Genetic variation for resistance to clinical and subclinical diseases exists in growing pigs

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Abstract

The objective of this study was to test that genetic variation for resistance to clinical and subclinical diseases exists in growing pigs. A total of 13 551 male growing pigs were assessed for resistance to five categories of clinical and subclinical disease: (i) any clinical or subclinical disease, (ii) lameness, (iii) respiratory diseases, (iv) diarrhoea, and (v) other diseases (i.e. any clinical or subclinical disease with the exception of (ii), (iii), and (iv)). Additive genetic variation for resistance to each disease category was estimated by fitting a Weibull, sire-dam frailty model to time until the pigs were first diagnosed with a disease from that category. Genetic correlations among the resistances to each disease category were approximated as product-moment correlations among predicted breeding values of the sires. Additive genetic variation was detected for resistance to (i) any clinical or subclinical disease (additive genetic variance for log-frailty (± s.e.) = 0·18 ± 0·05, heritability on the logarithmic-time scale = 0·10), (ii) lameness (0·29 ± 0·11, 0·16), (iii) respiratory diseases (0·24 ± 0·16, 0·12), (iv) diarrhoea (0·30 ± 0·27, 0·16), and (v) the other diseases (0·34 ± 0·15, 0·19) and there were generally positive and low-to-moderate correlations among the predicted breeding values (–0·03 to + 0·65). These results demonstrate that additive genetic variation for resistance to clinical and subclinical diseases does exist in growing pigs, and suggests that selective breeding for resistance could be successful.

Keywords: disease resistance, genetic variation, pigs.

Introduction

Pig production is often hindered by disease, which can cause mortality, reduced production performance, increased costs and poor animal welfare. Methods currently used to control disease include eradication, sanitation, quarantine, culling, vaccination and medication. A complementary, albeit longer-term, approach to disease control is to selectively breed pigs for resistance. Selective breeding should be possible given that genetic variation for resistance to specific pathogens is present in most, if not all, animal populations (Nicholas, 1987; Müller and Brem, 1991; Straw and Rothschild, 1992) and this is the case for pigs in relation to pathogens that have been investigated (Straw and Rothschild, 1992; Rohrer and Beattie, 1999). During pig production, resistance is assessed, not in relation to specific pathogens, but as the incidence of clinical and subclinical disease (e.g. lameness, respiratory diseases, diarrhoea, reduced food consumption). This has the advantage of enabling large numbers of pigs to be assessed while they are exposed to the pathogens encountered during production. However, clinical and subclinical diseases can be the outcome of infection by many different pathogens, and much of the variation for resistance among pigs is due to environmental factors, such as unpredictable exposure to the pathogens. Despite these drawbacks, in the species where most work has been done in this field, namely adult dairy cattle, resistance to economically important clinical diseases (e.g. mastitis, digestive diseases, feet and leg disorders) still exhibit low
levels of additive genetic variation ($h^2 < 0.10$ for disease incidence assessed as a categorical trait) (e.g. Philipson et al., 1980; Lyons et al., 1991; Mäntysaari et al., 1991; Simianer et al., 1991; Uribe et al., 1995; Heringstad et al., 2000). This has led to the inclusion of resistance to clinical diseases in cattle breeding programmes (e.g. Pedersen et al., 1993; Pedersen and Aamand, 1999). Similarly, in the few studies presented to date on piglets and growing pigs, low levels of additive genetic variation have been documented for resistance to respiratory diseases, diarrhoea, and arthritis (Smith et al., 1962; Lundeheim, 1979 and 1988; Lingaas and Rønningen, 1991). These results suggest that at least low levels of additive genetic variation for resistance to clinical and subclinical diseases exists in pigs, and that selection for resistance to clinical and subclinical disease can be successful.

In this study, additive genetic variation was estimated for resistance to clinical and subclinical diseases in growing pigs. Male growing pigs from the nucleus breeding population of the Danish pig breeding programme (DanAvl) were assessed for resistance to five categories of disease (i.e. any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and other diseases) while they were performance tested for production traits (e.g. growth rate, food efficiency, and lean tissue content). Additive genetic variation was estimated for resistance to each disease category, while genetic correlations among the resistances were approximated as product-moment correlations among predicted breeding values. The objective was to test that additive genetic variation for resistance to clinical and subclinical diseases exists in growing pigs.

Material and methods

Performance test

Between 1995 and 1998, 13,551 male growing pigs from the Duroc, Yorkshire, Landrace, and Hampshire breeds were assessed for clinical and subclinical diseases while they were performance tested for production traits at Bøgildgård test station. Bøgildgård is the central test station of DanAvl and is used to performance test approximately 5000 male pigs each year. On average, the performance test for each pig lasted 83 days, beginning when the pigs were 9 weeks old ($\pm 4$ days) (approx. 30 kg live body weight) and finishing when they attained slaughter weight (90 kg) at approximately 21 weeks of age. However, there were pigs that were removed from the performance test as early as day 7 and as late as day 123. Pigs removed during early stages of the performance test either died, were injured, or were severely ill (i.e. growth was severely affected, and they would not respond to treatment).

