Factors influencing Danish veterinarians’ choice of antimicrobials prescribed for intestinal diseases in weaner pigs

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Abstract

Background  Antimicrobial resistance is a worldwide human and animal health problem, and there is an urgent need to promote prudent use of antimicrobials among veterinarians. In order to do so, it is important to understand the factors that determine their use of antimicrobials. This questionnaire-based study aimed to determine which factors that influence the Danish veterinarians’ choice of antimicrobials prescribed for intestinal diseases in weaner pigs.

Methods  The survey was completed by 83.3 per cent (n=105) of all veterinarians accountable for a Veterinary Advisory Contract in Danish weaner pig herds (n=126). The participants scored to which extent 29 different factors influenced their antimicrobial choice on a five-point Likert scale (1-5).

Results  The veterinarian’s own experiences of clinical efficacy in the herd exerted the greatest influence (94.4 per cent scored ≥4). The Danish authorities have directed a threshold of the antimicrobial use and made some antimicrobials less favourable to use in pig production through The Yellow Card Initiative, and this influenced the choice of antimicrobials significantly (78.1 per cent scored ≥4). Microbiological laboratory diagnostics influenced the choice of antimicrobial for most veterinarians (78.1 per cent scored 4 or 5), and therefore the Danish statutory requirement of laboratory diagnostics before flock treatment was considered reasonable.

Conclusion  The study concluded that many factors influenced the veterinarians choice of antimicrobials, and that statutory requirements can be used to support prudent use of antimicrobials.

Introduction

Antimicrobial resistance is a worldwide problem for which there is an urgent need to find solutions. A key point is to secure prudent antimicrobial usage (PAMU). PAMU involves both reducing the total use and making an appropriate choice of antimicrobial treatment. Denmark has a long tradition for promoting PAMU in food-producing animals. This includes banning use of antimicrobials for growth promotion in 1995–1999 and the introduction of the Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) in 1995. Since then, several other initiatives have followed. However, the amount of therapeutic antimicrobial used in proportion to the kilogram-produced meat rose by 53 per cent in the Danish pig production during the years 2001–2009. To reverse this trend, Danish authorities introduced The Yellow Card Initiative (TYCI) in 2010. TYCI introduced thresholds for antimicrobial use on herd level and penalties for exceeding these. Hereby TYCI motivated the implementation of health strategies in Danish pig herds. This lead to a reduction in the antimicrobial use. In 2014, a statutory requirement of laboratory diagnostics for group-treatment of pigs (hereon denoted SRLD) was introduced in Denmark. According to this order, a bacteriological pathogen must be detected by microbiological laboratory diagnostics (MLD) (eg, culturing or quantitative PCR on faeces for intestinal diseases) at least once a year in order to obtain...
permission for group-treatment in a herd.\textsuperscript{9,10} As of March 31, 2017, TYCI was ‘differentiated’, meaning that some classes of antimicrobials carried a higher penalty and the consumption was multiplied with certain factor (eg, 1.2 for tetracycline) when the total antimicrobial use in a herd was calculated.\textsuperscript{11} The Danish Veterinary and Food Administration (DVFA) has also produced Evidence-based Prudent Use Guidelines (EPUG), which advises on first, second and third choices of antimicrobials for treatment of bacteriological pathogens in pigs and cattle.\textsuperscript{12}

Denmark is a major pig-producing country with 19 million slaughtered pigs and 12 million 30kg fatteners exported in 2015.\textsuperscript{13} Pigs accounted for 75 per cent of the total Danish antimicrobial consumption for livestock in 2015, and weaners accounted for 42 per cent of the antimicrobials used in pig production. When adjusted for body weight, the consumption of antimicrobials in weaner herds was about five times higher than in both finisher herds and sow herds.\textsuperscript{4} During 2002–2012, 75 per cent of antimicrobials used for Danish weaners were prescribed for intestinal diseases.\textsuperscript{6} Therefore, the antimicrobial choice for intestinal diseases in Danish weaners is especially interesting in relation to promoting veterinary PAMU in Denmark.

The World Health Organization has pointed out identification and implementation of national action plans as a crucial point in succeeding the achievement of PAMU.\textsuperscript{1} Despite the many initiatives in Denmark, some knowledge gaps are still present. For instance, little is known about the line of thought that leads to the veterinarian’s choice of a specific antimicrobial.

Therefore, the aim of this study was to determine which factors that influence the Danish veterinarians’ choice of antimicrobials prescribed for treatment of intestinal diseases in weaner pig herds.

Methods

Design of the questionnaire

The investigation was conducted as a questionnaire-based study. The questionnaire was designed in accordance to the principles described by Stone,\textsuperscript{14} supplemented by guidance from Nielsen and others\textsuperscript{15} and Münster.\textsuperscript{16} Questions were formulated based on relevant literature. Three veterinary students did a preparatory review of the questionnaire to identify errors. A researcher with 36 peer-reviewed papers on veterinary antimicrobial usage and resistance was chosen as expert to comment on the questionnaire. Finally, the questionnaire was reviewed by five veterinary students for self-typing and by three veterinarians (not included in study population) as telephone interview. The veterinarians were asked about their perception of specific words, and thus provided clarity to certain wordings.

