before turning into a bass-dominated state (Batt et al., 2013), and humans showed increased variance and autocorrelation in their emotional state when the transition to a depressed or a healthy state was nearby (van de Leemput et al., 2014; Wichers and Groot, 2016). Scheffer et al. (2018) suggested that generic resilience indicators based on critical slowing down may apply in animals as well.

This thesis contains an extensive study on the use of these resilience indicators based on daily milk yield and step count in dairy cattle. Moreover, throughout the course of this study, many other studies have been conducted on resilience indicators based on longitudinal data in animals (Elgersma et al., 2018; van Dixhoorn et al., 2018; Berghof et al., 2019a; Putz et al., 2019; Adriaens et al., 2020; Cheng et al., 2020; van der Zande et al., 2020; Kok et al., 2021). Based on all these studies and this thesis, a road map can be designed that can be used by future researchers to develop resilience indicators that are suitable for implementation in practice, both for breeding and for management purposes. The proposed road map is shown in Figure 8.1. The four elements of this road map will be discussed in the following paragraphs, including all issues to consider based on results from this thesis and other studies.

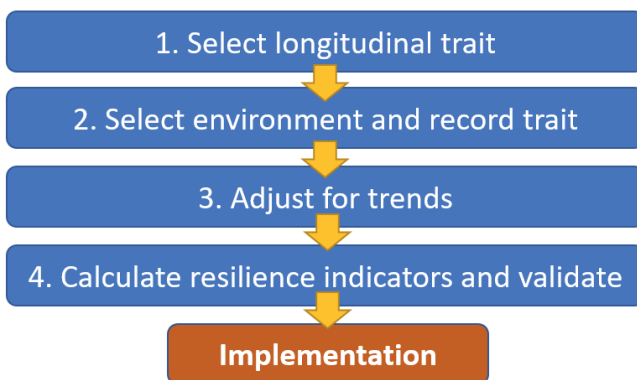


Figure 8.1 Road map for developing resilience indicators for animals with the aim of implementing them in practice

8.2.1 Selection of longitudinal trait

When selecting a longitudinal trait to calculate resilience indicators from, a number of issues are important to consider: (1) the trait should be vulnerable to many disturbances, (2) the trait should be measured frequently, (3) the trait should have sufficient number of records per animal, and (4) the quality of the data should be adequate. I will discuss these considerations below.

First of all, the longitudinal trait should be vulnerable to many disturbances to be able to show critical slowing down (increased variance and autocorrelation) (Carpenter et al., 2008; Batt et al., 2013; Boettiger et al., 2013; Dakos et al., 2015). Based on this criterion, milk yield and activity were selected in this thesis; they are vulnerable to many types of disturbances (Hasegawa et al., 1997; Fourichon et al., 1999; Kadzere et al., 2002; Edwards and Tozer, 2004; Yagi et al., 2004; Pesenhofer et al., 2006; Nielsen et al., 2007; Abeni and Galli, 2017). Other studies selected traits like feed intake and body weight (González et al., 2008; Berghof et al., 2019a; Putz et al., 2019). Traits exist as well that are sensitive to 1 type of disturbance, and such traits are excellent indicators for a specific disorder (e.g. somatic cell count for mastitis (de Haas et al., 2003)). However, such traits are less suitable as an indicator of general resilience.

While traits exist that are vulnerable to many disturbances, it is important to realize that there is no trait that is equally sensitive to every disturbance. For example in this thesis, variance and autocorrelation of milk yield were mostly related to udder health problems but not to claw health problems, while autocorrelation of activity was mostly related to claw health problems but not udder health problems. Additional support is given by the weak genetic correlations between resilience indicators based on milk yield and the same resilience indicators based on activity (-0.29 for variance and -0.01 for autocorrelation; estimated with data and models Chapter 5). Because longitudinal traits differ in their sensitivity to different disturbances, it is recommended to combine resilience indicators based on different traits together, to generate a more complete picture of resilience of an animal.

The second issue to consider when selecting a longitudinal trait for calculation of resilience indicators, is the frequency with which it is measured. According to theory about critical slowing down, the interval between data points should be shorter than the time scale of the slowest return rate of the system (Dakos et al., 2012). Otherwise short-term fluctuations due to minor disturbances may be missed. According to this statement, the use of daily measurements of milk yield and activity as in this thesis seems appropriate. Milk yield and activity both recover often after more than 1 day upon many types of disturbances (Hasegawa et al.,

1997; Fourichon et al., 1999; Hayes et al., 2003; Edwards and Tozer, 2004; Pesenhofer et al., 2006). For traits that react more slowly to disturbances, longer intervals between measurements may be sufficient. For example, Berghof et al. (2019a) had body weight in chickens available with 4-weekly intervals and still found genetic variation in resilience indicators and a favorable genetic correlation of variance with lesion scores after inoculation with *Escherichia coli*.

Even though frequent (e.g. daily) measurements are preferred, it would be useful to test if resilience indicators based on less frequent measurements are really genetically different from resilience indicators based on daily measurements. If not, in cows this would open up the opportunity to calculate resilience indicators using 3- to 6-weekly test-day milk yield records, which are available on more cows than daily milk yield records. Patterns in test-day somatic cell count have already been shown to indicate mastitis and are used in practice in the Dutch udder health index (de Haas et al., 2004). For autocorrelation, which is specifically informative about short-term fluctuation patterns, a lot of information will probably be missed when using test days. However, for variance based on test-days, several indications exist that it may be informative about resilience. First of all, averaged at herd level, variance based on test-day milk yield gave similar results as variance based on daily milk yield studied in Chapter 6 (Rocland et al., 2021). Secondly, several studies showed genetic variation in residual variance of test-day milk yield using double hierarchical generalized linear models (Rönnegård et al., 2013; Vandenplas et al., 2013; Ehsaninia et al., 2019). Genetic variance was somewhat lower than for variance based on daily milk yield in this thesis (Chapter 2, 3). However, a genetic correlation with variance based on daily milk yield is lacking and therefore no final conclusions can be drawn.

In addition to traits with lower than daily frequency, traits that are measured multiple times per day can be considered. Such traits offer great opportunities to use regularity of daily patterns as indicators of resilience. For example, Van Dixhoorn et al. (2018) showed that cows with irregular circadian behavior patterns before calving were prone to health problems after calving, and were thus not resilient.

The third issue to consider when selecting a longitudinal trait for calculation of resilience indicators is the number of records per animal. Especially for an accurate estimation of the autocorrelation, a long and equidistant time series is required (Dakos et al., 2012), and a minimum of 50 records has been recommended (DeCarlo and Tryon, 1993; Box et al., 2008). As far as I know, no recommendation is given for the minimum number of records for variance or skewness. The minimum of 50 records was therefore applied as a requirement in this thesis. The amount of

longitudinal data records is also specifically important for genetic selection: a higher number of records per animal has been shown to increase the heritability of the trait variance (Berghof et al., 2019b). Furthermore, a long time series per animal increases the probability to capture response to disturbances (Berghof et al., 2019b). A challenge is, that there can be large differences in the amount of records per animal because of differences in survival, leading to differences in reliability of resilience indicators. This was accounted for in the genetic models in this thesis by including a fixed effect describing the number of records on which the resilience indicator was based.