The pigs performance tested at Bøgildgård were from DanAvl’s nucleus breeding population (Figure 1). Each was bred at one of 49 breeding farms and was selected to be performance tested because it had the potential to be genetically superior for the production traits by virtue of its ancestry. At the conclusion of the performance test, those pigs found to be genetically superior were selected to produce semen used to artificially inseminate sows at the breeding farms. The remaining pigs were slaughtered. The artificial insemination of the sows at the breeding farms resulted in the next generation of the nucleus breeding population.

The 49 breeding farms were responsible for maintaining DanAvl’s nucleus breeding population. The majority of the farms maintained one or two of the pig breeds, although there were farms that maintained as many as all four breeds.

Pedigree

The pigs performance tested at Bøgildgård were from 1032 sires and out of 7104 dams. The number of pigs from each sire ranged between 1 and 101 (mean 13.1 (s.e. 5.2)) and the number of pigs out of each dam ranged between 1 and 11 (1.9 (s.e.1.2)). The total number of individuals in the pedigree structure after tracing animals back from the sires and dams of the pigs was 14,458.

Rearing of pigs

Bøgildgård operates by an ‘all in-all out’ policy. The pigs were performance tested in stall groups, where the pigs in each group started and finished the performance test at the same time. Specifically, the pigs arrived at Bøgildgård from their respective breeding farms as 4-week-old piglets (approx. 8 kg live body weight). Upon arrival, they spent 5 weeks in acclimatization pens (Figure 2). The pigs were then allocated to a stall within a test facility to be performance tested.

The test facility consisted of 16 stalls. Each stall was divided into eight pens, and each pen maintained between 12 and 14 pigs (i.e. approx. 100 pigs per stall). Pigs allocated to the same stall finished the period of acclimatization at the same time. However, pigs allocated to the same pen within each stall were from the same breed and were a mixture of pigs from different acclimatization pens. After each stall group had been performance tested, the pigs were removed.
and the stall made ready for the next group to be performance tested.

Diagnosis of clinical and subclinical diseases
During the performance test, a pig was assumed to have been diagnosed with a clinical or subclinical disease when it was treated for the disease. Each time a pig was treated, a record was made of the disease and the date of treatment. The clinical and subclinical diseases diagnosed are presented in Table 1.

There were cases where non-diagnosed pigs were treated to prevent them from being infected with a clinical or subclinical disease (i.e., majority of pigs within a pen group were treated for a disease although only a few individuals in the group were diagnosed with the disease). However, preventive treatments were not recorded in a way that was distinguishable from the treatments of diagnosed pigs. Therefore, to account for the preventive treatments, when more than 75% of the pigs in a pen group were treated for a particular disease on a given day, all of these treatments were assumed to be preventive and removed from the data set. This enabled pigs treated on subsequent days to be identified as the diagnosed pigs.

The clinical and subclinical diseases were grouped into the following categories: (i) any clinical or

Table 1 Clinical and subclinical diseases diagnosed while growing pigs were performance tested for production traits at Bøgildgård test station

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Subclinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lameness, respiratory diseases, diarrhoea, skin disorders, sneezing, snout deformation, boils, cramp, tail bitten</td>
<td>Reduced food consumption</td>
</tr>
</tbody>
</table>
subclinical disease (i.e. includes all diseases), (ii) lameness, (iii) respiratory diseases, (iv) diarrhoea, and (v) other diseases, which included reduced food consumption and all the clinical diseases with the exception of (ii), (iii), and (iv).

The diseases were grouped into these categories, as preliminary analysis demonstrated that lameness, respiratory diseases, diarrhoea, and reduced food consumption were the most prevalent diseases. By contrast, less than 0.6% of the pigs were treated for skin disorders, sneezing, snout deformation, boils, cramp and tail bitten.

Assessment of disease resistance
Resistance of the pigs to each disease category was assessed as time (days) from the start of the performance test until first diagnosis of a disease from that category. By assessing resistance in this way, it was assumed that all pigs would eventually be diagnosed with a disease from each category. Pigs that were not diagnosed with a particular disease category were assumed to have a censored record for that category (i.e. assumed that they would be diagnosed some time after the performance test).