The final questionnaire consisted of three modules. The first module surveyed demographical characteristics. The second module was created based on comments from the expert and consisted of two questions measuring the respondents’ behaviour towards microbiological tests. The third module was the main module. Factors that could possibly influence the choice of antimicrobials for treatment of intestinal diseases in weaners were listed in four sections to be scored by the respondents: sources of information, properties of the drug, clinical and paraclinical factors and other relevant factors. Altogether 29 factors were scored on a Likert scale with rising agreement: 1: no influence, 2: little influence, 3: some influence, 4: great influence or 5: decisive influence.

Suggested factors were determined by reviewing literature.\textsuperscript{7,17–27} Finally, the respondents were given the opportunity to state up to five additional factors in an open-ended question, recognising that other factors than the suggested ones could be influential. The questionnaire was in Danish, and a translated version in English is enclosed as supplementary material.

Obtainment of study population

A Veterinary Advisory Contract (VAC) is an agreement on terms for continuous herd health service between a herd owner and one veterinarian and that implies mandatory on-farm veterinary consultancy on a regular basis. According to Danish law, antimicrobials must be prescribed by a veterinarian, but a farmer will have more liberal access to use of antimicrobials (eg, store antimicrobials and execute treatments on own initiative) if they enter into a VAC. This study included all Danish veterinarians accountable for at least one VAC in a pig weaner herd and that met both of the criteria: Active January 1, 2017 and in a herd comprising of at least 100 weaners as of January 2017. The cut-off by 100 weaners was set, as done by Jensen and others,\textsuperscript{27} to exclude VACs in sow herds with no regular weaner production.

Since 2000, VETSTAT has been the Danish system for surveillance of veterinary antimicrobial usage. All agreed VACs must be registered in VETSTAT.\textsuperscript{9,28} Information can be obtained from VETSTAT for any herd with a VAC. This includes details such as number of pigs, age groups and the prescribed amounts of antimicrobials in the herd on a monthly basis. Statements from VETSTAT were obtained from all 5479 Danish pig herds with an active VAC January 1, 2017. These data were used to determine which veterinarians that met the criteria of inclusion. Consequently, the study population included 126 veterinarians.

Data collection

Answers were collected as self-typed in a web-based setting or as telephone interviews, both facilitated by SurveyXact version 12.6 by Rambøll Management
Consulting. Contact information on respondents was identified primarily through Google search engine. The data collection period lasted from April 20 to May 5, 2017. In total 105 respondents were contacted by email at least once. Telephone numbers were identified for all 126 veterinarians. In the period April 24–May 5, respondents were contacted by phone and asked to participate by telephone interview or encouraged to participate online.

The order of the scored factors in the third questionnaire module was randomised within each of the four sections by SurveyXact for both self-type-answering and telephone interviews. The exact same wording was used for the self-type-answering and the telephone interviews. The two authors, EOE and SS, undertook the telephone interviews. The chapter on interviewing technique was studied in Oppenheim29 and attempted to be adapted by both interviewers. Furthermore, the interviewers practised interviewing each other several times. Thereby, discrepancies were discussed and corrected before the data collection started.

**Data processing**

It was ensured that the self-typed answers were completed with the necessary attention from the respondents. This was managed by checking for suspiciously low total response time, defined as less than three minutes, or stereotypical scoring in the third module. The coding of gender was checked according to the name of the respondent. Age and year of obtained veterinary licence were probed for extreme and strange values. This proofreading led to no exclusions. Finally, the answers were anonymised by replacing name and licence number with a respondent number.

**Statistical analyses**

Descriptive statistics provided a summary of the demographical distribution of the respondents. R version 3.4.0 was used for estimates of proportions, means and medians. Veterinary experience was estimated by the calculation:

\[ 2017 - h_d. \]

Descriptive statistics provided a summary of the responses on the Likert scale-scored factors in the third questionnaire module; guided by Heiberger and Robbins30 diverging stacked bar charts were created with R version 3.4.0 with ‘HH’ package. The order of the factors was randomised during the data collection, but in figure 1A,B, the diverging stacked bar charts were ranked according to the sum of respondents that scored great influence or decisive influence plus half of the sum that scored some influence.

It was investigated whether certain demographical characteristics or behaviour towards microbiological tests were associated with certain patterns in the scoring of the Likert scale-scored factors. The following generic null hypothesis was tested with non-parametric Mann-Whitney U tests: respondent group A and respondent group B have the same distribution of Likert scale-scoring of a certain factor. Table 1 defines how the respondents were grouped in group A and group B for each independent variable. All 29 factors were tested for differing distributions of the scoring. In total, 638 tests were performed using R version 3.4.0 and the Wilcox.test function.
A multiple comparisons problem was present, but it would probably lead to a low sensitivity if a correction (eg, Bonferroni) for 638 comparisons were applied. In addition, the controversy on p values and fixed significance levels\(^3\) was recognised, and therefore, the following approach was chosen: no statistically significance level were specified for the p values, but diverging stacked bar charts were made for comparison between groups where comparison showed p<0.01, and these bar charts where provided with both p values and q values. Q values were defined by Storey and Tibshirani\(^4\) and can be explained as the probability of getting a false positive at a given significance level. The q values were estimated by using the ‘qvalue’ package in R.

