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# Application of multiblock modelling to identify key drivers for antimicrobial use in pig production in four European countries

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## Abstract

Antimicrobial use in pig farming is influenced by a range of risk factors, including herd characteristics, biosecurity level, farm performance, occurrence of clinical signs and vaccination scheme, as well as farmers' attitudes and habits towards antimicrobial use. So far, the effect of these risk factors has been explored separately. Using an innovative method called multiblock partial least-squares regression, this study aimed to investigate, in a sample of 207 farrow-to-finish farms from Belgium, France, Germany and Sweden, the relative importance of the six above mentioned categories or 'blocks' of risk factors for antimicrobial use in pig production. Four country separate models were developed; they showed that all six blocks provided useful contribution to explaining antimicrobial use in at least one country. The occurrence of clinical signs, especially of respiratory and nervous diseases in fatteners, was one of the largest contributing blocks in all four countries, whereas the effect of the other blocks differed between countries. In terms of risk management, it suggests that a holistic and country-specific mitigation strategy is likely to be more effective. However, further research is needed to validate our findings in larger and more representative samples, as well as in other countries.

## Introduction

Because of the rising threat from antimicrobial resistance (AMR), livestock farmers are strongly encouraged to reduce their antimicrobial usage [1, 2]. Pig farming in particular contributes to an important part of overall veterinary antimicrobial usage [3]. Previous research has demonstrated that antimicrobial usage in food-producing animals is influenced by different categories of risk factors. First, the herd health status significantly influences the need for antimicrobial treatments, and the observation of clinical signs was reported as the main risk factor for farmers to initiate antimicrobial treatment [4]. In pig medicine, gastro-intestinal disorders in weaners and fatteners, respiratory clinical signs in fatteners as well as lameness and reproductive clinical signs in sows represent major indications for antimicrobial treatments [5, 6]. Antimicrobial usage is also likely influenced by the herd vaccination scheme; for example, Raith *et al.* showed a significant effect of porcine circovirus type 2 vaccination on the reduction of antimicrobial use at farm level [7].

However, non-medical risk factors are also playing a role. Herd characteristics, such as farm size, production type or management (e.g. farrowing rhythm) were shown to be significantly associated with the amount of antimicrobials used in a herd [8, 9]. Farm management practices, especially those related with internal and external biosecurity, also have an impact; the higher the level of biosecurity in a herd, the lower the antimicrobial usage [10]. However, the association between the level of therapeutic antimicrobial usage in a herd and the farm technical performances is not very strong [9, 10]. Recent studies have also looked at the influence of farmers' attitudes and habits towards antimicrobial usage [11, 12]. Farmers who believed more strongly in their ability to reduce antimicrobial usage had higher intention to reduce it [13], and farmers who perceived higher risk of using antimicrobials had lower actual antimicrobial usage [14]. The social context and the professional network of the farmer, especially the relationship with the herd veterinarian or technical advisor, also strongly influences the farmer's practices in terms of antimicrobial treatments [15].



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In brief, previous literature has shown that antimicrobial usage in livestock is influenced by a range of risk factors, namely herd characteristics, biosecurity level, occurrence of clinical signs and vaccination scheme, as well as the farmer's attitudes and habits towards antimicrobial usage. Especially two studies conducted by Postma *et al.* and Visschers *et al.* as part of the European research project MINAPIG investigated, in a sample of farrow-to-finish pig farms located in Belgium, France, Germany and Sweden, the influence of technical [8], as well as social and psychological risk factors [14] on antimicrobial usage in pig production. However, little is known about the relative importance of the different categories of risk factors to explain antimicrobial usage in pig production.

The objective of this study was to investigate, within the same sample of farrow-to-finish pig farms previously used by Postma *et al.* and Visschers *et al.*, the relative importance of different categories of risk factors for antimicrobial usage in pig production, by using an innovative statistical analysis method called multi-block partial least-squares (*mbPLS*) regression. We especially explored the following research questions: (i) which category (ies) of risk factors are mainly associated with overall antimicrobial usage in each country and (ii) within each category, which risk factors mainly explain antimicrobial usage.

## Methods

### Study design

A cross-sectional study was conducted among 227 farrow-to-finish pig farms located in Belgium ($n = 47$), France ($n = 60$), Germany ($n = 60$) and Sweden ($n = 60$) between December 2012 and January 2014. Recruitment of farm is described by Postma *et al.* [8]. Briefly, a convenient sample of farms willing to participate and having more than 70 sows and 500 finishers produced annually was enrolled in the study. Each farm was visited once and data collected using a harmonised procedure prepared in collaboration within the research consortium. Collected data related to antimicrobial usage, herd characteristics and technical performance, biosecurity practices, occurrence of selected clinical signs of disease, vaccination scheme and farmers' attitudes and habits towards antimicrobial usage.

### Antimicrobial usage data

Detailed description of antimicrobial usage data collection is provided by Sjölund *et al.* [16]. Briefly, antimicrobial usage data of participating farms were collected for 1 year preceding the farm visit in Belgium, Germany and Sweden and for the last batch in France, using invoices from veterinarians and feed companies, farmers' treatment records or farmers' directed interview. Collected data included the product commercial name, total volume or mass, concentration of active substance and target animal age category. In each herd, the average number of animals of each age category present in a batch was estimated using data from the herd management information system.

Antimicrobial usage was expressed in terms of 'treatment incidence' (TI) that represents the number of animals per 1000 receiving a daily dose of an antimicrobial during their production period [17]. The TI was calculated using standardised daily doses as defined by Postma *et al.* [18] and harmonised weights at treatment [16]. For each farm were computed separately the TI of sucklers, weaners, fatteners and sows/gilts, the TI of oral and parenteral antimicrobial treatments, the TI of macrolides and the TI of cephalosporins/fluoroquinolones treatments; the latter antimicrobial classes were considered of special interest as they are considered as highest priority critically important for human medicine by the World Health Organization [19]. Glycopeptides are not licensed for use in pig production in the European Union and were therefore not included in the analysis. Topical antimicrobial treatments were excluded from the analysis because they represented a negligible part of total antimicrobial usage [16].

### Herd characteristics and technical performances

Herd characteristics were collected using farmer's interviews and included information on the farm management, i.e. number of present sows, number of employees per 100 sows, farrowing rhythm, weaning age and post-weaning use of zinc oxide, as well as information on the farmer, i.e. age, years of experience with pig farming and highest educational level.

Technical performance data included both production (i.e. mortality rates, daily weight gain and feed conversion ratio) and reproductive (i.e. number of litters and weaned pigs per sow and per year) performance and were retrieved from the farm management system or via farmer's interviews.

### Data on biosecurity practices

Farm biosecurity status was described using the risk-based Biocheck.UGent™ scoring system [20]. A farm visit together with farmer's interview was used to complete a questionnaire that provided detailed description of farms' practices to prevent pathogens from entering into the farm (i.e. external biosecurity) and to spread within the farm once they entered (i.e. internal biosecurity). Scores between 0 and 100 were then computed for six sub-categories each of external and internal biosecurity practices [8, 21].

### Occurrence of clinical signs and vaccination scheme

Farmers were asked to indicate on a scale from 1 (never) to 5 (every batch) whether they had to treat their sucklers, weaners, fatteners and sows because of lameness, gastro-intestinal, respiratory or nervous clinical signs, and their sows because of metritis or mastitis. The information was provided for the year preceding the farm visit, and was used as a proxy for the occurrence of clinical signs at the farm. Vaccination scheme at the time of the visit was also collected; farmers reported whether they were implementing vaccination against porcine parvovirus, *Escherichia coli*, *Clostridium* spp., atrophic rhinitis, porcine reproductive and respiratory syndrome virus (PRRS), influenza virus, *Mycoplasma hyopneumoniae*, *Actinobacillus pleuropneumoniae* and porcine circovirus type 2.