Assessing resistance as time until first diagnosis provides a measure of the degree of resistance (i.e. the longer it takes before a pig is diagnosed, the greater the resistance). In terms of a selective breeding programme, the aim is to produce pigs whose time until diagnosis would be some time after they have been performance tested. For growing pigs, this is after they have been slaughtered.
**Statistical analysis**

*Kaplan-Meier estimate of the survival function.* The Kaplan-Meier estimate of the survival function (Kaplan and Meier, 1958) was plotted for any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and the other diseases. The slope of the survival functions estimate the daily rate (i.e. proportion) of pigs first diagnosed over the course of the performance test.

*Model.* Variance components, and breed and environmental effects, for resistance to any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea, and the other diseases were estimated by fitting a Weibull, sire-dam frailty model to the times until first diagnosis for each disease category (after Ducrocq and Casella, 1996). In the Weibull, sire-dam frailty model, the hazard function for time, \( t \), from the start of the performance test until first diagnosis of pig \( i \), conditional on random effects, is given by

\[
\lambda_i(t | u) = \lambda_0(t) \exp(\mathbf{x}_i(t)' \mathbf{b} + \mathbf{z}_i(t)' \mathbf{u}),
\]

where the baseline hazard function, \( \lambda_0(t) \), is assumed to be Weibull distributed [i.e. \( \lambda_0(t) = \rho(t)^{\beta_1} \)], \( \mathbf{x}_i(t) \) and \( \mathbf{z}_i(t) \) are vectors of time-independent and/or time-dependent covariates with associated fixed (\( \mathbf{b} \)) and random (\( \mathbf{u} \)) effects, and \( \lambda \) and \( \rho \) are parameters of the Weibull distribution. The hazard for time until first diagnosis of pig \( i \), describes the instantaneous probability (i.e. risk) of it being diagnosed at time \( t \), conditional upon it not being diagnosed up to \( t \). Modelling the hazard of the pigs accounted for the performance test of the pigs (i.e. period of risk) varying from 7 to 123 days and enabled censored observations (i.e. pigs that were not diagnosed during the performance test) and time-dependent effects to be included in the analyses.

The Weibull, sire-dam frailty model fitted to the times until first diagnosis for each disease category was:

\[
\begin{align*}
\lambda_i(t | v, a) &= \lambda_0(t) \exp[\tau_i(t) + \mathbf{m}_i + \delta_i + \kappa_m + \phi_q(t) + \eta(t) + \theta_g + (a_{i,t} + a_{i,d})]\quad (1)
\end{align*}
\]

with equation symbols defined as follows.

\( \tau_i(t) \) = time-dependent piece-wise constant function, which changed when pig \( i \) was in the \( j \)th pre-defined period of the performance test. The \( j \) pre-defined periods differed when the model was fitted to any clinical or subclinical disease (i.e. periods were between days 1-6, 7-16, 17-57, and \( \geq 58 \)), lameness (days 1-6, 7-17, 18-73, and \( \geq 74 \)), respiratory diseases (days 1-6, 7-17, 18-45, and \( \geq 46 \)), diarrhoea (days 1-6, 7-15, and \( \geq 16 \)), and the other diseases (days 1-6, 7-17, 18-65, and \( \geq 66 \)). By fitting the piece-wise constant function, the Weibull distribution was an appropriate fit of \( \lambda_i(t) \) over the course of the performance test.

\( \delta_i \) = time-independent fixed effect of the \( i \)th disease category.

\( \kappa_m \) = time-independent fixed effect of the \( m \)th stall group in which pig \( i \) was performance tested \((m = 1, \ldots, 134) \).

\( \phi_q(t) \) = time-dependent fixed effect of the \( q \)th pen group in which pig \( i \) was performance tested \((q = 1, \ldots, 1053) \).

\( \beta_1 \) = regression coefficient associated with \( \eta(t) \).

\( \eta^2(t) \) = square of \( \eta(t) \). The square of the number of diagnosed pigs was only included when the model was fitted to any clinical or subclinical disease and respiratory diseases.

\( \beta_2 \) = regression coefficient associated with \( \eta^2(t) \).

\( \theta_g \) = time-independent random effect of the \( g \)th pen group in which pig \( i \) was performance tested \((g = 1, \ldots, 1053) \). The vector of pen group effects, \( v = (\theta_1, \ldots, \theta_{1053}) \).
\(\theta_{(053)}\), was assumed to be iid and follow a log-gamma distribution (–log-gamma(\(\gamma, \gamma\)), where \(\gamma\) is the parameter of the log-gamma distribution).

\(\frac{1}{2}(a_{s} + a_{d})\) = time-independent random effect, where \(a_{s}\) and \(a_{d}\) are the breeding values of sire, \(s\), and dam, \(d\), of pig \(i\). The vector of sire and dam breeding values, \(\mathbf{a} = (a_{1}, ..., a_{8136})\), was assumed to follow a normal distribution (~\(N(0, A\sigma_{a}^2)\)), where \(A\) is the numerator relationship matrix).