The final issue to consider when selecting a longitudinal trait for calculation of resilience indicators is data quality; the data should not contain too many missing values and not too many measurement errors. Especially if missing values exist due to disease, the resilience indicators do not reflect response to that disease. Kok et al. (2021) studied associations between resilience indicators based on milk yield deviations and clinical mastitis. The authors mentioned missing records during mastitis treatment as a possible reason why they saw a negative instead of a positive relation of autocorrelation with clinical mastitis. Still, a positive relation between variance of daily milk yield deviations and clinical mastitis was observed, which suggests that for variance the presence of missing values is less important than for autocorrelation: apparently in the periods before or after the disease event deviations were sufficiently large to result in an increase in variance (Kok et al., 2021).

The issue with measurement errors, is that it is difficult to distinguish measurement errors from extreme values that are due to impaired resilience. Therefore, it is impossible to be strict on removal of outliers, and if measurement errors exist they have an effect on the resilience indicators. We observed this problem especially for the trait skewness (Berghof et al., 2019b), which needs a single outlier to become extremely low or high (Chapter 2). Therefore, skewness is recommended to be calculated only on longitudinal traits that are extremely reliably measured.

8.2.2 Selection of recording environment

After selecting the longitudinal trait, it is important to consider if the trait is recorded on animals that are sufficiently exposed to disturbances. If not, there will be no information about resilience in the fluctuations of the trait. For dairy cattle, often there is no issue here, because many longitudinal traits are measured on commercial farms, for example by sensors or automated systems. On commercial farms there are plenty of disturbances, such as pathogens, changes in feed ration,

changing weather circumstances and movement between groups, which will be visible in the longitudinal traits. Nevertheless, it is good to note that the disturbance regime between dairy farms differs largely, as suggested by the large herd level differences in variance and autocorrelation between herds in Chapter 6. More genetic variation in resilience may be present on farms with severe disturbances present (Mulder et al., 2013a).

For pigs and poultry, even larger differences in exposure to disturbances exist, depending on if they are housed on nucleus farms or commercial farms. Breeding animals are often kept on nucleus farms with high biosecurity and a very limited number of disturbances (Sevillano, 2018; Duenk, 2020). Longitudinal traits measured on such farms likely do not reflect resilience sufficiently. Therefore, it is important to obtain resilience indicator phenotypes under commercial circumstances. This was successfully done in pigs by exposing them to a multifactorial natural disease challenge that was similar to a commercial environment (Putz et al., 2019; Cheng et al., 2020). The fact that exposure to disturbances is important for longitudinal traits to reflect resilience was confirmed by Van der Zande et al. (2020) in pigs. These authors found that resilience indicators based on longitudinal activity data were able to predict morbidity and mortality upon a disease challenge when measured only during, but not before, the disease challenge. Moreover, other researchers (Bedere, N., Pegase, INRAE, Institut Agro, Saint Gilles, France, unpublished data) found low genetic correlations between resilience indicators calculated on egg production in purebred layer hens kept in high biosecurity environments and in crossbred layer hens kept in commercial environments. These low genetic correlations may be partly caused by the difference in disturbances between the environments, although a genotype by genotype and a genotype by environment interaction probably plays a role too.

8.2.3 Adjustment for trends

After the longitudinal trait is recorded, it is important to correct it for continuous trends in the mean of the trait that can have an effect on the resilience indicators (Scheffer et al., 2009; Dakos et al., 2012; Lenton et al., 2012; Boettiger et al., 2013). Examples of trends in animals are growth curves and lactation curves. The importance of adjusting milk yield for the lactation curve before calculating the resilience indicator variance was illustrated by Elgersma et al. (2018) and Chapter 2. When milk yield was not adjusted for lactation curve shape, variance was genetically related with the persistency of milk yield: cows with a flatter lactation curve had lower variance than cows with a high peak and rapid decline. After adjusting for the lactation curve shape, the genetic correlation with persistency

virtually disappeared (Chapter 2). In other species, the correction for long-term trends was recognized and applied as well, such as correction for age in layer chickens (Berghof et al., 2019a) and pigs (Putz et al., 2019; Cheng et al., 2020). Seasonal trends can be observed in animals as well, such as for daily step count in Chapter 5. The seasonal trend was accounted for by correcting step count for month of the year before calculating the resilience indicators.

When correcting for long-term trends it is important to avoid overfitting to ensure that the dynamics of interest remain in the data (Dakos et al., 2012). In other words, disturbances should have a limited effect on the fitted trend, so that the residuals contain as much information about resilience as possible. For this reason, polynomial quantile regression was applied with a quantile of 0.7 in this thesis. The quantile of 0.7 ensures that temporary declines in milk yield or activity have little effect on the fitted curve. Alternative methods have been proposed, such as an iterated Wood curve (Adriaens et al., 2020), where extreme negative deviations are excluded from fitting the curve. Which method is used to fit a lactation curve or other long-term trend is probably not important (at least for genetic selection): in Chapter 2 the resilience indicators based on different lactation curves were genetically very similar, except for skewness, which turned out not to be a good resilience indicator based on milk yield anyway.

In addition to correction for trends in the mean of a longitudinal trait, it may also be necessary to adjust for trends in variance. This is the case for growing animals, where the variance of traits increases with an increasing mean of traits over time. In such case, when calculating the variance of the trait as a resilience indicator, it is too much determined by fluctuations at older age. For this reason, Berghof et al. (2019a) standardized body weight to an average of zero and a standard deviation of one across cohorts. In dairy cows, the same probably plays a role, where mean milk yield increases over lactations, resulting in higher variance at later ages. Therefore, resilience indicators based on milk yield were treated as different traits in different lactations (Chapter 3).

8.2.4 Validation of calculated resilience indicators

After calculation of resilience indicators on longitudinal traits adjusted for trends, it is important to validate if they really represent resilience. It can occur that a resilience indicator does not behave according to expectation. For example, in this thesis, skewness based on milk yield had unfavorable genetic correlations with some health traits (Chapter 2). In addition, low variance based on step count was genetically associated with poor health (Chapter 5), while according to theory of Scheffer et al. (2009), it should be associated with good health. If such

unexpected characteristics are not recognized, implementation can give unwanted results, for example no change in resilience or even a decline in resilience.

The validation method depends on the purpose of the resilience indicators: should they be used as an early warning signal for management purposes, or for genetic selection? If the purpose is to serve as an early warning signal for a specific disease or disturbance, the validation can be performed using an experiment. In such an experiment, resilience indicators should be calculated on animals, and the association between the resilience indicators and response to an experimental disturbance should be investigated. This approach was performed by Van Dixhoorn et al. (2018) for predicting resilience to the disturbance of calving in dairy cattle, and by Van der Zande et al. (2020) for predicting resilience to a disease disturbance in pigs. An observational study can be performed as well, such as the one by Kok et al. (2021), who investigated the association between resilience indicators and occurrence of mastitis cases.

When the aim is to develop a resilience indicator that can be used to genetically improve resilience to all types of environmental disturbances, validation is less straightforward. Resilience has no golden standard, and therefore it is not possible to simply estimate a genetic correlation with 'true' resilience. The only way to validate resilience indicators then, is to gain as much information about them as possible, to get a well-informed impression if selection on them will improve resilience. In this thesis, two methods were used to gain information about the resilience indicators. The first was estimating genetic correlations with current health, longevity and fertility traits, which are traits related with resilience as well (Chapter 2, 3, 5). This method was applied in other studies too (Elgersma et al., 2018; Putz et al., 2019; Cheng et al., 2020). If unfavorable genetic correlations with other resilience-related traits exist, selection on the resilience indicator will result in deterioration of certain aspects of resilience and is therefore not a good resilience indicator. The other method used, was to investigate genetic associations with response and recovery to actual disturbances (Chapter 4). It is impossible to apply this method to all possible disturbances that exist. However, the more types of disturbances are proven to be associated with the resilience indicators, the stronger the confirmation that the resilience indicators indicate 'general' resilience.