### Farmers' attitudes and habits towards antimicrobial usage

The collection of data related to farmers' attitudes and habits towards antimicrobial usage was already described by Visschers *et al.* [22]. Briefly, a seven-page questionnaire was sent to each farmer and collected during the farm visit. Questionnaire items were assessed on six-point Likert scales and were grouped into eight constructs exploring the farmer's worries about infectious diseases in the pigs, worries about AMR and worries about

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financial/legal issues, the farmer's perceived benefits of, need for and risks of using antimicrobials in pig production and the farmer's perceptions of the role of the veterinarian and feed expert regarding the reduction of antimicrobial usage [13, 22]. After checking the internal reliabilities of the items per construct (i.e. Cronbach $\alpha > 0.5$), mean scores over the items were calculated per constructs and used in all further analyses. Two items related to the farmers' habits towards antimicrobial usage ('I only administer antimicrobials to diseased pigs after having consulted my veterinarian' and 'All administrations of drugs are recorded and archived in my farm') had poor internal reliability and were included as individual items in further analysis. Although farmers have to record every antimicrobial treatment administered to their pigs in accordance with the EU legislation, in practice this is not done systematically (especially individual treatments are sometimes missing). The item 'All administrations of drugs are recorded and archived in my farm' was therefore included to test the underlying assumption that farmers recording every antimicrobial administration were paying more attention to their antimicrobial usage, and potentially used fewer or less important antimicrobials than the other farmers.

## Data analysis

### *Principle of* mbPLS *regression*

Data were analysed using a *mbPLS* regression [23]; the method initially used in the field of chemometrics and sensometrics was recently applied to the field of veterinary epidemiology [24, 25]. Briefly, multiblock regressions are especially suitable when data are organised in $(K+1)$ blocks of variables, consisting in a block of several variables to be explained **Y**, and a large number of explanatory variables, i.e. the potential risk factors, organised in $K$ meaningful blocks ($\mathbf{X_1}$; …; $\mathbf{X_k}$).

An overall factor analysis, which reflects the sum of the links between each explanatory block and the response one, is performed to summarise the information contained in each block $\mathbf{X_k}$ into $K$ partial components $t_k$.

$$t_k = \sum_i X_{ki} w_{ki}, \tag{1}$$

where $k$ refers to the block's number, $i$ refers to the variable's number within the block $\mathbf{X_k}$ and $w_{ki}$ to the weight of $X_{ki}$ within $t_k$.

A global component $t$ is later defined as a linear combination of the $t_k$; higher weights $a_k$ are allocated to $t_k$ explaining a bigger proportion of the variability in the block **Y**, and $a_k$ satisfy the condition $\sum_k a_k^2 = 1$. The global component $t$ therefore compiles the information provided by all explanatory variables.

$$t = \sum_k a_k t_k = \sum_k a_k X_k w_k = Xw. \tag{2}$$

Subsequently, a multiple linear regression of **Y** against $t$ is performed:

$$\mathbf{Y} = tc + \varepsilon, \tag{3}$$

where $c$ is the regression coefficient of **Y** upon $t$ and $\varepsilon$ represents the residuals of the regression models [26, 27].

Combining Equations (2) and (3), one can explore the direct relationship between the block **Y** and the explanatory variables of the blocks $\mathbf{X_k}$:

$$\mathbf{Y} = Xwc + \varepsilon. \tag{4}$$

The description of the relationships between explanatory and response blocks via the use of partial and global components is presented in Figure 1.

Compared with traditional linear regression modelling, *mbPLS* regression presents three main advantages: (i) it allows for multiple response variables to be studied simultaneously, (ii) it is stable in case of multicollinearity within explanatory blocks [28], (iii) it allows not only to explore the associations between explanatory and response variables, but also between explanatory and response blocks of variables.

### *Interpretation of* mbPLS *models*

Two interpretation tools called 'block importance index (BlockImp)' and 'variable importance index (VarImp)' describe, respectively, the relative contribution of each explanatory block and each explanatory variable to the explanation of the **Y** block [25, 29]. If $K$ is the number of explanatory blocks, $\text{BlockImp}_k$ is defined as:

$$\text{BlockImp}_k = a_k^2. \tag{5}$$

As previously mentioned, $a_k^2$ satisfies $\sum_k a_k^2 = 1$ (see Equation (2)). $\text{BlockImp}_k$ can therefore be expressed as a percentage [29].

If $P$ is the total number of explanatory variables included in the model, $\text{VarImp}_p$ is defined as

$$\text{VarImp}_p = a_k^2 w_p^2, \tag{6}$$

With $w_p^2$ the squared weight for the explanatory variable $p = (1, \ldots, P)$. After normalisation, $\text{VarImp}_p$ can also be expressed as a percentage [25].

Ninety per cent tolerance intervals around VarImp and BlockImp estimates can also be computed using bootstrap simulation [29].

### *Application to the present study*

The *mbPLS* regression was applied to the present study to achieve two objectives: (i) describe, in each country, the relative contribution of selected explanatory blocks of variables to the explanation of antimicrobial usage (block **Y**) and (ii) identify within each block, the variables mainly contributing to the explanation of antimicrobial usage (block **Y**). Collected data were organised into seven meaningful blocks of variables, namely: a block of response variables (block **Y**) describing the herd level of antimicrobial usage, and six blocks of explanatory variables, i.e. the potential risk factors, that related with the herd characteristics (block $\mathbf{X_1}$), biosecurity scores (block $\mathbf{X_2}$), occurrence of clinical signs (block $\mathbf{X_3}$), vaccination scheme (block $\mathbf{X_4}$), farmer's attitudes and habits (block $\mathbf{X_5}$) and herd technical performance (block $\mathbf{X_6}$). Potential explanatory variables were selected from available data on the basis of the main risk factors reported in the literature [6, 8, 10, 14] and the authors' expertise, as well as univariate screening using generalised linear regression analysis applied to each variable of the block **Y**. The composition of the blocks and the distribution of the potential risk factors in each participating country are presented in Table 1. Only three variables were included in the block $\mathbf{X_6}$ because too many data (>20% of the farms) were missing for the other variables of interest.