In this model, exp\{\(\theta_{i} + \frac{1}{2}(a_{s} + a_{d})\}\} is the frailty variable of pig \(i\), while the log-frailty variable is \(\theta_{i} + \frac{1}{2}(a_{s} + a_{d})\). The model was fitted using ‘The Survival Kit’ developed by Ducrocq and Sölkner (1998).

Model (1) was fitted to each disease category after the following preliminary analyses.

Validation of the Weibull baseline hazard assumption and establishment of the \(j\) pre-defined periods of the performance test (i.e. when including the time-dependent piece-wise constant function, \(\tau(t)\)) were carried out empirically (Kalbfleisch and Prentice, 1980). Specifically, a semi-parametric Cox model (Cox, 1972) was fitted to the times until first diagnosis. The model included the fixed and regression effects included in model (1) (i.e. excluded the random pen group effects and random breeding values of the sires and dams) and the distribution of \(\lambda_{0}(t)\) was not specified [i.e. \(\lambda_{0}(t)\) was arbitrarily defined]. Solving for the fixed and regression effects enabled \(\lambda_{0}(t)\) and the interrelated baseline survival function, \(S_{0}(t)\), to be evaluated. A graphical test for the suitability of a Weibull distribution (i.e. plot of \(\ln[-\ln[S_{0}(t)]\]) against \(\ln(t)\) produces a straight line) demonstrated that the Weibull distribution was an appropriate fit of \(\lambda_{0}(t)\) when the performance test was divided into the \(j\) pre-defined periods.

The fixed and regression effects included in model (1) were arrived at through backward elimination of non-significant effects (Myers, 1989) from a Weibull model. The Weibull model included all available fixed and regression effects (i.e. piece-wise constant function, breed, breeding farm, stall group, treatment level, and number and square of the number of diagnosed pigs), but no random effects. The test criterion was the difference in –2ln(L (L = likelihood)) between a full and a reduced model, where the full model was the Weibull model following each round of elimination, and the reduced model was the full model following each round of elimination with the effect being assessed removed. The critical \(\chi^2\)-value for elimination was \(\chi^2_{\text{uav}}\) with \(P > 0.10\), where \(\chi^2_{\text{uav}}\) is the \(\chi^2\)-value of the \(w\)th effect with \(v\) d.f. The \(\chi^2\)-values and associated d.f. for significant fixed and regression effects (i.e. fixed and regression effects included in model (1)) are presented in Table 2. These values were obtained for each effect as the difference in –2lnL when the effect was removed from the Weibull model after non-significant fixed and regression effects had been eliminated.

Pig \(i\) was considered treated for 2 days following treatment (i.e. when including the fixed effect of treatment level, \(\Phi_{w}(t)\), in model (1) fitted to respiratory diseases and diarrhoea) for two reasons. First, veterinarians working at Bøgildgård advised that the pigs be considered treated for 2 days following treatment. Second, when treatment level was included in a Weibull model fitted to the times until first diagnosis (i.e. model (1) without the random pen group effects and random breeding values of the sires and dams), considering pig \(i\)

<table>
<thead>
<tr>
<th></th>
<th>Any disease</th>
<th>Lameness</th>
<th>Respiratory</th>
<th>Diarrhoea</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>d.f.</td>
<td>(\chi^2)</td>
<td>d.f.</td>
<td>(\chi^2)</td>
<td>d.f.</td>
</tr>
<tr>
<td>Piece-wise constant</td>
<td>3</td>
<td>434·6</td>
<td>3</td>
<td>275·0</td>
<td>3</td>
</tr>
<tr>
<td>Breed</td>
<td>3</td>
<td>78·2</td>
<td>3</td>
<td>25·0</td>
<td>3</td>
</tr>
<tr>
<td>Breeding farm</td>
<td>48</td>
<td>66·6</td>
<td>48</td>
<td>63·3</td>
<td>45</td>
</tr>
<tr>
<td>Stall group</td>
<td>133</td>
<td>593·3</td>
<td>133</td>
<td>311·8</td>
<td>97</td>
</tr>
<tr>
<td>Treatment</td>
<td>1</td>
<td>186·0</td>
<td>1</td>
<td>177·0</td>
<td>1</td>
</tr>
<tr>
<td>No. diagnosed</td>
<td>1</td>
<td>39·0</td>
<td>1</td>
<td>104·4</td>
<td></td>
</tr>
<tr>
<td>(No. diagnosed)²</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† Some levels of the fixed breeding farm and stall group effects were not estimable for respiratory diseases, diarrhoea, and the other diseases because no pigs in these levels were diagnosed.
Genetic variation of disease resistance in growing pigs