If the new resilience indicator does not behave according to expectation, it is important to return to the previous steps on the road map to see if any improvements can be made. For example, it could be that the longitudinal trait on which the resilience indicator is based should be recorded in an environment with more disturbances, or that more data per animal should be included. Sometimes it is possible to account for unwanted side effects in the implementation stage. For

example, I accounted for differences in amount of data records per cow by including a fixed effect on lactation length in the genetic model for the resilience indicators (Chapter 2). Only if the resilience indicators then behave according to expectation, they can be implemented in practice.

8.2.5 Concluding remarks

Variance, autocorrelation and skewness of longitudinal traits have been studied as resilience indicators in many species and for many longitudinal traits so far. Based on these studies a recommendation can be provided about which steps to follow to develop a new resilience indicator using longitudinal data that is suitable for implementation. First of all, a longitudinal trait should be selected that is vulnerable to many disturbances, is measured frequently, and provides a sufficient number of records per animal with good data quality. Then, the selected trait should be recorded in an environment with many disturbances, to be able to display response and recovery patterns. After recording, the longitudinal trait should be corrected for any long-term trends, and then resilience indicators can be calculated. Finally, the resilience indicators should be thoroughly validated to investigate if their implementation will result in improvement of resilience. Only if the last step is successful, the resilience indicator can be implemented in practice. Based on these steps, in this thesis variance and autocorrelation of milk yield deviations were concluded to be good resilience indicators that can be implemented in practice. Skewness of milk yield deviations was concluded not to be a good resilience indicator at the moment, and it can possibly be improved by improving data quality of daily milk yield. Resilience indicators based on step count data are still in the phase of validation, so no conclusions can be drawn.

8.3 Application in breeding programs

This thesis contains a genetic analysis of resilience indicators, both based on milk yield and on step count. From the estimates of heritability we know that resilience indicators are heritable and potentially can be selected for, and, at least for resilience indicators based on milk yield, selection will result in more resilient cows. Therefore, it is now time to discuss if and how the genetic improvement for the resilience indicators should be applied in breeding programs. Because research on the resilience indicators based on activity is not complete yet, discussion of the application in breeding programs will mainly focus on variance and autocorrelation based on milk yield (from now on called **LnVar** and **r_{auto}**, respectively). However, recommendations will be given for resilience indicators based on activity as well.

I will focus on inclusion of the resilience indicators in the Dutch-Flemish breeding program and discuss the following topics that are important to decide if and how the resilience indicators should be included. First of all, it is important to know if the resilience indicators explain additional genetic variation that is not covered by the existing national index traits, so that additional genetic gain can be achieved. If not, resilience indicators do not add anything to the traits under current selection and should not be included as an additional trait in the breeding goal. If resilience indicators do contain additional genetic variation, the second step will be to discuss the usefulness of this additional genetic variation. Only if the resilience indicators contain useful information for the farmer and for the cow, they should be included in the breeding goal. These considerations will be discussed in the following paragraph. However, before starting that discussion, I will deliberate how LnVar should be dealt with, given its strong genetic correlation with mean milk yield. After discussing the expression of LnVar and the usefulness of selection on the resilience indicators, this section concludes with an outlook to the future.

8.3.1 How to deal with the strong genetic correlation between LnVar and mean milk yield

Before we can discuss if the resilience indicators should be included in breeding programs, it is important to discuss the interpretation and use of the trait LnVar. This trait had a strong unfavorable genetic correlation with mean milk yield (0.79). This makes it difficult to discuss in the following subchapters if LnVar contains useful information about resilience beyond its relation with mean milk yield. Furthermore, the strong genetic correlation with milk yield makes the trait LnVar difficult for interpretation for farmers: bulls with the highest estimated breeding value (**EBV**) for resilience (lowest EBV for LnVar) will often be bulls with low EBV for milk yield. Because milk yield is such an economically important trait, it would be beneficial to make LnVar independent of milk yield level.

To deal with the genetic correlation between mean milk yield and LnVar, it is good to realize that both traits are calculated from the same underlying milk yield data. Positive genetic correlations between mean and variance of the same trait recorded multiple times within an animal have been shown before, for example for test-day milk yield (Rönnegård et al., 2013) and somatic cell score (Urioste et al., 2012; Rönnegård et al., 2013) and daily milk yield in dairy cattle (Elgersma et al., 2018), and for birth weight of piglets (Damgaard et al., 2003; Sell-Kubiak et al., 2015). For variance based on step count we saw a strong positive genetic correlation with mean step count as well (Chapter 5). The positive genetic

correlation between the mean and variance of the same measurements could be partly attributed to a scale effect (Mulder et al., 2007; Rönnegård et al., 2013; Sell-Kubiak et al., 2015; Tatliyer et al., 2019). A scale effect occurs when the increase of the mean of a trait is accompanied by an increase of the variance of the trait, while the variance relative to the mean stays the same (Falconer and Mackay, 1996; Tatliyer et al., 2019). Scaling is however not the only explanation for a positive genetic correlation. The other explanation is that animals with high means truly are more vulnerable to disturbances than animals with low means, resulting in higher variance. For LnVar based on milk yield this is likely. When resources are limiting, cows with high genetic tendency to produce milk are known for allocating resources to production rather than other functions that are needed to cope with disturbances, such as the immune system (Beilharz, 1998; Rauw et al., 1998; Veerkamp et al., 2009). However, for variance based on step count, it is less likely that the strong positive genetic correlation with mean step count is due to higher vulnerability to disturbances of highly active cows. It is even more likely that high activity is a sign of good health and resilience (Chapter 5; Edwards and Tozer, 2004; Kamphuis et al., 2013; Thorup et al., 2015). Nevertheless, for LnVar based on milk yield, the positive genetic correlation between mean and LnVar is probably due to a combination of scaling and higher environmental sensitivity of cows with high mean milk yield.

Whatever the reason for the strong genetic correlation between LnVar and milk yield, the consequence is that it is difficult to interpret if LnVar contains any additional genetic variation about resilience that is not explained yet by genetic variation in milk yield. Therefore, it is easier for interpretation if LnVar would be adjusted for the trait milk yield. Literature on the genetic correlation between mean and variance of traits recommends transforming the variance, with the most commonly mentioned transformation being the coefficient of variation (Rönnegård and Valdar, 2011; Tatliyer et al., 2019). The coefficient of variation is the ratio of the standard deviation over the mean of a trait. If I analyze the coefficient of variation of daily milk yield using the data from Chapter 2 (standard deviation of the deviations from expected milk yield over mean daily milk yield, transformed with a natural logarithm to make it normally distributed), I find a heritability of 0.083, a genetic correlation with LnVar of 0.57 and a genetic correlation with mean milk yield of -0.09. These results indicate that the coefficient of variation is indeed practically genetically independent of milk yield level, while still genetically related with LnVar. Therefore, this may be a suitable way of presenting the variance independent of milk yield. However, this outcome should be investigated more

thoroughly first to see if it reflects resilience to the same extent as LnVar does. This can for example be done using the validation method described in Chapter 4.

While the coefficient of variation may be easier to interpret than LnVar, genetic selection for a ratio trait is not recommended. The genetic variance of the coefficient of variation is a function of the genetic variances of mean milk yield and variance of deviations in milk yield and the covariance between them (Lynch and Walsh, 1996), which makes it difficult to predict improvement in the component traits (Gunsett, 1984). Furthermore, although selection on ratio traits is possible, it is shown less effective than selection on the components of the ratio (Gunsett, 1984; Zetouni et al., 2017). Therefore, for genetic selection, it is still recommended to select for LnVar and mean milk yield using a multi-trait approach to simultaneously increase milk yield and decrease LnVar, although this does not solve the problem of interpreting LnVar.