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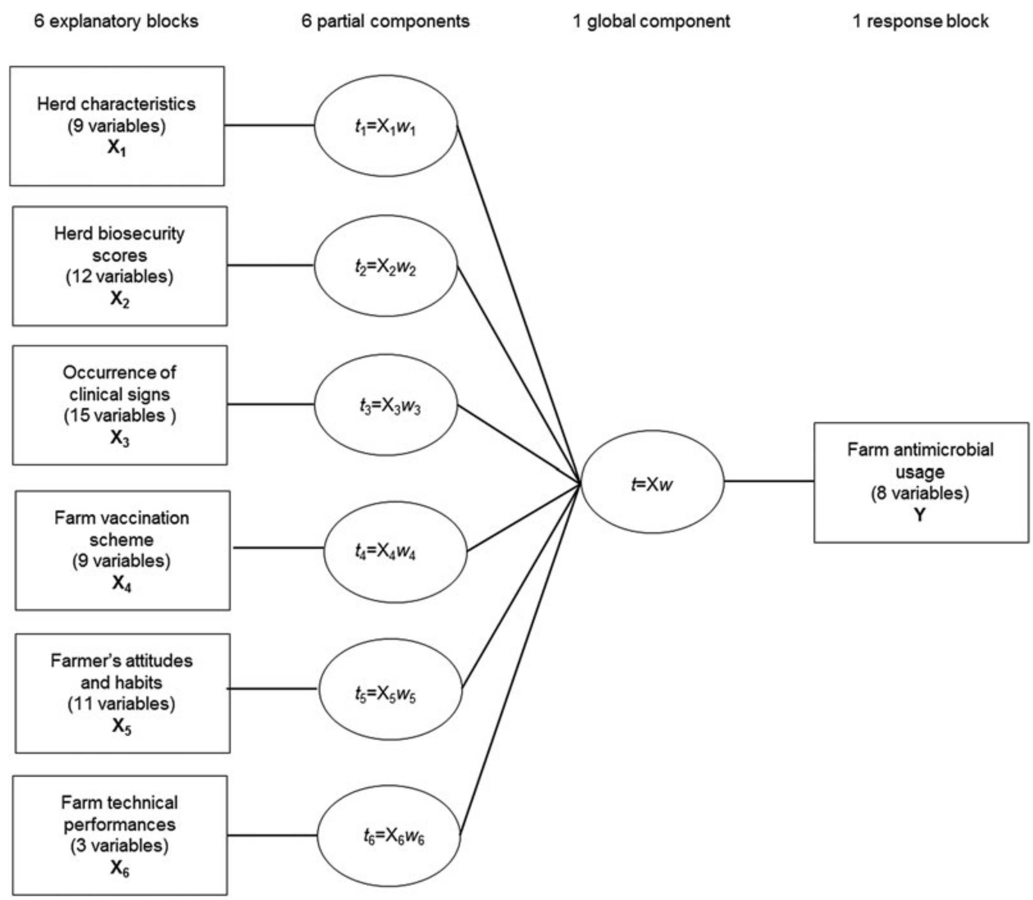


**Fig. 1.** Conceptual scheme of the relationships between explanatory blocks ($\mathbf{X_1}$, …, $\mathbf{X_6}$) and the response block **Y**.

### *Data pre-processing*

The *mbPLS* regression did not allow for missing data in the dataset; 20 farms were therefore excluded from further analysis because they had missing data for an entire explanatory block. Thus, 207 farms, including 38 Belgian, 56 French, 54 German and 59 Swedish farms were included in the models. Remaining farms had sparse missing data for few variables (i.e. <3% of the farms); missing values were imputed using regularised iterative principal component and multiple correspondence analyses algorithms for quantitative and qualitative variables, respectively [30, 31]. Besides, variables of the block **Y** were normalised using logarithm transformation, after adding one to the original variable to adjust for zero values in the data. The herd farrowing rhythm was converted into a dummy variable, using a 3-week system as the reference class. As all variables were expressed in different units, they were column centred and scaled to unit variance.

### *Preliminary study of the relationships between antimicrobial usage variables*

Principal component analyses were first performed in each country-specific model to explore the relationships between the eight variables describing antimicrobial usage within the block **Y** [32]. At the difference of the blocks $\mathbf{X_k}$, multi-collinearity between variables of the block **Y** is desired as it increases the predictive power of the model (i.e. more similar outcomes have to be predicted).

### *Implementation of the multiblock procedure*

Blocks $\mathbf{X_k}$, initially made of a total of 59 potential explanatory variables (Table 1), were defined and included in the model attributing equal weight to every variable in each block and equal weight to every block in the overall model. The VarImp index of the full models (i.e. with 59 explanatory variables) were computed, and following the parsimony principle, only those variables with a contribution >1% to the explanation of the block **Y** were retained in the final, reduced models. The BlockImp and VarImp indexes of the reduced models were then computed, as well as their 90% tolerance intervals using bootstrap simulation with 500 repetitions. The overall model fit was described as the proportion of variance in the block **Y** explained by the model.

Subsequently, non-parametric Friedman rank-sum testing was used within each country to test for differences in BlockImp indexes between blocks (group variable), using the iteration identifier as the blocking variable. Post-hoc comparison was performed using pairwise sign testing with Bonferroni correction for multiple comparisons. The null hypothesis was that each block contributed equally to the explanation of the block **Y**. This analysis was based on the outcomes of a bootstrap simulation with 50 repetitions only, in order to prevent an artificial exaggeration of the statistical power of the study. Statistical analyses were performed in the open-source environment R version 3.3.1 [33].

## Results

### *Relationships between antimicrobial usage variables*

Detailed results of the principal components analyses performed among the **Y** block variables in each participating country are

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**Table 1.** Definition and distribution of the variables included in the *mbPLS* regression