Additive genetic variation. Additive genetic variation was estimated as the variance of log-frailty associated with the random breeding values of the sires and dams ($\sigma^2_a$). A heritability was estimated by noting that model (1) is also a log-linear model when no time-dependent effects are included (cf. Kalbfleisch and Prentice, 1980; Ducrocq and Casella, 1996). Hence, the heritability was presented for the time until diagnosis on the logarithmic-time scale as if there were no time-dependent effects. It was calculated as:

$$h^2_{log} = \frac{\sigma^2_a}{\frac{1}{2}\sigma^2_a + \psi^{(1)}(\gamma) + \pi^2/6}$$

(after Ducrocq and Casella, 1996), where $\psi^{(1)}(\gamma)$ is the variance of log-frailty associated with the random pen group effects, $\psi^{(1)}(.)$ is a trigamma function, and $\pi^2/6$ is the error variance of an extreme value distribution. Other definitions of heritability for Weibull distributed traits have also been proposed (e.g. Korsgaard et al., 1999; Yazdi et al., 2000).

To illustrate the additive genetic variation for resistance to clinical and subclinical diseases in the nucleus breeding population, predicted survival functions were plotted for resistance to any clinical or subclinical disease. Specifically, a predicted survival function of pigs expected from mating a sire and dam with high resistance to any clinical or subclinical disease was plotted alongside a predicted survival function of pigs expected from mating a sire and dam with low resistance. The survival functions were obtained using solutions to model (1) fitted to any clinical or subclinical disease. The sires and dams were chosen after ranking them by predicted breeding values. The sires and dams with high resistance were chosen from the 90th percentile, while the sires and dams with low resistance were chosen from the 10th percentile. Two assumptions were made. First, the pigs were assumed to be from the same breed, and performance tested under identical environmental conditions (i.e. fixed, regression, and random effects were the same, with the exception of the predicted breeding values of the sires and dams). Second, the risk of a diagnosed disease was assumed to be high (i.e. there were always diagnosed pigs in the same stall and/or pen group).

Correlation among predicted breeding values. Genetic correlations among the resistances to any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea, and the other diseases were approximated as product-moment correlations among the predicted breeding values (i.e. solutions to model (1)) of sires with more than 40 offspring. Sires with more than 40 offspring were chosen for two reasons. First, product-moment correlations of the same sign and similar magnitude were obtained when correlating the predicted breeding values of all sires and dams, and when correlating the predicted breeding values of sires with more than 10, 20, and 30 offspring. Second, product-moment correlations obtained using sires with more than 40 offspring were considered more reliable approximations of the genetic correlations than the product-moment correlations using sires (and dams) with less than 40 offspring.

Breed and environmental effects. The levels of the breed and environmental effects are presented for each disease category as their relative effects on the hazard. Specifically, the effects of the Duroc, Yorkshire, Landrace, and Hampshire breeds on the hazard are presented relative to the Duroc breed as $\exp(\sigma_1 - \sigma_{Duroc})$, where $\sigma_1$ is the effect of the Duroc breed, $\sigma_{Duroc}$ is the effect of the Duroc breed. The effect of treatment level is presented as $\exp(\phi_{\text{treated}} - \phi_{\text{untreated}})$, where $\phi_{\text{treated}}$ and $\phi_{\text{untreated}}$ are the treatment and non-treatment effects. Differences among the breed and treatment level effects were tested for significance by $\chi^2$-test. That is, the difference between the $i$th and $v$th breeds or treatment levels was tested by fitting model (1) with the $i$th breed or treatment level effect constrained to zero. The difference was significant ($P < 0.05$) when $\chi^2 > 3.8$, where $\chi^2$ is the $\chi^2$-value of the $i$th breed or treatment level effect with 1 d.f.

For the breeding farm and stall group effects, a range is presented by ranking the effects and calculating $\exp(\alpha_{\text{high}} - \alpha_{\text{low}})$, where $\alpha_{\text{high}}$ is the mean of the highest 25th percentile of effects and $\alpha_{\text{low}}$ is mean of the lowest 25th percentile. The effect of the number of diagnosed pigs on the hazard was presented by plotting the function $f(\eta) = \exp(\eta \beta_1 + \eta^2 \beta_2)$ against $\eta$, where $\eta$ is the number of diagnosed pigs, and $\beta_1$ and $\beta_2$ are the regression coefficients associated with $\eta$ and $\eta^2$.

Results

Incidence of disease

A total of 3 256 (24.0%) of the 13 551 pigs were diagnosed with at least one clinical or subclinical
Table 3  Number of growing pigs (from a total of 13 551) that were diagnosed for five categories of clinical and subclinical diseases, the average number of days taken for those pigs that were diagnosed for each category of disease to be diagnosed, and estimates of variance components. The disease categories are any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and other diseases. The variance components are additive genetic variance ($\sigma^2_a$ ± standard error) and pen group variance ($\psi(1)(\gamma)$) for log-frailty. A heritability ($h^2_{\log}$) for resistance to each disease category is presented for the time until diagnosis on the logarithmic-time scale.