Other methods exist to adjust traits for other traits as well. For example, the trait longevity is in some countries adjusted for milk production to obtain functional longevity, by including milk production of the cow as a covariate in the genetic model (van der Linde et al., 2007). Feed intake is another example, which is sometimes adjusted for production and other energy sinks phenotypically or genetically to obtain residual feed intake. Residual feed intake is modelled phenotypically as the feed intake of the cow minus the predicted feed intake based on energy sinks, such as milk yield and growth (Tempelman et al., 2015; Martin et al., 2021b). Feed efficiency can be modelled genetically by performing a genotypic regression of feed intake on production (Kennedy et al., 1993). Resulting genetic residual feed intake is genetically independent of production, and selection on this trait is equivalent to using a selection index with both feed intake and production, where production is kept constant (Kennedy et al., 1993). Genotypic regression was used by Veerkamp and Brotherstone (1997) too, to make the trait live weight genetically independent of body condition score.

The method of genotypic regression seems so far the most appropriate method to correct LnVar for mean milk yield. This method does make LnVar genetically independent of milk yield, while not having the problem of selecting on a ratio trait, which was the case for the coefficient of variation. Making LnVar genetically independent of milk yield does remove the correlation due to vulnerability to disturbances of highly productive cows as well. However, it improves understandability of the trait. Therefore, I performed genotypic regression to obtain genetic (co-)variances for LnVar adjusted for milk yield (**LnVar_{adj}**). Following Kennedy et al. (1993) and Veerkamp and Brotherstone (1997), the genetic regression coefficient of LnVar on mean milk yield (b) was calculated as:

$$b = \frac{\sigma_{A_{LnVar},milk}}{\sigma_{A_{milk}}^2},$$

where $\sigma_{A_{LnVar},milk}$ was the genetic covariance between LnVar and mean milk yield and $\sigma_{A_{milk}}^2$ was the genetic variance of mean milk yield. Genetic variance of LnVar_{adj} ($\sigma_{A_{LnVar_{adj}}}^2$) was then calculated as:

$$\sigma_{A_{LnVar_{adj}}}^2 = \sigma_{A_{LnVar}}^2 - b * \sigma_{A_{LnVar},milk},$$

where $\sigma_{A_{LnVar}}^2$ was the genetic variance of LnVar. Phenotypic variance of LnVar_{adj} ($\sigma_{P_{LnVar_{adj}}}^2$) was calculated as:

$$\sigma_{P_{LnVar_{adj}}}^2 = \sigma_{P_{LnVar}}^2 - 2b * \sigma_{P_{LnVar},milk} + b^2 * \sigma_{P_{milk}}^2$$

where $\sigma_{P_{LnVar}}^2$ and $\sigma_{P_{milk}}^2$ were phenotypic variance of LnVar and mean milk yield, respectively, and $\sigma_{P_{LnVar},milk}$ was the phenotypic covariance between LnVar and mean milk yield. Using as input estimated variance components from Chapter 2, variance components for LnVar_{adj} were $\sigma_{A_{LnVar_{adj}}}^2 = 0.021$ and $\sigma_{P_{LnVar_{adj}}}^2 = 0.27$.

Heritability was then $h^2 = \frac{\sigma_A^2}{\sigma_P^2} = 0.079$, which is similar to the heritability of the coefficient of variation calculated earlier. Applying this method, EBVs for LnVar_{adj} can be calculated that make it easy for farmers to select the bulls with the best resilience, independent of their genetic merit for production. Furthermore, the variance components calculated using this method are useful for the next subchapter, where I will investigate if LnVar, adjusted for mean milk yield, contains any genetic variation that cannot be explained by the current national index traits.

8.3.2 Do the resilience indicators explain additional genetic variation that is not covered by the existing national index traits?

To decide if an additional trait should be added to a selection index, it is important that it is heritable and that it contains more than just the genetic variation that is already selected for by current traits in the index. Therefore, it is important to test if genetic variation in LnVar and r_{auto} can be explained by the traits in the current Dutch-Flemish national index (**NVI**), which are lactose, fat,

protein, longevity, udder health, interval first to last insemination, calving interval, udder conformation, feet & legs, birth ease, calving ease, livability, maternal livability, claw health and saved feed costs (CRV, 2020b).

To investigate if genetic variation in LnVar and r_{auto} can be explained by genetic variation in the existing NVI, a selection index calculation was performed. A similar approach was used as described by van Pelt (2017) for longevity. The breeding goal trait was $\text{LnVar}_{\text{adj}}$ or r_{auto} , and the index traits were the traits currently in the NVI (CRV, 2020b). The calculations were performed using SelAction (Rutten et al., 2002), and the accuracy of the index was calculated for sires with 10,000 daughters with phenotypes. The remaining settings were set the same as in Berghof et al. (2019b) who performed a selection index calculation on LnVar and a number of breeding goal traits. Genetic correlations of $\text{LnVar}_{\text{adj}}$ and r_{auto} with the traits in the NVI used as input were MACE correlations estimated in Chapter 2. For $\text{LnVar}_{\text{adj}}$, these MACE correlations were adjusted for correlations with milk yield using the equations from Veerkamp and Brotherstone (1997). Heritability and phenotypic variance of the traits in the NVI and genetic correlations among them were taken from CRV (CRV, 2020b). Phenotypic correlations were unavailable and were therefore assumed the same as genetic correlations.

The accuracy of the index consisting of the current NVI traits with $\text{LnVar}_{\text{adj}}$ as the breeding goal trait was 0.51 and with r_{auto} as the breeding goal trait was 0.44. This means that only 26% of genetic variation in $\text{LnVar}_{\text{adj}}$ (0.512) and only 19% of genetic variation in r_{auto} can be explained by all traits in the NVI. The other 74% of genetic variation in $\text{LnVar}_{\text{adj}}$ and 81% of genetic variation in r_{auto} are not explained yet. Therefore, the resilience indicators do contain new information. It should be studied further if this new information is useful for describing resilience, both for the farmer and for the cow, to be able to finally conclude if resilience should be included in the breeding goal.

8.3.3 What do the resilience indicators explain about resilience, that is not explained by current national index traits?

As explained in the previous subchapter, 74% of variation in $\text{LnVar}_{\text{adj}}$ and 81% of variation in r_{auto} is not explained yet by the traits that are currently in the Dutch national index. However, addition of the resilience indicators as breeding goal traits is only useful and justified if the unexplained genetic variation contains information about resilience. This subchapter contains a discussion of what additional information the resilience indicators LnVar ($\text{LnVar}_{\text{adj}}$) and r_{auto} contain about resilience, beyond their relation with current national index traits.