| Definition of variables | % or median (Q25–Q75) | | | |
|---|---|---|---|---|
| | Belgium (*n* = 38 herds) | France (*n* = 56 herds) | Germany (*n* = 54 herds) | Sweden (*n* = 59 herds) |
| **Y** block: farm antimicrobial usage[a] | | | | |
| Treatment incidence in sucklers | 2.11 (1.73–2.36) | 1.18 (0.65–1.87) | 2.14 (1.88–2.59) | 1.73 (1.35–2.06) |
| Treatment incidence in weaners | 2.42 (1.83–2.86) | 2.51 (1.83–2.83) | 2.69 (2.45–3.02) | 0.85 (0.49–1.28) |
| Treatment incidence in fatteners | 1.26 (0.23–1.67) | 0.00 (0.00–0.11) | 1.29 (0.41–1.75) | 0.58 (0.43–0.86) |
| Treatment incidence in sows/gilts | 0.83 (0.39–1.27) | 0.20 (0.10–0.87) | 1.03 (0.66–1.57) | 0.98 (0.75–1.22) |
| Treatment incidence via oral route | 2.51 (1.91–2.85) | 2.57 (1.89–2.84) | 2.73 (2.53–3.03) | 0.52 (0.00–1.12) |
| Treatment incidence via parenteral route | 2.17 (1.86–2.40) | 1.30 (0.86–1.89) | 2.29 (2.02–2.61) | 1.88 (1.52–2.15) |
| Treatment incidence with cephalosporins/fluoroquinolones | 1.50 (0.79–2.10) | 0.10 (0.00–0.62) | 1.11 (0.73–1.43) | 0.00 (0.00–0.24) |
| Treatment incidence with macrolides | 1.50 (0.68–2.23) | 0.05 (0.00–1.97) | 2.06 (0.73–2.45) | 0.23 (0.00–0.93) |
| $\mathbf{X_1}$ block: herd characteristics | | | | |
| Number of present sows | 287 (211–388) | 174 (120–236) | 300 (230–495) | 190 (138–275) |
| Number of employees per 100 present sows | 0.7 (0.5–0.8) | 1.05 (0.9–1.3) | 0.9 (0.6–1.1) | 1.6 (1.2–2.2) |
| Farrowing rhythm | | | | |
| 1–2-week system (%) | 23.7 | 14.3 | 46.3 | 13.6 |
| 3-week system (%) | 26.3 | 53.6 | 42.6 | 18.6 |
| 4–8-week system (%) | 50 | 32.1 | 11.1 | 67.8 |
| Piglets weaning age (days) | 24.0 (21.0–25.0) | 28.0 (21.0–28.0) | 24.0 (21.0–27.0) | 35.0 (33.0–35.0) |
| Farm using zinc oxide at therapeutic dose post-weaning (%) | 10.5 | 1.8 | 7.4 | 42.4 |
| Age of the farmer (years) | 45.5 (33.0–49.0) | 44.5 (41.0–52.3) | 44.5 (36.5–50.8) | 47.0 (43.0–55.5) |
| Experience with pig farming (years) | 23.0 (17.0–26.0) | 23.0 (20.0–29.3) | 25.0 (16.0–34.3) | 22.0 (15.0–30.0) |
| Highest education level of farm personnel (1 = basic to 5 = advanced) | 3 (3–4) | 4 (3–4) | 4 (3–5) | 3 (3–5) |
| $\mathbf{X_2}$ block: herd biosecurity scores[b] | | | | |
| Purchasing policy | 88.0 (84.0–99.0) | 70.0 (64.0–78.0) | 90.0 (84.5–95.5) | 100.0 (84.0–100.0) |
| Transport, elimination of manure and carcasses | 63.0 (57.5–70.0) | 61.0 (52.0–70.0) | 78.0 (74.5–87.0) | 54.0 (40.0–65.0) |
| Water and feed supply | 31.5 (19.5–43.0) | 27.0 (27.0–40.8) | 47.0 (30.8–47.0) | 40.0 (30.0–50.0) |
| Policy regarding farm visitors | 65.0 (53.0–71.0) | 59.0 (53.0–71.0) | 71.0 (65.0–82.0) | 65.0 (47.0–85.0) |
| Birds, vermin control | 55.0 (50.0–70.0) | 60.0 (50.0–80.0) | 70.0 (60.0–90.0) | 80.0 (70.0–90.0) |
| Farm location | 60.0 (30.0–80.0) | 55.0 (27.5–70.0) | 30.0 (10.0–57.5) | 90.0 (70.0–95.0) |
| Infectious diseases management | 60.0 (40.0–60.0) | 40.0 (40.0–60.0) | 60.0 (40.0–80.0) | 80.0 (40.0–100.0) |
| Management of the maternity unit | 50.0 (36.0–57.0) | 57.0 (43.0–65.8) | 50.0 (36.0–71.0) | 57.0 (43.0–71.0) |
| Management of the nursery unit | 57.0 (43.0–71.0) | 71.0 (55.3–74.8) | 71.0 (64.0–86.0) | 86.0 (71.0–86.0) |
| Management of the fattening unit | 79.0 (57.0–79.0) | 79.0 (62.3–79.0) | 79.0 (58.8–93.0) | 86.0 (79.0–93.0) |
| Farm compartmentation | 39.0 (29.0–50.0) | 50.0 (42.0–71.0) | 39.0 (32.0–50.0) | 43.0 (32.0–54.0) |
| Cleaning and disinfection | 44.0 (29.8–63.0) | 45.0 (35.0–65.0) | 45.0 (30.0–55.0) | 55.0 (35.0–55.0) |
| $\mathbf{X_3}$ block: occurrence of clinical signs[c] (occurrence of) | | | | |
| Lameness in sucklers | 3.0 (2.0–3.8) | 3.0 (2.0–5.0) | 3.0 (2.0–3.0) | 3.0 (2.0–3.0) |
| Gastro-intestinal in sucklers | 2.0 (2.0–3.0) | 3.0 (2.0–4.0) | 2.5 (2.0–3.0) | 2.0 (2.0–3.0) |
| Respiratory signs in sucklers | 1.0 (1.0–1.8) | 1.0 (1.0–1.0) | 2.0 (1.0–2.0) | 1.0 (1.0–2.0) |
| Lameness in weaners | 3.0 (2.0–3.0) | 2.0 (1.0–3.0) | 3.0 (2.0–3.0) | 2.0 (2.0–2.0) |
| Gastro-intestinal in weaners | 3.0 (1.3–3.0) | 2.5 (1.0–4.0) | 3.0 (2.0–4.0) | 2.0 (2.0–3.0) |
| Respiratory signs in weaners | 2.0 (1.0–2.0) | 2.0 (1.0–2.3) | 3.0 (2.0–3.0) | 2.0 (1.0–2.0) |
| Nervous signs in weaners | 3.0 (2.0–3.0) | 2.0 (1.0–2.0) | 3.0 (2.0–3.0) | 2.0 (1.0–2.0) |
| Lameness in fatteners | 2.0 (2.0–3.0) | 2.0 (1.0–3.0) | 2.0 (2.0–3.0) | 2.0 (2.0–2.0) |

(*Continued*)

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**Table 1.** (*Continued.*)

| Definition of variables | % or median (Q25–Q75) | | | |
|---|---|---|---|---|
| | Belgium (*n* = 38 herds) | France (*n* = 56 herds) | Germany (*n* = 54 herds) | Sweden (*n* = 59 herds) |
| Gastro-intestinal in fatteners | 1.0 (1.0–1.0) | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) |
| Respiratory signs in fatteners | 2.0 (2.0–3.0) | 2.0 (1.0–3.0) | 2.0 (2.0–3.0) | 2.0 (1.0–2.0) |
| Nervous signs in fatteners | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) | 1.8 (1.0–2.0) | 2.0 (1.0–2.0) |
| Lameness in sows | 3.0 (2.0–3.0) | 2.0 (2.0–3.0) | 2.5 (2.0–3.0) | 2.0 (2.0–2.0) |
| Respiratory signs in sows | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) | 2.0 (2.0–2.0) | 1.0 (1.0–2.0) |
| Metritis in sows | 2.0 (2.0–3.0) | 2.0 (1.0–2.3) | 2.0 (2.0–3.0) | 2.0 (1.0–2.0) |
| Mastitis in sows | 2.5 (2.0–3.0) | 2.0 (1.0–2.0) | 3.0 (2.0–3.0) | 3.0 (2.0–3.0) |
| $\mathbf{X_4}$ block: vaccination scheme (vaccination against) | | | | |
| Porcine parvovirus (%) | 73.7 | 98.2 | 100.0 | 83.1 |
| *Escherichia coli* (%) | 73.7 | 69.6 | 44.4 | 83.1 |
| *Clostridium spp* (%) | 2.6 | 50.0 | 27.8 | 3.4 |
| Atrophic rhinitis (%) | 55.3 | 73.2 | 3.7 | 1.7 |
| Porcine reproductive and respiratory syndrome virus (%) | 81.6 | 64.3 | 87.0 | 0.0[d] |
| Influenza virus (%) | 18.4 | 42.9 | 85.2 | 0.0 |
| *Mycoplasma hyopneumoniae* (%) | 84.2 | 96.4 | 88.9 | 47.5 |
| *Actinobacillus pleuropneumoniae* (%) | 10.5 | 5.4 | 35.2 | 1.7 |
| Porcine circovirus type 2 (%) | 34.2 | 66.1 | 94.4 | 83.1 |
| $\mathbf{X_5}$ block: farmer's attitudes and habits | | | | |
| Worries about infectious diseases in his/her pigs[e] | 4.3 (3.0–5.0) | 5.5 (3.9–6.0) | 3.5 (3.0–5.0) | 3.0 (2.0–4.0) |
| Worries about antimicrobial resistance[e] | 4.2 (3.7–5.0) | 5.0 (3.6–5.7) | 3.0 (2.3–4.3) | 4.0 (3.2–4.7) |
| Worries about financial/legal issues[e] | 5.3 (4.7–6.0) | 5.7 (4.9–6.0) | 4.3 (3.7–4.7) | 4.7 (4.0–5.2) |
| Perceived benefits of antimicrobial usage in pig production[f] | 4.3 (3.7–4.8) | 4.0 (3.4–4.5) | 4.0 (3.4–4.4) | 4.4 (3.6–5.2) |
| Perceived need for antimicrobial usage in pig production[f] | 2.8 (2.7–3.3) | 2.0 (1.3–2.7) | 2.2 (1.7–2.9) | 2.7 (2.3–3.5) |
| Perceived risks of antimicrobial usage in pig production[f] | 3.4 (3.0–4.0) | 3.5 (2.7–4.1) | 3.3 (2.7–4.0) | 3.3 (2.7–4.0) |
| Perceived role of the veterinarian[f] | 4.4 (3.8–5.0) | 5.0 (4.4–5.3) | 4.8 (4.1–5.4) | 5.3 (4.9–5.9) |
| Perceived role of the feed expert[f] | 2.1 (1.6–3.3) | 3.8 (2.9–4.5) | 1.9 (1.5–2.3) | 1.3 (1.0–1.6) |
| Perceived impact of selected policy measures to reduce antimicrobial usage[f] | 4.4 (3.8–4.8) | 3.5 (2.9–4.5) | 3.7 (3.1–4.5) | 3.8 (2.8–4.5) |
| 'I only administer antimicrobials to diseased pigs after having consulted my veterinarian'[f] | 4.0 (2.3–5.0) | 3.0 (2.0–5.0) | 5.0 (3.0–5.8) | 5.0 (4.0–6.0) |
| 'All administrations of drugs are recorded and archived in my farm'[f] | 4.0 (4.0–6.0) | 5.1 (4.8–6.0) | 6.0 (5.0–6.0) | 6.0 (6.0–6.0) |
| $\mathbf{X_6}$ block: farm technical performances | | | | |
| Number of litters per sow per year | 2.38 (2.35–2.42) | 2.47 (2.42–2.54) | 2.37 (2.30–2.42) | 2.20 (2.20–2.30) |
| Number of weaners per sow per year | 26.2 (25.5–28.7) | 26.2 (25.3–28.2) | 26.9 (25.5–29.2) | 23.6 (22.4–24.2) |
| Mortality in sucklers (%) | 12.3 (10.1–14.9) | 20.3 (16.9–23.8) | 15.0 (11.5–17.5) | 18.3 (15.6–20.9) |