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>No. diagnosed</th>
<th>Days to first diagnosis</th>
<th>$\sigma^2_a$ ± standard error</th>
<th>$\psi(1)(\gamma)$</th>
<th>$h^2_{\log}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any disease</td>
<td>3256</td>
<td>39</td>
<td>0.18 ± 0.05</td>
<td>0.01</td>
<td>0.10</td>
</tr>
<tr>
<td>Lameness</td>
<td>1351</td>
<td>46</td>
<td>0.29 ± 0.11</td>
<td>0.04</td>
<td>0.16</td>
</tr>
<tr>
<td>Respiratory</td>
<td>697</td>
<td>55</td>
<td>0.24 ± 0.16</td>
<td>0.21</td>
<td>0.12</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>428</td>
<td>28</td>
<td>0.30 ± 0.27</td>
<td>0.10</td>
<td>0.16</td>
</tr>
<tr>
<td>Other</td>
<td>1174</td>
<td>33</td>
<td>0.34 ± 0.15</td>
<td>0.00</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Figure 3  Kaplan-Meier estimate of the survival function for first diagnosis of growing pigs with any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and other diseases during performance test. The survival functions represent resistance of the pigs (i.e. proportion not diagnosed on each day of the performance test).

As an illustration of the additive genetic variation, there was a large difference in the predicted survival functions of pigs expected from mating sires and dams with high and low resistance to any clinical or subclinical disease (Figure 4). Approximately half of the pigs from the sire and dam with high resistance were predicted to be diagnosed with any clinical or subclinical disease during the performance test. On the other hand, approximately 70% of the pigs from the sire and dam with low resistance were predicted to be diagnosed.

Correlation among predicted breeding values
There were generally favourable correlations among the predicted breeding values for resistance to any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and the other diseases (Table 4). Correlations between the predicted breeding values for any clinical or subclinical disease and the predicted breeding values for lameness, respiratory diseases, diarrhoea and the other diseases were...
Genetic variation of disease resistance in growing pigs

Figure 4 Predicted survival function of growing pigs expected from mating a sire and dam with high resistance to any clinical or subclinical disease plotted alongside the predicted function of pigs expected from mating a sire and dam with low resistance. The survival functions represent resistance of the pigs (i.e. proportion not diagnosed on each day of the performance test).

Table 4 Product-moment correlations among predicted breeding values for resistance of growing pigs to any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and other diseases

<table>
<thead>
<tr>
<th></th>
<th>Lameness</th>
<th>Respiratory</th>
<th>Diarrhoea</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any disease</td>
<td>0.65</td>
<td>0.52</td>
<td>0.32</td>
<td>0.59</td>
</tr>
<tr>
<td>Lameness</td>
<td>0.24</td>
<td>0.08</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>–0.03</td>
<td>0.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

positive and moderately large (0.32 to 0.65). By contrast, correlations among the predicted breeding values for lameness, respiratory diseases, diarrhoea, and the other diseases were positive but weak (0.04 to 0.24). The only exception was the correlation between the predicted breeding values for respiratory diseases and diarrhoea, which was negative and weak (–0.03).

Breed effects

Pigs from the Duroc and Yorkshire breeds were generally more resistant to the clinical and subclinical diseases than pigs from the Landrace and Hampshire breeds (Table 5). Specifically, the hazard of the Duroc and Yorkshire breeds for any clinical or subclinical disease, lameness, respiratory diseases and the other diseases was 1.4 to 3.0 times lower than the hazard of the Landrace and Hampshire breeds. The only exception was diarrhoea, where pigs from the Landrace breed tended to be more resistant. The hazard of the Landrace breed for diarrhoea was 1.8 and 2.2 times lower than the hazard of the Yorkshire and Hampshire breeds. However, the hazard of the Duroc breed was not significantly higher than that of the Landrace breed and the hazards of the Duroc, Yorkshire, and Hampshire breeds were not significantly different.

Environmental effects

There was a large range among the breeding farm and stall group effects. For the breeding farm effects, there was a 1.6-fold difference between the hazard of the highest and lowest 25th percentile means for any clinical or subclinical disease. A larger difference was found for lameness (2.0-fold difference), diarrhoea (3.4) and the other diseases (2.3). Similarly, for the stall group effects, there was a 3.7-fold difference between the hazard of the highest and lowest 25th percentile means for any clinical or subclinical disease and a larger difference for lameness (4.1), respiratory diseases (11.4), diarrhoea (11.2), and the other diseases (6.8).