The resilience indicators have additional value over the traits currently in selection indices for several reasons. The first reason is that the resilience indicators quantify response in milk yield to all possible disturbances and not just a specific disturbance or disease. Vulnerability to some disturbances is already captured by traits that are currently genetically evaluated, such as mastitis resistance (Heringstad et al., 2000; de Haas et al., 2004; Weigel and Shook, 2018; Cole, 2020) and ketosis resistance (Vosman et al., 2015). However, not all diseases are genetically evaluated in all countries, while daily recording of milk yield is becoming available in an increasing number of countries (de Koning, 2010; Rutten et al., 2013). For such countries, resilience indicators based on daily milk yield could assist in improving resistance to diseases. Moreover, cows encounter many more disturbances than only diseases, and resilience to those disturbances is important too. Milk yield has for example been shown to be sensitive to heat stress (Kadzere et al., 2002; Garner et al., 2016; Corazzin et al., 2020), stress of relocation and movement between groups (Varner et al., 1983; Hasegawa et al., 1997; Broucek et al., 2015), stress of transport (Yagi et al., 2004), hoof trimming (Pesenhofer et al., 2006; Montgomery et al., 2012; Janßen et al., 2016) and nutritional challenges (Nielsen et al., 2007; Codrea et al., 2011). Selection for lower LnVar and r_{auto} is likely to improve resilience to such disturbances. For heat stress, this has already been confirmed in Chapter 4, and also for unknown disturbances affecting herd milk yield, which likely consist of a combination of the above mentioned disturbances. Nevertheless, it would be valuable to validate LnVar and r_{auto} for additional common sources of stress.

Another reason why selection on the resilience indicators has additional value, is that they indicate the yield loss and recovery of milk yield to disturbances. Disease traits are used to select against occurrence of the disease, but are not informative about differences between cows in how much they are affected and how quickly they recover. Studies on genetic selection for recovery rate of mastitis (Franzén et al., 2012; Welderufael et al., 2017) have been performed and other studies characterized degree of mastitis infection (Højsgaard and Friggens, 2010) and yield loss due to infection (Adriaens et al., 2021). However, as far as known, no genetic selection on such traits is performed in practice.

Chapter 4 showed that LnVar was associated with the amount of yield loss upon disturbances, and that r_{auto} was associated with how quickly milk yield recovers. To indicate how response in milk yield to disturbances would change upon selection for lower LnVar_{adj} and r_{auto} , correlated responses were calculated for the yield response traits upon disturbances (herd disturbance and heat wave) using the genetic parameters from chapter 4. When LnVar_{adj} would be decreased with 1

genetic standard deviation through selection, correlated response in total yield loss after general disturbances at herd level would be -0.24 kg (cows would lose on average 3.3% less milk upon a herd disturbance), and a correlated response in total yield loss after a heat wave similar to the one of July 2015 of -0.53 kg (cows would lose on average 10.0% less milk upon this heat wave). Furthermore, if r_{auto} would be decreased with 1 standard deviation, correlated response in length of the yield drop would be -0.063 days upon herd disturbances (cows would have a 1.8% quicker recovery) and -0.13 days upon a heat wave similar to the one of July 2015 (cows would have a 4.3% quicker recovery). These responses indicate that selection on LnVar and r_{auto} will decrease the yield loss upon disturbances and will increase recovery rate. The responses seem small, but considering that many disturbances happen throughout the life of a cow, the accumulated effect may be substantial.

8.3.4 Should resilience be included in the breeding goal?

Based on the paragraphs above, the resilience indicators clearly have additional value to the traits under current selection. Now the question is if, based on this additional value, resilience should be included in the breeding goal. To include a new trait in a breeding goal, it is important that it has an economic value, or a non-economic emotional or societal value (Kanis et al., 2005; Nielsen et al., 2014). Resilience is expected to have both, which will be discussed below.

8.3.4.1 The economic value of resilience

Resilience can have economic value through (1) higher longevity, (2) lower treatment costs, (3) lower labor costs, and (4) lower milk yield losses. Resilient cows probably have higher longevity, as suggested by favorable genetic and phenotypic associations between LnVar and longevity (Chapter 2, 7). A higher longevity means that less replacement animals are needed and rearing costs are lower per year of life, as confirmed in Chapter 7. However, longevity is in most countries included as a breeding goal trait (Forabosco et al., 2009), and therefore the economic value of resilience should not include economic effects through increased longevity.

Cows with good resilience probably need less treatments than cows with poor resilience, because they are ill less often and because they are less severely affected. This is confirmed in Chapter 7, where low r_{auto} was associated with low yearly treatment costs. Low LnVar was not associated with treatment costs, but was associated with occurrence of some specific diseases, such as mastitis. The association between LnVar and mastitis was confirmed by Kok et al. (2021). However, treatment costs for most of the diseases covered in Chapter 7 are already

accounted for in selection for disease traits in the Netherlands (CRV, 2020c; d; e; f) and in some other countries (Kargo et al., 2014). Therefore, the added value of LnVar and r_{auto} through less treatments should be through treatments for traits that are not selected for. As treatment of individual cows is mostly needed for diseases, and not for other sources of stress (e.g. heat stress, relocation stress, hoof trimming stress, nutritional challenges), the economic value based on treatments is only valuable for countries where selection is performed on a limited number of health traits.

Cows with good resilience probably need less labor from the farmer than cows with poor resilience, because they are relatively ‘problem-free’. However, similar to treatment costs, labor costs for many diseases are already accounted for in the breeding goal in the Netherlands and some other countries (Huijps et al., 2008; Kargo et al., 2014; CRV, 2020c). Therefore, for these countries labor should be considered that is needed for individual cows affected by disturbances other than diseases. A method to value resilience through labor requirements was proposed by Berghof et al. (2019b). This method relies on the assumption that farmers receive alerts from the automatic milking system based on drops in milk yield caused by all kinds of disturbances. In case of an alert, the cow needs to be checked by the farmer, and this way she requires labor. A cow with high LnVar has more drops in milk yield, generates more alerts, and therefore requires more labor than a cow with low LnVar. However, the disadvantage of this method is that a decrease in milk yield does not always lead to an increase in labor in reality. If a farm has no automatic milking system, or if the automatic milking system does not provide alerts the way assumed in Berghof et al. (2019b), no extra labor is involved for cows with a drop in milk yield that are not ill. Literature suggests that in reality automatic milking systems mainly generate alerts for clinical mastitis and not other disturbances, and these are based on declines in milk yield as well as increases in milk conductivity and changes in milk color (Kamphuis et al., 2010; Steeneveld et al., 2010). As indicated before, labor costs for clinical mastitis are already accounted for in the economic value of udder health (Kargo et al., 2014; CRV, 2020c). Therefore, the economic value of resilience through increased labor due to alerts generated by automatic milking systems is not confirmed and needs validation on real farms. An example of a study to investigate the association between resilience indicators and labor could be to have farmers with automatic milking systems record every instance where they need to spend individual attention on a cow. The associations between the number of attention moments per cow and the resilience indicators should then be investigated.

The last economic advantage of resilience is that cows with good resilience have smaller yield loss upon disturbances than cows with poor resilience, as shown for LnVar in Chapter 4 and subchapter 8.3.3. Even though milk loss upon disturbances seems an important and straightforward economic advantage of LnVar, this milk loss may be partly accounted for by the breeding values for milk yield. Breeding values for milk yield are generally based on a random regression test-day model (Schaeffer et al., 2000; de Roos et al., 2001; Jakobsen et al., 2002). If drops in milk yield occur on test-days, the breeding value for milk yield may be decreased. However, test-days are recorded only once every 3-6 weeks, so the chance that a drop in milk yield occurs exactly on the test-day may be small. Moreover, drops in milk yield on a test-day, if severe enough, may be detected as outliers, and outliers are generally excluded or corrected for in genetic evaluation (Yang et al., 2004; Jamrozik et al., 2007; CRV, 2020g). Hence, drops in milk yield due to lack of resilience may be partly expressed in the breeding value for milk yield, but there is probably still an additional economic value.