Because the *mbPLS* regression did not allow for missing data, these were imputed for the following variables: Block $\mathbf{X_1}$: age of the farmer (*n* = 6 farms) and experience with pig farming (*n* = 6); block $\mathbf{X_2}$: management of the nursery unit (*n* = 2); block $\mathbf{X_3}$: occurrence of gastro-intestinal signs in fatteners (*n* = 2), nervous signs in fatteners (*n* = 3) and metritis in sows (*n* = 1); block $\mathbf{X_5}$: perceived impact of selected policy measures to reduce antimicrobial usage (*n* = 4), 'I only administer antimicrobials to diseased pigs after having consulted my veterinarian'(*n* = 2) and 'All administrations of drugs are recorded and archived in my farm' (*n* = 6); block $\mathbf{X_6}$: number of litters per sow per year (*n* = 2) and number of weaners per sow per year (*n* = 2). Missing data belonged to different farms and different countries (with a maximum of three missing data per variable and per country).

[a] Treatment incidences were log-transformed.

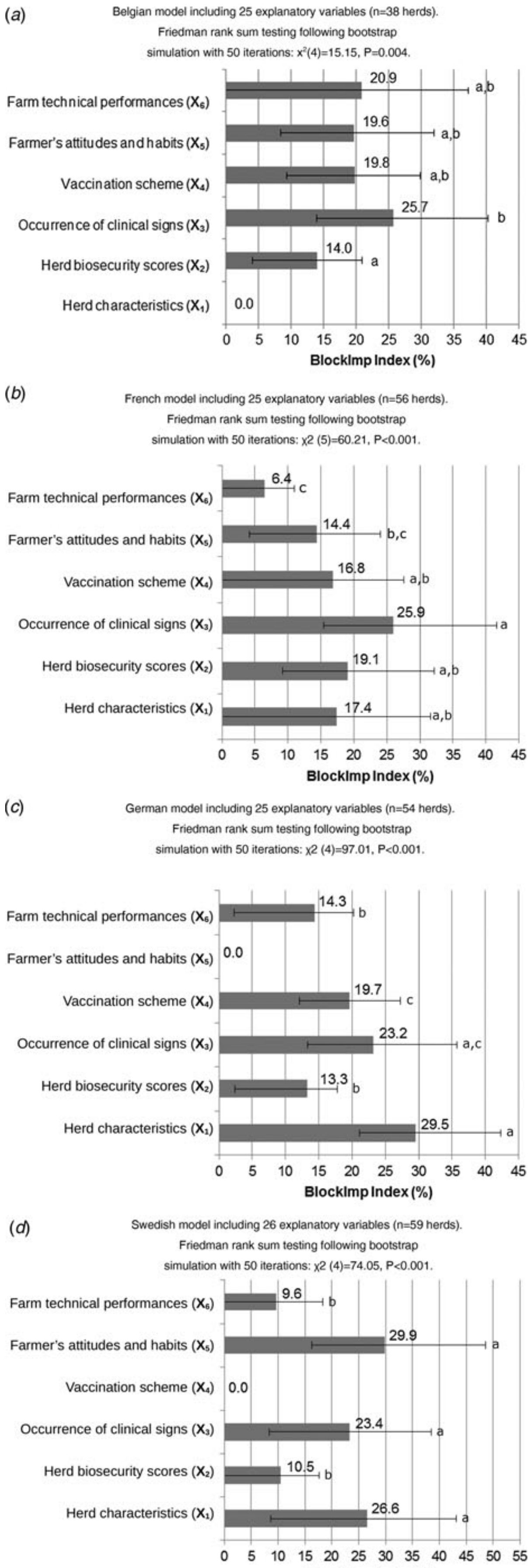
[b] For each sub-category of external and internal biosecurity practices, scores were attributed from 0 (absence of biosecurity) to 100 (very strict biosecurity) using the Biocheck.UGent™ scoring system [20].

[c] Occurrence of clinical signs in each age group were based on farmer's indication of whether he/she had to treat his/her pigs because of given clinical signs (score from 1 = never to 5 = every batch).

[d] Vaccination against PRRS is not allowed in Sweden.

[e] Items were measured on six-point response scales, ranging from 1 = very little worry to 6 = very much worry.

[f] Items were measured on six-point response scales, ranging from 1 = do not agree at all to 6 = fully agree see Visschers *et al.* [22].




provided as Supplementary material (see Fig. S1). In each country, correlation was high between variables of the **Y** block. Especially TI via oral route was highly correlated with TI in weaners; this is because weaners are generally treated with antimicrobials via feed or water routes [16]. TI via parenteral route was highly correlated with TI in sucklers in the four countries, and with TI in fatteners and sows in Sweden. TI with cephalosporins/fluoroquinolones was mainly correlated with TI in sucklers and via the parenteral route in Belgium and France, and with TI in fatteners in Germany and Sweden.

### *Relative contribution of explanatory blocks and explanatory variables to the explanation of antimicrobial usage*

Figure 2 and Table 2 present, in each participating country, the relative contribution of explanatory blocks $\mathbf{X_k}$ and explanatory variables to the explanation of antimicrobial usage (block **Y**). After the variables selection procedure, five blocks made of a total of 25, 25 and 26 variables were retained in the Belgian, German and Swedish models, respectively, whereas six blocks (made of 25 variables) were retained in the French model. The models explained between 26.6% and 51.6% of variance in the block **Y** (Table 2). Within each country, Friedman rank sum testing showed that the contribution of the explanatory blocks significantly differed (Fig. 2).