The hazard for respiratory diseases and diarrhoea was 1.6 and 7.0 times lower (P < 0.05) when the pigs

Table 5 Effect of Duroc, Yorkshire, Landrace and Hampshire breeds on the hazard for time until diagnosis of growing pigs with five categories of clinical and subclinical diseases during performance test. The disease categories are any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and other diseases. The effect of each breed on the hazard is presented relative to the Duroc breed†

<table>
<thead>
<tr>
<th></th>
<th>Any disease</th>
<th>Lameness</th>
<th>Respiratory</th>
<th>Diarrhoea‡</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duroc</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Yorkshire</td>
<td>1.05</td>
<td>0.77</td>
<td>1.15</td>
<td>1.25</td>
<td>1.17</td>
</tr>
<tr>
<td>Landrace</td>
<td>1.52</td>
<td>1.37</td>
<td>2.07</td>
<td>0.63</td>
<td>2.16</td>
</tr>
<tr>
<td>Hampshire</td>
<td>1.92</td>
<td>1.57</td>
<td>2.99</td>
<td>1.44</td>
<td>1.66</td>
</tr>
</tbody>
</table>

† Values in the same column with different superscripts are significantly different (P < 0.05).
‡ Differences between the Landrace and Yorkshire breeds (P = 0.06), and the Landrace and Hampshire breeds (P = 0.08), were approaching significance for diarrhoea.
The hazard for any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and the other diseases increased with the number of diagnosed pigs in the stall and/or pen groups (Figure 5). However, there were two distinct differences among the disease categories. First, the effect of the number of diagnosed pigs on the hazard was largest for lameness, for which the hazard was increased 29-fold when six pigs in a pen were diagnosed with lameness. Diagnosed pigs increased the hazard by up to 11-fold for respiratory diseases and by up to between five- and six-fold for any clinical or subclinical disease, diarrhoea, and the other diseases. Second, there was a diminishing effect on the hazard for any clinical or subclinical disease and respiratory diseases as the number of diagnosed pigs in a stall increased, and the effect on the hazard reached a plateau (i.e. as the number of diagnosed pigs increased, the effect of an additional diagnosed pig on the hazard was lower than the effect of the previous diagnosed pig). A diminishing effect was not apparent for lameness, diarrhoea, and the other diseases. Instead, for these disease categories, there was an increasing effect on the hazard as the number of diagnosed pigs in a pen increased (i.e. as the number of diagnosed pigs increased, the effect of an additional diagnosed pig on the hazard was higher than the effect of the previous diagnosed pig).

The pen group variation for log-frailty was larger for respiratory diseases (0.21) and diarrhoea (0.10) than for any clinical or subclinical disease, lameness and the other diseases (0.00 to 0.04) (Table 3).

### Discussion

This study established that additive genetic variation for resistance to clinical and subclinical diseases exists in growing pigs. Additive genetic variation was detected for resistance to any clinical or subclinical disease, lameness, respiratory diseases, diarrhoea and the other diseases and there were generally favourable correlations among the predicted breeding values for resistance to these disease categories. These results indicate that selection of pigs for resistance to clinical and subclinical diseases could be successful.

The additive genetic variation detected in the nucleus breeding population indicates that there were genes within the population that conveyed resistance to the pathogens encountered during the production test. However, the pathogens encountered, and the immunological mechanisms controlled by these genes to resist infection, remain unclear. All forms of micro-organisms (i.e. bacteria, virus, and protozoa) may have been encountered, and the mechanisms of resistance could have involved all aspects of the immune system (i.e. innate and/or acquired immunity). Despite this uncertainty, there was presumably greater variation in the pathogens encountered among disease categories than there was within the categories. For this reason, it was not surprising to find that the additive genetic variation and heritability for resistance to any clinical or subclinical disease were lower than the additive genetic variation and heritabilities for the resistances to lameness, respiratory diseases, diarrhoea and the other diseases.

Favourable and moderately-strong correlations were found between the predicted breeding values for resistance to any clinical or subclinical disease and the predicted breeding values for lameness, respiratory diseases, diarrhoea and the other diseases. These correlations existed because resistance to any clinical or subclinical disease was a composite of the resistances to lameness, respiratory diseases, diarrhoea and the other diseases and because of the generally favourable correlations among the predicted breeding values for lameness, respiratory diseases, diarrhoea and the other diseases. This result could have particular implications for selective breeding programmes with...
pigs. In such programmes, selection may need only be placed on resistance to any clinical or subclinical disease for there to be simultaneous and favourable responses in the resistance of the pigs to lameness, respiratory diseases, diarrhoea and the other diseases.