The same may account for heat tolerance based on yield loss in Australia (Nguyen et al., 2017a): the economic value was originally proposed as a sum of the amount of money lost due to decreased production on days with temperature-humidity index higher than 60. Still, the breeding value for milk yield is based on phenotypes that are part of the time under heat stress (DataGene, 2020), and thus may partly cover sensitivity to heat stress already. For LnVar specifically, the economic value due to milk loss could potentially be determined by calculating the difference between realized lactational milk yield based on automatic milking system records and estimated lactational milk yield based on test-day records. This difference should then be related to LnVar to see how much milk is lost due to increased LnVar.

8.3.4.2 *The non-economic value of resilience*

From the previous subchapter it is clear that with the current knowledge it is difficult to exactly quantify the economic advantage of the resilience indicators. However, farmers do prefer to have robust or resilient cows (Egger-Danner and Heringstad, 2020). Therefore, for farmers resilience may have a so-called ‘non-market economic value’ (Nielsen et al., 2005).

A possibility to get a better understanding of the non-market economic value of the resilience indicators for farmers, is to perform a survey to understand how much they value a gain in resilience. Stated preference techniques could be used, such as choice experiments based on stated choices (Carlsson and Martinsson, 2001; Nielsen et al., 2011). With a choice experiment, respondents are presented a

number of scenarios, where they have to choose their preferred alternative of the two presented options. Each option consists of a number of attributes and options are created by changing the levels of the attributes. By asking a series of these choices, the respondents underlying preference (utility) for attributes can be determined. In case of resilience indicators, the respondents could be asked which cow out of a few options they would prefer. The attributes that can differ between cows then consist of LnVar, r_{auto} , and price. It is important that LnVar and r_{auto} are visualized for the respondents, because they have no experience with these traits (Byrne et al., 2012). Figure 8.2 shows an example of visualization of pairs of cows with the same milk yield but different LnVar and r_{auto} . By applying a choice experiment on a sufficient number of farmers, it should be possible to determine the maximum prize difference for which they prefer a resilient over a less-resilient cow. Another way to determine a non-market economic value is through quantifying the loss in selection response in milk yield resulting from stronger emphasis on the resilience indicators (Nielsen et al., 2005). It can then be determined through surveys how much loss in response in milk yield farmers are willing to accept to obtain a better resilience.

In addition to the non-market economic value for farmers, resilience also has a non-economic societal value through its positive association with animal welfare (Colditz and Hine, 2016; Berghof et al., 2019b). Indeed, selection on reduced LnVar and r_{auto} will likely reduce vulnerability of production to many sources of stress. However, it is currently unknown if it will also reduce feelings of stress for the cow. Literature shows that many disturbances that result in a temporary decline in milk yield, result in an increase in stress hormone levels as well (Varner et al., 1983; Yagi et al., 2004; Pesenhofer et al., 2006). It is however unknown if cows with a small decline in milk yield have a smaller increase in stress hormone levels than cows with a large decline in milk yield. At least for heat stress it has been shown that cows with small declines in milk yield during an experimental heat challenge, had smaller increases in rectal and intra-vaginal temperatures than did cows with large declines in milk yield (Garner et al., 2016). This suggests that the cows with smaller declines in milk yield felt less heat stressed than the cows with larger declines. Therefore, selection for smaller decline in milk yield in response to heat waves would be beneficial for animal welfare. Another confirmation that selection for lower vulnerability of milk yield to disturbances is beneficial for animal welfare is provided in Chapter 2 and 3: selection for lower LnVar and r_{auto} will result in fewer cases of disease and higher longevity, and thus probably better welfare. Of course, it could be that for certain cows it is better for their welfare if they do drop their milk yield severely to be able to survive. However, if animals exist that keep

producing while it is detrimental for their future health and survival, this will be reflected by their breeding values for health and longevity, and such animals will probably not be selected.

It is difficult to assign a non-economic or non-market economic value to the resilience indicators through improved animal welfare. An option is to apply a restricted index, where the non-economic value of the resilience indicators is determined by the weight that is required to obtain zero change (Nielsen et al., 2005). This is a form of desired gains approach (Brascamp, 1984). However, the question is if we want zero change, or if we want a reduction in LnVar and r_{auto} . If we want a reduction, it is still unknown how large the reduction should be. Another method is the use of stated preference techniques (Nielsen et al., 2011) as explained in the previous paragraph, but applied to consumers instead of farmers. However, it is even more difficult to explain LnVar and r_{auto} and their effects on animal welfare to consumers than to farmers, because consumers probably have difficulties with interpreting visualizations as in Figure 8.2. Therefore, probably the most practical option to obtain a non-market economic value for the resilience indicators is to define it based on farmer surveys, and this will probably automatically result in improvements of animal welfare.

8.3.5 Outlook

There are plenty of reasons why we should select for lower LnVar and r_{auto} . However, additional studies are needed to determine their weight in the breeding goal. Until such studies have been finished, I recommend to include the resilience indicators in genetic evaluation and present them to farmers separately from the national index. Similarly, in Australia the new breeding value for heat tolerance is published but not included in the national index (DataGene, 2017, 2020). Moreover, in the Netherlands, for several traits breeding values are published and sometimes included in alternative indexes but not included in the national index. Examples are ketosis and reproduction disorders (Vosman et al., 2015; CRV, 2020b; e). The recommended approach towards including LnVar and r_{auto} in the breeding goal is summarized in Figure 8.3.

8 General discussion

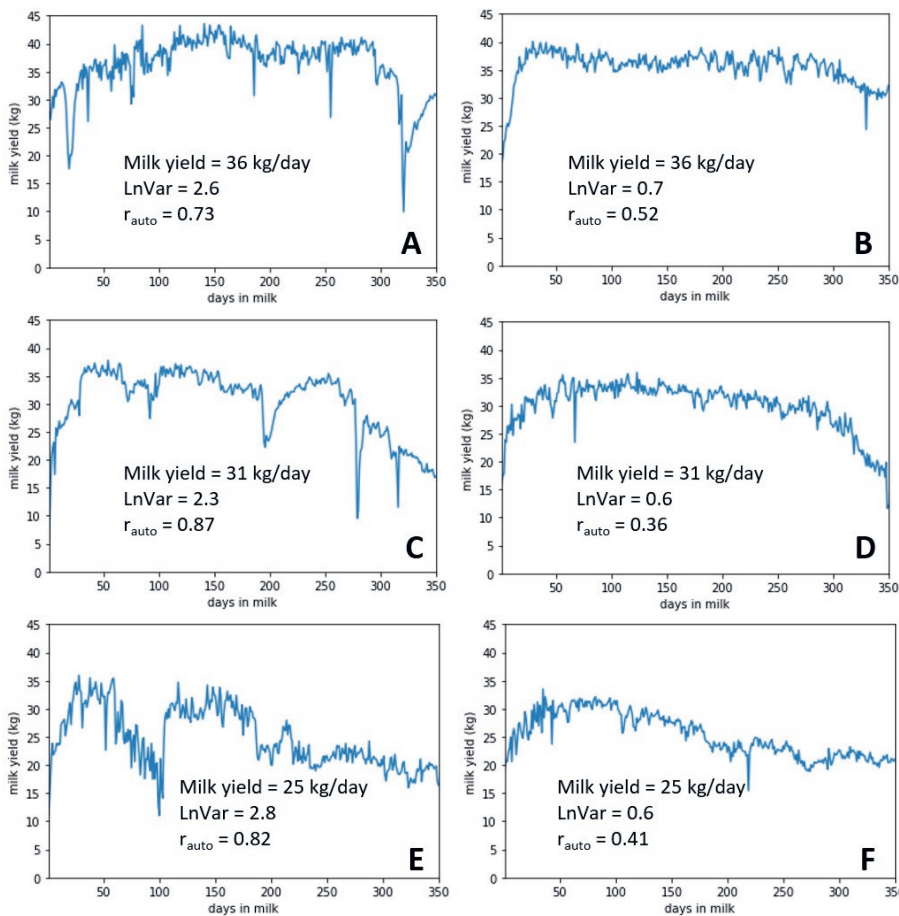


Figure 8.2 Illustrations of lactations of cows with low and high variance (LnVar) and autocorrelation of milk yield deviations (r_{auto}). A, C and E are cows with high LnVar and r_{auto} , and B, D and F are cows with respectively the same milk yield level but a low LnVar and r_{auto} .