The occurrence of clinical signs (block $\mathbf{X_3}$) and the farm technical performances (block $\mathbf{X_6}$) were the largest contributors to the Belgian model (Fig. 2). Among clinical signs, mainly the occurrence of clinical signs of respiratory diseases in sows and fatteners and the occurrence of clinical signs of nervous diseases in fatteners were positively associated with antimicrobial usage (Table 2). Belgian herds with more litters per sow per year and higher mortality in sucklers also had higher antimicrobial usage (Table 2). Vaccination scheme (block $\mathbf{X_4}$) and farmer's attitudes and habits towards antimicrobial usage (block $\mathbf{X_5}$) had a lower contribution to the Belgian model and related, respectively, to the vaccination against PRRS virus (i.e. farms implementing vaccination also had higher antimicrobial usage) and to the perceived risk of using antimicrobial usage in pig production (i.e. the higher the perceived risk, the lower the usage). The herd biosecurity scores (block $\mathbf{X_2}$) only had a minor contribution to the model, whereas no herd characteristics variable (block $\mathbf{X_1}$) was retained in the Belgian model (Fig. 2).

In the French model, antimicrobial usage was primarily associated with the occurrence of clinical signs (block $\mathbf{X_3}$) and with the vaccination scheme (block $\mathbf{X_4}$). The contribution of these two blocks related, respectively, to the occurrence of respiratory signs in fatteners and lameness in sows, and to the vaccination against *Clostridium* spp, PRRS and influenza viruses (Table 2).

**Fig. 2.** Graphical representation of the BlockImp index of the explanatory blocks. Multiblock partial least-squares (*mbPLS*) regression of farm antimicrobial usage (**Y**) explained by six blocks of variables: herd characteristics ($\mathbf{X_1}$), herd biosecurity scores ($\mathbf{X_2}$), occurrence of clinical signs ($\mathbf{X_3}$), vaccination scheme ($\mathbf{X_4}$), farmer's attitudes and habits ($\mathbf{X_5}$) and farm technical performances ($\mathbf{X_6}$). BlockImp index represents the relative contribution of each explanatory block to the explanation of antimicrobial usage (block **Y**) and satisfies the condition $\sum_k \text{BlockImp}_k = 100\%$ for $K = 1$ to 6. Bars represent the 90% tolerance interval around the BlockImp index estimate. Blocks where BlockImp = 0 are those for which no variable was kept in the block after the variable selection procedure. BlockImp indexes with different superscripts significantly differ based on post-hoc pairwise comparison with Bonferroni correction ($P < 0.05$).

**Table 2.** Variable importance index of the reduced country-specific *mbPLS* regressions and sign of the association between explanatory variable and antimicrobial usage (block **Y**)

| | Belgium ($n = 38$ herds) | | France ($n = 56$ herds) | | Germany ($n = 54$ herds) | | Sweden ($n = 59$ herds) | |
|---|---|---|---|---|---|---|---|---|
| | VarImp index (%) (90% CI)[a] | Sign[b] | VarImp index (%) (90% CI)[a] | Sign[b] | VarImp index (%) (90% CI)[a] | Sign[b] | VarImp index (%) (90% CI)[a] | Sign[b] |
| $\mathbf{X_1}$ block: herd characteristics | | | | | | | | |
| Number of present sows | | | | | 7.0 (1.9–12.2) | + | 4.7 (−5.2 to 9.3) | + |
| Number of employees per 100 present sows | | | | | 10.8 (6.4–19.2) | – | | |
| Farrowing system: 1–2-week system (*vs*. 3-week) | | | | | 11.7 (7.2–20.8) | + | | |
| Farrowing system: 4–8-week system (*vs*. 3-week) | | | 5.0 (−13.7 to 10.0) | – | 3.5 (−6.9 to 6.9) | – | 5.2 (−9.5 to 10.3) | – |
| Piglets weaning age | | | | | 3.0 (−2.7 to 5.9) | – | 14.0 (1.6; 26.4) | – |
| Farm using zinc oxide post-weaning | | | | | | | 6.2 (−6.3 to 12.4) | + |
| Experience with pig farming | | | 11.1 (−16.3 to 22.2) | + | | | | |
| Highest education level of farm personnel | | | | | 2.8 (−1.9 to 5.5) | + | | |
| $\mathbf{X_2}$ block: herd biosecurity practices | | | | | | | | |
| Purchasing policy | 0.8 (−2.8 to 1.6) | – | | | 1.7 (−1.8 to 3.2) | – | 0.7 (−2.1 to 1.4) | – |
| Transport, elimination of manure and carcasses | 2.0 (−2.5 to 4.0) | – | 2.2 (−3.8 to 4.4) | – | 1.8 (−4.4 to 3.5) | – | 0.5 (−3.1 to 1.1) | – |
| Water and feed supply | 0.7 (−1.5 to 1.4) | – | 6.0 (0.1–12.0) | – | | | 0.9 (−3.6 to 1.8) | – |
| Policy regarding farm visitors | 1.2 (−2.1 to 2.5) | + | 1.3 (−4.4 to 2.6) | – | 2.4 (−1.3 to 4.7) | – | 0.3 (−3.0 to 0.6) | – |
| Farm location | 1.3 (−5.1 to 2.6) | – | 5.6 (0.7–11.1) | – | 2.6 (−3.4 to 4.5) | – | | |
| Infectious diseases management | | | | | | | 1.1 (−4.2 to 2.1) | – |
| Management of the nursery unit | 1.6 (−2.5 to 3.1) | – | | | 1.6 (−6.7 to 3.0) | + | 0.6 (−3.1 to 1.1) | – |
| Management of the fattening unit | | | 2.3 (−0.9 to 4.5) | – | | | | |
| Farm compartmentation | | | 2.1 (−3.4 to 4.3) | – | | | 0.6 (−4.2 to 1.2) | – |
| Cleaning and disinfection | 1.8 (−2.1 to 3.5) | – | | | | | | |
| $\mathbf{X_3}$ block: occurrence of clinical signs (occurrence of) | | | | | | | | |
| Lameness in sucklers | | | | | 4.7 (−4.7 to 9.0) | + | 3.5 (−0.8 to 6.9) | + |
| Gastro-intestinal in sucklers | | | | | | | 1.5 (−1.8 to 2.9) | + |
| Respiratory signs in sucklers | | | | | | | 1.7 (−3.0 to 3.3) | + |
| Lameness in weaners | | | | | 4.5 (−5.5 to 9.0) | + | | |
| Gastro-intestinal in weaners | 3.0 (−1.3 to 5.9) | + | | | | | 3.8 (−2.6 to 7.5) | + |
| Respiratory signs in weaners | 2.2 (−3.9 to 4.4) | + | | | | | 1.8 (−2.2 to 3.7) | + |
| Nervous signs in weaners | 2.4 (−3.5 to 4.7) | + | | | | | 0.9 (−2.1 to 1.8) | + |
| Gastro-intestinal in fatteners | | | 5.0 (−4.7 to 10.0) | + | | | 4.1 (−1.3 to 8.0) | + |
| Respiratory signs in fatteners | 5.9 (1.0–11.6) | + | 15.5 (7.2 to 30.0) | + | 6.0 (−3.7 to 11.6) | + | 1.7 (−0.5 to 3.4) | + |
| Nervous signs in fatteners | 4.8 (−1.1 to 9.5) | + | 4.1 (−7.3 to 8.1) | + | | | | |
| Lameness in sows | | | 11.4 (−0.6 to 22.6) | + | | | | |
| Respiratory signs in sows | 8.1 (3–15.4) | + | | | | | 0.7 (−2.1 to 1.3) | + |
| Metritis in sows | 2.5 (−2.8 to 5.0) | + | | | 8.9 (−0.6 to 17.3) | + | 1.7 (−1.5 to 3.3) | + |
| Mastitis in sows | 3.2 (−2.3 to 6.3) | + | | | | | 1.8 (−2.2 to 3.6) | + |
| $\mathbf{X_4}$ block: vaccination scheme (vaccination against) | | | | | | | | |
| Porcine parvovirus: yes (*vs*. no) | 3.8 (−5.3 to 7.7) | – | | | | | | |
| *Escherichia coli*: yes (*vs*. no) | | | | | 4.5 (0.7–8.1) | + | | |
| *Clostridium spp*: yes (*vs*. no) | 2.3 (−1.9 to 4.7) | + | 5.9 (−16.7 to 11.8) | + | 2.0 (−1.0 to 3.7) | + | | |
| Atrophic rhinitis: yes (*vs*. no) | 4.4 (−9.2 to 8.8) | + | | | 1.3 (−1.8 to 2.5) | + | | |
| Porcine reproductive and respiratory syndrome virus: yes (*vs*. no) | 8.4 (−7.6 to 16.6) | + | 5.1 (−13.9 to 10.1) | + | 1.8 (−3.8 to 3.4) | + | | |
| Influenza virus: yes (*vs*. no) | | | 4.2 (−9.4 to 8.3) | + | 2.5 (−3.9; 5.0) | + | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *Mycoplasma hyopneumoniae*: yes (*vs.* no) | | | | | 3.0 (−1.5 to 5.8) | − | | |
| *Actinobacillus pleuropneumoniae*: yes (*vs.* no) | | | | | 2.6 (−1.2 to 4.8) | + | | |
| **$X_5$** block: farmer's attitudes and habits | | | | | | | | |
| Worries about infectious diseases in his/her pigs | | | 1.1 (−3.0 to 2.1) | − | | | | |
| Worries about antimicrobial resistance | | | 3.8 (−0.3 to 7.6) | − | | | 25.4 (−1.1 to 49.1) | + |
| Worries about financial/legal issues | 5.4 (−7.0 to 10.8) | + | | | | | | |
| Perceived benefits of antimicrobial usage in pig production | | | 1.4 (−2.2 to 2.8) | + | | | | |
| Perceived need of antimicrobial usage in pig production | | | 1.8 (−5.0 to 3.6) | + | | | | |
| Perceived risks of antimicrobial usage in pig production | 7.8 (−4.5 to 15.4) | − | 1.0 (−3.1 to 2.0) | − | | | | |
| Perceived role of the feed expert | | | 1.0 (−1.3 to 1.9) | − | | | | |
| 'All administrations of drugs are recorded and archived in my farm' | 5.4 (−8.8 to 10.7) | − | 0.9 (−3.3 to 1.9) | − | | | 12.7 (−8.4 to 25.3) | − |
| **$X_6$** block: farm technical performances | | | | | | | | |
| Number of litters per sow per year | 8.4 (−16.7 to 16.8) | + | 0.1 (−9.5 to 0.3) | + | 0.9 (−7.4 to 1.6) | + | | |
| Number of weaners per sow per year | 0.7 (−19.8 to 1.4) | − | 0.7 (−9.6 to 1.4) | + | 5.5 (−1.1 to 10.6) | − | 2.3 (−18.7 to 4.7) | + |
| Mortality in sucklers | 11.9 (−13.9 to 23.6) | + | 1.4 (−5.2 to 2.8) | − | 2.9 (−10.9 to 5.4) | + | 1.6 (−20.6 to 3.3) | − |
| Proportion of explained variance in the block **Y** (%) | 29.8 | | 26.6 | | 51.6 | | 38.6 | |