The correlations among the predicted breeding values are approximations of the genetic correlations and should be interpreted accordingly for two reasons. First, strong assumptions were made when calculating these approximations, most notably independence among residual terms. This assumption was unlikely to hold, given that the same pigs were used to assess resistance to each disease category. Second, the predicted breeding values were estimated with uncertainty, suggesting that the correlations among the predicted breeding values underestimated the genetic correlations. Despite these drawbacks, while multivariate Weibull frailty models remain undeveloped (Ducrocq, 1999), ad hoc methods, such as correlations among predicted breeding values, remain the only alternative to approximate genetic correlations.

Assessing resistance to clinical and subclinical disease has the drawback that the outcome of infection can be caused by many different pathogens and much of the variation for resistance among pigs is due to environmental factors. A complementary approach to increase the reliability of resistance estimates could involve indirect, multitrait selection for phenotypes reflecting variation in the immunocompetence of the pigs (e.g. antibody and cell-mediated immune response). Such phenotypes would need to be well defined, accurately measured, heritable and highly correlated with the incidence of clinical and subclinical disease. As yet, no suitable phenotypes have been identified, although pigs performance tested at Bøgildgård are currently being tested to identify such phenotypes.

There are two areas that require consideration before resistance to clinical and subclinical diseases is included in breeding programmes for pigs. First, although there were generally favourable correlations among the predicted breeding values for each of the disease categories, it may be unrealistic to hope to achieve resistance to all forms of disease. Diseases differ in their aetiologies, each requiring a different mechanism of immunity on the part of the pigs to prevent infection and there is evidence to suggest that some of these mechanisms of immunity may be negatively intercorrelated (cf. Biozzi et al., 1982). Second, during selection of pigs resistant to a pathogen, the pathogen is likely to evolve to survive in the pig (Nicholas, 1987). Increased resistance in the pathogen may offset at least some of the progress made in the resistance of the pigs. These two considerations are certain to make selective breeding for resistance challenging.

The Kaplan-Meier estimate of the survival function demonstrated that the daily rate of pigs first diagnosed for each disease category was highest between days 7 and 18 (approx.) of the performance test. This period followed transfer of the pigs from the acclimatization pens to the test facility, where pigs from different acclimatization pens were mixed together in the same pen group. Such a practice could have increased the risk of diagnosed disease in two ways. First, both transfer to a new environment and mixing of pigs are stressors that have a detrimental effect on the immunocompetence of pigs (Curtis and Backstrom, 1992). Second, the mixing of pigs could have increased the risk of infection by bringing together pigs from acclimatization pens where pathogens were encountered, and pigs from acclimatization pens where such pathogens were not present.

Pigs from Duroc and Yorkshire breeds were more resistant to the clinical and subclinical diseases than pigs from the Landrace and Hampshire breeds. The only exception was diarrhoea, where pigs from the Landrace breed tended to be most resistant. These findings suggest that there were genes specific to Duroc and Yorkshire breeds that provided greater resistance against the pathogens encountered during the performance test. Breed differences for resistance to respiratory diseases and diarrhoea have also been reported in previous studies (e.g. Lundehem, 1979 and 1988; Straw et al., 1983 and 1984; Jørgensen, 1992). However, the rank of the breeds for resistance in these studies varied, and in turn differed from the rank found for the nucleus breeding population in the present study. The differences in rank were presumably because the pigs were reared under different environmental conditions and management practices, and were exposed to different pathogens. Therefore, breed differences for resistance to clinical and subclinical diseases appear to exist in pigs, although the relative resistance of the breeds is dependent upon environmental conditions and management practices, and the pathogens to which they are exposed.

The most important environmental effects affecting the hazard for each disease category were the breeding farm (with the exception of respiratory diseases) and stall group effects, and the number of diagnosed pigs in the stall and/or pen groups. The breeding farm effects were important presumably because pigs from different breeding farms differed
in immune status (i.e. pigs bred on different breeding farms were exposed to different pathogens, causing variation for resistance to specific pathogens among the farms). The stall group effects and the number of diagnosed pigs were important as they represent exposure of the pigs to pathogens during the performance test.

The increase in hazard with the number of diagnosed pigs in the stall and/or pen groups is of particular interest for breeding programmes for resistance. It indicates that a successful breeding programme for resistance would not only reduce the number of diagnosed pigs at any time but simultaneously reduce the risk of susceptible pigs being diagnosed (cf. Knap and Bishop, 2000). In this way, breeding for resistance may have a dramatic impact on the incidence of clinical and subclinical diseases at the population level, whereby the population could carry a sizeable proportion of susceptible pigs without the risk of disease outbreak.

The additive genetic variation for resistance to clinical and subclinical diseases detected in this study demonstrates that selective breeding could be successful, providing a complementary approach to disease control in pig production. Pigs selectively bred for resistance may provide additional benefits by reducing the reliance on current methods of disease control, in particular, vaccines, medicines, and animal culling.

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References


Genetic variation of disease resistance in growing pigs


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