Figure 8.3 Recommended approach towards including a resilience index in the breeding goal.

LnVar and r_{auto} based on milk, and potentially resilience indicators based on activity, are recommended to be combined in a ‘resilience index’. This resilience index needs proper introduction, and any worries that farmers may have about unwanted side effects of selection for resilience should be addressed. One worry could be whether a cow is really resilient if she keeps producing milk upon disturbances, or if it is a more resilient approach to decrease milk yield temporarily to recover. This worry can be addressed by explaining that resilience means that a cow is allowed to decrease her milk yield, as long as the decrease is not too severe and she recovers quickly (Berghof et al., 2019b). This is why r_{auto} is part of the index. Figure 8.2 can help to explain this concept: cows with low LnVar and r_{auto} still have temporary decreases in milk yield (panels B, D, F), but there are only few and recovery is quick. In addition, the favorable genetic correlations of the resilience indicators with health traits and longevity can be presented. Selection on the resilience indicators is not detrimental for health and longevity of cows; it is even beneficial. Apparently, resilience is partly a matter of resistance, and if a cow is resistant to e.g. pathogens, it is not even necessary to decrease milk yield. Another worry could be that selection on resilience will lead to cows that are not feed

efficient, because they have too high maintenance requirements. Cows with low LnVar indeed genetically had higher dry matter intake than cows with higher LnVar at the same milk yield level, and this genetic correlation was considerably strong (Chapter 2). From the other side, this correlation stresses that focusing on only feed efficiency can be detrimental for resilience. Luckily, the genetic correlation between resilience and dry matter intake was not 1, and therefore animals can be selected that combine a high breeding value for resilience with a high breeding value for feed efficiency. After proper introduction and addressing the potential worries of farmers about resilience, experience can be gained with the trait resilience. Once the weight of resilience in the breeding goal is determined, it can be included in the breeding goal.

In addition to LnVar and r_{auto} based on milk yield, more research should be performed into resilience indicators based on activity data. The resilience indicators based on daily step count were heritable and some of them were genetically associated with health traits (Chapter 5). However, it is still unknown if they add any information about resilience on top of the current breeding goal traits. A validation similar to chapter 4 could be performed. Furthermore, the accelerometers that provided daily step count in chapter 5, also provide traits like lying time and standing time. Additional resilience indicators could potentially be calculated from these traits. If resilience indicators based on activity become available, it is recommended to add them to the proposed resilience index based on LnVar and r_{auto} of milk yield, to generate a more complete picture of the genetic merit for resilience.

8.4 Concluding remarks

This thesis focused on development of resilience indicators for genetic selection from longitudinal milk yield and step count data. Several of the investigated resilience indicators seem successful, because they are related with resilience and can be genetically selected for. These resilience indicators are the natural log-transformed variance and lag-1 autocorrelation of daily deviations from expected milk yield. Selection on these traits will likely result in cows that are less severely affected by disturbances and that recover more quickly than the current population. Moreover, these cows are expected to make more profit throughout life and have lower treatment costs. Furthermore, in addition to indicating resilience at individual cow level, the variance of milk yield deviations can be used to indicate resilience at the herd level. Lag-1 autocorrelation based on step count data and mean step count were promising resilience indicators as well, because they were heritable and genetically related with health traits. However, more

research is needed to determine to what extent they represent resilience beyond information captured by current health traits. To improve resilience, a resilience index composed of multiple resilience indicators is recommended to improve all aspects of resilience simultaneously. Once the economic or non-economic value of such a resilience index is determined, it should be included in the breeding goal.

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Summary

Summary

Resilience is the ability of a cow to be minimally affected by disturbances and if affected, to recover quickly. Improving resilience is important for animal welfare and for the benefit of the farmer wanting to work with trouble-free cows. I investigated new traits based on daily recorded milk yield and activity sensor data to indicate how resilient a cow is; resilience indicators. I investigated if these indicators can be used in genetic selection and what the economic relevance was and the usefulness at herd level.

The resilience indicators were the variance, autocorrelation, and skewness of the deviations of daily milk yield and activity from the expected values. Resilient cows are expected to fluctuate closely around the expected milk yield, and therefore have low variance. They are also expected to have little dependency between subsequent deviations, and therefore have weak autocorrelation. They are also expected to have a symmetrical distribution of negative and positive deviations, and therefore have little skewness.

Chapters 2, 3, and 4 focused on genetic analysis of the resilience indicators based on daily deviations from expected milk yield. These chapters showed that variance and autocorrelation were promising resilience indicators, while skewness was not suitable due to low heritability and unfavorable genetic correlations with health traits. Variance and autocorrelation were both heritable and had favorable genetic correlations with other resilience-related traits such as udder health and longevity. Moreover, variance had moderate to strong genetic correlations with magnitude of the production response to unidentified disturbances at herd level and to a heat wave. Autocorrelation had moderate to strong genetic correlations with recovery time from these disturbances. Variance and autocorrelation of daily deviations from expected milk yield thus covered different aspects of resilience.

Chapter 5 contains a genetic analysis of potential resilience indicators as well, but based on deviations from expected step count instead of expected milk yield. The variance and autocorrelation of daily step deviations were studied, but also some additional traits, including activity level. Most of the studied resilience indicators were heritable, and especially the activity level had considerable heritability. The resilience indicators based on step count had genetic correlations with different health, fertility and longevity traits than the resilience indicators based on milk yield, which suggests that the indicators based on activity and milk yield indicated resilience to different types of disturbances.

Chapter 6 showed that large differences existed between herds in the variance and autocorrelation of their cows, that cannot be explained by differences in genetics. This suggests an effect of management on resilience. Furthermore, herds with cows with high variance, also tended to be herds with high incidence of rumen acidosis, high somatic cell score, low survival to second lactation, and high production level. This suggests these herds were herds with many disturbances. For autocorrelation, the correlations with herd performance traits were more ambiguous.

Chapter 7 showed the economic importance of variance and autocorrelation of daily milk yield deviations. Cows with low variance in lactation 1 had higher lifetime profit than cows with high variance, which was mainly due to longer herd life and also higher milk components. Cows with low autocorrelation did not have significantly different lifetime profit than cows with high autocorrelation, but they did have lower treatment costs, which stresses its importance for easy management.

Chapter 8 contains a general discussion consisting of two parts. In the first part I discuss the lessons learnt from this thesis and literature when developing a new resilience indicator based on fluctuations in longitudinal production or sensor data. The most important lessons are, that different longitudinal traits represent resilience to different disturbances, that resilience indicators measured in an environment with a lack of disturbances are not able to predict resilience well, and that correcting longitudinal data for long-term trends (e.g. lactation curves) before calculating resilience indicators is important. In the second part, I discuss the application of the resilience indicators in a dairy cattle breeding program. The resilience indicators based on milk yield express genetic variation that cannot be explained by the current traits in the national index. This new genetic variation is expected to have both economic and non-economic value. Economic value can be expected through labor time and milk losses. Non-economic value can be expected through improved animal welfare. Once the economic value and non-economic value are determined in more detail, the resilience indicators based on milk yield should be included as a resilience index in the breeding goal. The resilience indicators based on activity could be added to that resilience index once they have been studied in more detail, to offer a more complete representation of resilience.