VarImp index represents the relative contribution of each explanatory variable to the explanation of antimicrobial usage (block **Y**) and satisfies the condition $\sum_p \text{VarImp}_p = 100\%$, *P* being the number of explanatory variables (*P* = 25 for Belgium, France and Germany, and *P* = 26 for Sweden). The slash sign means the variable was not kept in the country-specific model after the variable selection procedure.
[a]Ninety per cent tolerance interval around the VarImp index estimate.
[b]The sign (+ or −) of the association was provided by the sign of the regression coefficients *β* of the models linking explanatory variables to every variable of the block **Y**, this information being also given by the *mbPLS* regression.

Herd biosecurity scores (block $\mathbf{X_2}$) and herd characteristics (block $\mathbf{X_1}$) had a lower contribution to the model (Fig. 2). Farms with better water and feed supply policy, as well as farms located in more favourable locations (i.e. with reduced pig density) had lower antimicrobial usage, whereas farmers with longer experience with pig farming were using more antimicrobials (Table 2). A lower contribution was observed for the farmer's attitudes and habits towards antimicrobial usage (block $\mathbf{X_5}$) and the farm technical performances (block $\mathbf{X_6}$).

In the German model, the herd characteristics block (block $\mathbf{X_1}$) was the largest contributor to antimicrobial usage and was in highest degree related to the herd size (i.e. the higher the herd size and the lower the number of employees per 100 present sows, the higher the antimicrobial usage) and to the farrowing system (i.e. herds with a 1- or 2-week farrowing rhythm had higher antimicrobial usage compared with those having a 3-week system). The occurrence of clinical signs (block $\mathbf{X_3}$) was the second largest contributor and was mainly related to the occurrence of metritis and the occurrence of clinical signs of respiratory diseases in fatteners (Table 2). The vaccination scheme (block $\mathbf{X_4}$) had a lower contribution that was related to a small contribution of vaccination against seven out of eight vaccines considered in the model (Table 2). Farm technical performances (block $\mathbf{X_6}$) and herd biosecurity scores (block $\mathbf{X_2}$) only had a minor contribution to the model, and no variable related to the farmer's attitudes and habits towards antimicrobial usage (block $\mathbf{X_5}$) was retained in the German model (Fig. 2).

The farmer's attitudes and habits towards antimicrobial usage (block $\mathbf{X_5}$), the herd characteristics (block $\mathbf{X_1}$) and the occurrence of clinical signs (block $\mathbf{X_3}$) were the largest contributors to the Swedish model (Fig. 2). Swedish farmers with higher worries about AMR also had higher antimicrobial usage, suggesting that Swedish farmers that had high antimicrobial usage were aware of being high users and worried about the consequences their usage could have on AMR. Among herd characteristics, especially herds with higher weaning age had lower antimicrobial usage. The contribution of the occurrence of clinical signs was related to a rather small contribution of a diversity of clinical signs in all age groups (Table 2). Besides, the herd biosecurity scores (block $\mathbf{X_2}$) and the farm technical performances (block $\mathbf{X_6}$) had a minor contribution to the model, and none of the variables related to the vaccination scheme (block $\mathbf{X_4}$) were kept in the Swedish model (Fig. 2).

## Discussion

The relative importance of the selected risk factors for antimicrobial usage in farrow-to-finish pig production was explored using an innovative analytical approach called *mbPLS* regression. To our knowledge, this is the first study that included both technical (i.e. herd characteristics, biosecurity level, occurrence of clinical signs and vaccination scheme) and psychosocial risk factors (i.e. farmer's attitudes and habits towards antimicrobial usage), organised in meaningful categories or 'blocks' of explanatory variables, in the same model and across four countries. The use of a composite block **Y** made of eight variables provided a better description of the herd-level antimicrobial usage in comparison with traditional methods based on a single outcome summary variable (e.g. TI from birth till slaughter), which typically give more weight to group treatment (i.e. via the oral route) or treatments of animal age categories with longer lifespan. On the contrary here, each variable describing antimicrobial usage in different age categories, as well as via different administration routes, had equal importance in the definition of the block **Y**. Additionally, not only the amount of antimicrobials that is used was considered, but also which antimicrobial classes.