Curriculum Vitae

About the author

Marieke Poppe was born on February 12, 1994 in Zwolle, the Netherlands. She grew up on a dairy farm, where she developed her passion for dairy cattle and in particular breeding. Because of this interest, she started her BSc in Animal Sciences at Wageningen University in 2012. She completed the BSc with honors.

Marieke continued her MSc in Animal Sciences at Wageningen University in 2015. She specialized in Animal Breeding and Genomics. To obtain additional knowledge about breeding, she spent 5 months at the Norwegian University of Life Sciences in Ås to attend courses on genetics. She wrote her MSc thesis on genetic selection for udder conformation using teat location records obtained by automatic milking systems. This thesis was partly carried out at CRV. She concluded her MSc with a 4 month internship at VikingGenetics in Denmark. There, she worked on implementation of optimum contribution selection in the Jersey breeding program.

In 2018, Marieke started as a PhD candidate at the Animal Breeding and Genomics group at Wageningen University. She was attracted by the combination of big data and breeding for resilience in this PhD project. The project was part of the Breed4Food consortium and of GenTORE. Since January 2022, Marieke works as a researcher for CRV.

Peer reviewed publications

- Poppe, M.,** H. A. Mulder, B. J. Ducro, and G. de Jong. 2019. Genetic analysis of udder conformation traits derived from automatic milking system recording in dairy cows. *J. Dairy Sci.* 102:1386-1396.
- Berghof, T. V. L., **M. Poppe,** and H. A. Mulder. 2019. Opportunities to improve resilience in animal breeding programs. *Front. Genet.* 9:692.
- Poppe, M.,** R. F. Veerkamp, M. L. van Pelt, and H. A. Mulder. 2020. Exploration of variance, autocorrelation, and skewness of deviations from lactation curves as resilience indicators for breeding. *J. Dairy Sci.* 103:1667-1684.
- Poppe, M.,** H. A. Mulder, C. Kamphuis, and R. F. Veerkamp. 2021. Between-herd variation in resilience and relations to herd performance. *J. Dairy Sci.* 104:616-627.
- Poppe, M.,** G. Bonekamp, M. L. van Pelt, and H. A. Mulder. 2021. Genetic analysis of resilience indicators based on milk yield records in different lactations and at different lactation stages. *J. Dairy Sci.* 104:1967-1981.
- Poppe, M.,** H. A. Mulder, and R. F. Veerkamp. 2021. Validation of resilience indicators by estimating genetic correlations among daughter groups and with yield responses to a heat wave and disturbances at herd level. *J. Dairy Sci.* 104:8094-8106.

Contributions to conferences

- Poppe, M.,** H. A. Mulder, and R. F. Veerkamp. 2018. Development of resilience indicators using deviations in milk yield from the lactation curve. 69th Annual Meeting of the European Federation of Animal Science (EAAP). Dubrovnik, Croatia.
- Poppe, M.,** H. A. Mulder, and R. F. Veerkamp. 2019. Breeding for resilience in dairy cows using daily milk yield recording. WIAS Science Day. Lunteren, the Netherlands.
- Poppe, M.,** H. A. Mulder, and R. F. Veerkamp. 2019. Breeding for resilience in dairy cows using daily milk yield recording. Annual Meeting of the American Dairy Science Association (ADSA). Cincinnati, USA.
- Poppe, M.,** C. Kamphuis, R. F. Veerkamp, and H. A. Mulder. 2020. Between-herd variation in cow resilience and relations to management. WIAS Annual Conference. Lunteren, the Netherlands.
- Poppe, M.,** H. A. Mulder, C. Kamphuis, and R. F. Veerkamp. 2020. Between-herd variation in cow resilience and relations to management. 71th Annual Meeting of the European Federation of Animal Science (EAAP). Online.
- Poppe, M.,** G. Bonekamp, M. L. van Pelt, and H. A. Mulder. 2020. Genetic analysis of resilience indicators based on different lactations and lactation stages. 71th Annual Meeting of the European Federation of Animal Science (EAAP). Online.
- Poppe, M.,** H. A. Mulder, and R. F. Veerkamp. 2020. Resilience indicators for dairy cattle based on longitudinal milk yield data. 6th International Conference of Quantitative Genetics (ICQG). Online.
- Poppe, M.,** H. A. Mulder, M. L. van Pelt, E. Mullaart, and R. F. Veerkamp. 2021. Validation of resilience indicators based on daily milk yield in dairy cows. WIAS Annual Conference. Online.
- Poppe, M.,** H. A. Mulder, M. L. van Pelt, and R. F. Veerkamp. 2021. Validation of resilience indicators based on daily milk yield in dairy cows. 72th Annual Meeting of the European Federation of Animal Science (EAAP). Davos, Switzerland.
- Poppe, M.,** H. A. Mulder, E. Mullaart, and R. F. Veerkamp. 2021. Resilience indicators calculated from daily activity in dairy cows. 72th Annual Meeting of the European Federation of Animal Science (EAAP). Davos, Switzerland.

Training and education

The Basic Package (1.8 ECTS)	
WIAS Introduction Day	2018
Course on philosophy of science and/or ethics	2018



Disciplinary Competences (18.5 ECTS)	
Writing WIAS research proposal	2018
Resilience of living systems – from fundamental concepts to interdisciplinary applications (Lunten, the Netherlands)	2018
NOVA course Linear models in animal breeding (Orsa Grönklitt, Sweden)	2018
NOVA course Biological consequences of animal breeding (Øyer, Norway)	2019
Applied economic modelling for the veterinary sciences (online)	2019
Genotype by environment interaction, uniformity and resilience (Wageningen)	2020
Quantitative Genetics Discussion Group	2018-2022
Study group Book Quantitative Genetics Falconer and Mackay	2018-2020

Professional Competences (5.0 ECTS)	
WGS course Posters and pitching	2019
WGS course Presenting with impact	2019
WGS course Scientific writing	2019
WGS course Supervising BSc and MSc students	2020
WGS course The final touch	2021

Societal Relevance (2.0 ECTS)	
Societal impact of your research	2019
Webinar for farmers who supplied data	2021

Presentation skills (maximum of 4.0 ECTS)	
EAAP, Dubrovnik, Croatia (Oral)	2018
WIAS Science Day, Lunten, the Netherlands (Oral)	2019
ADSA, Cincinnati, USA (Oral)	2019
GenTORE Annual Meeting, Frick, Switzerland (Oral)	2019
Vlaamse Fokkerijdag, Leuven, Belgium (Oral)	2019
WIAS Annual Conference, Lunten, the Netherlands (Oral)	2020
EAAP, online (Oral)	2020
ICQG, online (Oral)	2020
WIAS Annual Conference, online (Oral)	2021
EAAP, Davos, Switzerland (Oral)	2021
German National Congress on Breeding, Berlin, Germany (Oral)	2021

Curriculum vitae

Teaching Competences (maximum of 6.0 ECTS)	
Assisting MSc course Genetic Improvement of Livestock	2018 & 2019
Supervising MSc student	2019
Lecture training week for student Dairy Campus, Leeuwarden	2019
Lecture course Genotype by Environment Interaction, Uniformity and Resilience, Wageningen	2020
Supervising BSc student	2021
Total credits	37.3

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Colophon

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