The *mbPLS* regression showed that all six considered blocks provided useful contribution to explaining antimicrobial usage in at least one country, with no block dominating the effect of the other blocks when compared across countries (Fig. 2). It means that antimicrobial usage in pig production is influenced simultaneously by a wide range of risk factors, and that the reduction of antimicrobial usage should be addressed following a holistic approach, as recommended by national and European action plans against AMR [2]. However, the relative contribution of each block differed between the four countries, suggesting that country-specific measures to reduce antimicrobial usage are likely to be more effective.

The occurrence of clinical signs was one of the largest contributors to antimicrobial usage in all four countries. It suggests that participating farms primarily relied on antimicrobials for treatment of clinically sick animals or animals expected to become diseased [34]. This is in agreement with the current revision of EU Directive 90/167/EEC that proposes to introduce a ban of the preventive use of medicated feed containing antimicrobials in food-producing animals [35]. The in-depth study of the contribution of individual variables within the block 'occurrence of clinical signs' showed that the occurrence of respiratory signs in fatteners largely contributed to antimicrobial usage in Belgium, France and Germany (Table 2). This is in accordance with previous research that showed that respiratory infections were the main indication for using antimicrobials in pig production [6]. The occurrence of gastro-intestinal signs in weaners did not appear as a main risk factor in the present study, although these are known to account for an important part of antimicrobial usage in pig production [5, 6]. It probably relates to the fact that gastro-intestinal signs are often controlled via preventive antimicrobial treatments (especially in Belgium and France), i.e. using group treatments administered before the occurrence of clinical signs [36].

Herds vaccinating against PRRS in Belgium and France and against influenza in France had higher antimicrobial usage (Table 2). When combined with the observed contribution of the occurrence of respiratory signs in fatteners, our results suggest that Belgian and French farms vaccinating against PRRS, atrophic rhinitis and influenza were also likely to use more antimicrobials to control the associated respiratory clinical signs. This is in agreement with a recent Danish study that showed that vaccination against common endemic pig diseases is not necessarily associated with a reduced antimicrobial use [37]. The vaccination scheme did not contribute to the Swedish model. This might be related to the fact that the proportion of herds implementing vaccination in Sweden was lower than in the other countries, especially against PRRS (vaccination is not allowed as Sweden is officially declared free from PRRS) and influenza (see Table 1).

Nervous signs commonly occurred in weaners in most herds (see Table 1), but Belgian and French farms that had higher occurrence of nervous signs in fatteners also had higher antimicrobial usage. It could be related to an increased susceptibility to *Streptococcus suis*, known to be promoted by co-infection with PRRS, leading to nervous signs up to the fattening period [38]. Occurrence of lameness in sows also had a substantial contribution in France. It could be related to the recent implementation of group housing in sows [39], which could have led to an increase need for antimicrobials treatments, as previously suggested by Hémonic *et al.* [40]. This effect was however not observed in Belgium and Germany where sows group housing was also recently introduced, suggesting that other factors, including the housing conditions (e.g. use of slatted floors) could play a role. Occurrence of metritis was also identified as a risk factor for antimicrobial usage in Germany, as already shown by van Rennings *et al.* [6].

Non-medical risk factors also played a role in explaining antimicrobial usage, especially herd size, farrowing rhythm and weaning age, as well as increased biosecurity, as already shown in previous studies [9, 21], but the contribution of these risk factors differed between countries. Systems with longer between-farrowing periods are known to facilitate the implementation of a strict all-in all-out management of pig batches, and therefore to reduce the risk of infectious agents transmission, e.g. *M. hyopneumoniae* or *A. pleuropneumoniae* [41, 42]. Farm technical performances contributed to explaining antimicrobial usage in Belgium, but had a limited contribution in other countries. It might partly be explained by the limited number of variables included in this block (especially growth performances were not available), and by the cross-sectional design of the study, preventing the interpretation of the temporal association between antimicrobial usage and performances. Farmer's attitudes and habits towards antimicrobial usage contributed to the Belgian and Swedish models, and to a lower extent to the French model, but not to the German model. This could be related to the fact that the perceived risks about AMR, previously shown to be the main predictor for antimicrobial usage in pig production across the four countries [14], were lower and had lower variance in Germany than in the other countries. Further work is needed to explore the reasons behind these differences.

The present study however presented a number of limitations. First, it should be stressed that except in France, participating farms were recruited based on their willingness to participate, as it was very difficult to get a representative sample in each country. This likely introduced a selection bias towards farmers with a higher interest in the topic and potentially better pig farming practices than the average farrow-to-finish farm in the country. Besides, despite major efforts to harmonise study design and data collection between participating countries, some differences did remain. These were mostly due to the different channels available for the research partners to recruit participating farms, and to differences in the way antimicrobial usage is registered in each participating country. Although these differences in data collection may partly explain the observed differences in antimicrobial usage between countries, we are confident that these differences in antimicrobial usage do exist, as they are in lines with previous literature, e.g. from the monitoring of antimicrobial sales for veterinary use in Europe [43]. By combining TIs of sucklers, weaners and fatteners into a TI from birth until slaughter, Sjölund *et al.* [16] showed that participating countries ranked in the same order than observed in the European monitoring of antimicrobial sales for veterinary use. However, direct comparison is not possible as the European monitoring data combine all animal species together.

Besides, the sample size of the country-specific models was small, leading to very large tolerance intervals around the BlockImp and VarImp estimates. These estimates should therefore be interpreted with caution. An initial attempt was made to develop a multi-country model based on a bigger sample of farms from the four participating countries, including the farm country of origin as an extra block. This block was explaining

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33.0% of the variation in the block **Y** (data not shown). The country of origin was however not the effect of primary interest. Unfortunately, its effect could not be controlled for in a multi-country model, because at this stage, it is not possible to control for confounding or interaction in an *mbPLS* regression model. However, this feature is currently under development [44]. It was therefore decided to rather develop four separate, country-specific models. The proportion of explained variance in the block **Y** in each country-specific model was relatively low. It means that in addition to the 59 explanatory variables considered in the present study, there are other factors influencing antimicrobial usage in pig production in the four participating countries. These other factors are likely to be related to the country of origin, as the country of origin had a major effect in the multi-country model. They could relate, among others, to the structure of the pig sector, the regulation of antimicrobial usage or the influence of the socio-professional network of the farmer [15].

The fact that the model was built attributing equal weight to every variable in each block (by scaling them to unit variance) and equal weight to every block in the overall model partly influenced the observed contribution of the variables. For example, the variable 'All administrations of drugs are recorded and archived in my farm' had a large contribution to the Swedish model despite having low variability. This is partly because the variable was scaled to unit variance and because this block contained two variables only.

To conclude, by identifying the main risk factors and categories of risk factors associated with antimicrobial usage in each participating country, this study provided a basis for the prioritisation of future strategies to mitigate the risks associated with antimicrobial usage in pig production. Because several categories of risk factors were shown to be associated with antimicrobial usage, a holistic risk mitigation approach is highly recommended. Besides, the relative contribution of risk factors differed between the four participating countries, suggesting that country-specific mitigation activities are likely to be more effective. Further research is needed to validate our findings in larger and more representative samples, as well as in other countries.

**Supplementary material.** The supplementary material for this article can be found at https://doi.org/10.1017/S0950268818000742

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