Answers to the open-ended question were grouped if they, with good reason, could be understood as an expression of the same belief to determine frequently suggested additional factors.

**Factors influencing antimicrobial choice**

Sources of information and clinical and paraclinical factors influencing the choice of antimicrobials were scored as shown in figure 1. Knowledge from own education, recommendation and advice from colleagues and scientific literature were ranked the highest among sources for information on the appropriate choice of antimicrobials, while information from medical companies scored the lowest. Most of the clinical and paraclinical factors were generally counted to have a great extent of influence on the choice of antimicrobials, except for the herd manager’s tentative diagnose that scored more modestly. The experiences with clinical efficacy in the specific herd was scored highest overall (94.4 per cent scored ≥4), and 53.3 per cent of the pig practitioners stated the factor had decisive influence on their choice. Similarly, the influence of properties of the drug and other relevant factors influencing the choice of antimicrobials were scored as shown in figure 2. The possible route of administration was the most important factor for the drug, while treatment duration, frequency and the associated time interval between administrations ranked below this factor. TYCI also greatly influenced the choice of antimicrobials (78.1 per cent scored ≥4). The geographical location did in general not influence the choice, while a number of

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**Table 1** Overview of the grouping of Danish veterinarians made for statistical comparisons between groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male, female</td>
</tr>
<tr>
<td>Veterinary experience</td>
<td>≤3 years, 6–20 years, 21–35 years, ≥35 years</td>
</tr>
<tr>
<td>Age</td>
<td>≤42 years, 43–51 years, 52–61 years, ≥61 years</td>
</tr>
<tr>
<td>Primary region of practice*</td>
<td>Northern Jutland, Central Jutland, Southern Denmark, Zealand, Capital Region including Bornholm*</td>
</tr>
<tr>
<td>Proportion of total working time serving as a pig practitioner</td>
<td>0%–24.9%, 25%–49.9%, 50%–74.9%, 75%–100%</td>
</tr>
<tr>
<td>Position in practice</td>
<td>Owner/coowner, assistant</td>
</tr>
<tr>
<td>Part of a practice with other pig practitioner(s)</td>
<td>Yes, no</td>
</tr>
<tr>
<td>Completed supplementary education</td>
<td>DVA Certificate in Swine Health Management, not DVA Certificate in Swine Health Management</td>
</tr>
<tr>
<td>Conduction of microbiological laboratory diagnostics for intestinal pathogens more often than the statutory requirement for group treatment dictates</td>
<td>More often, only when dictated</td>
</tr>
<tr>
<td>Proportion of weaner herds, where an antimicrobial sensitivity testing for intestinal pathogens, performed within the past year, is available</td>
<td>0%–24.9%, 25%–100%</td>
</tr>
<tr>
<td>Sampling method</td>
<td>Self-typed by respondent, telephone interview</td>
</tr>
</tbody>
</table>

\(^*\)As the capital region including Bornholm only consisted of one respondent, no comparison was made between this region and the other regions.

\(\dagger\)For this category, each group was tested in a running fashion; that is, the 0%–24.9% group was tested against the remaining groups joined, then the groups were joined as 0%–49.9% and 50%–100% and tested against each other, and finally the 75%–100% group was tested against the remaining groups joined.

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**Results**

Useful answers were obtained from 105 respondents making the response rate 83.3 per cent. The answers were collected as 53 self-typed on web, 51 by telephone interview and 1 partly as self-typed and partly as telephone interview. One telephone-interviewed respondent was excluded, because the interviewer was not able to make the respondent collaborate with the Likert scale-scored questions. The 21 non-participating veterinarians distributed as following: one was excluded, five refused to participate, one had retired in the period between obtainment of the study population and the data collection, four was out of reach due to maternity leave or vacation and with four respondents contact was established at least once but not at an appropriate time for telephone interview. With the final six veterinarians, no contact was established.

**Danish pig practitioners’ demographical characteristics**

The majority of the respondents (74.3 per cent) were male, and 72.4 per cent were part of a practice with at least one other pig practitioner. More than half of the practitioners (63.8 per cent) were either owner or co-owner of their practice and correspondingly 36.2 per cent were working as assistants. The remaining results of the surveyed demographical characteristics of the respondents are shown in table 2. Most of the pig practitioners (68.6 per cent) stated that they conduct MLD more often than dictated by the SRLD.

Table 3 shows how the respondents reported their use of antimicrobial sensitivity testing. Only a small fraction (16.2 per cent) of the respondents had performed a susceptibility test within the past year in all the herds where they were accountable for the VAC.
other factors were scored somewhat influential by the veterinarians.

**Associations between respondents’ characteristics and factors influencing antimicrobial choice**

In total 638 Mann-Whitney U tests were performed in order to analyse the scoring depending on the grouping of veterinarians into relevant groups (Table 1). This resulted in p<0.01 for 16 of the comparisons. Diverging stacked bar charts are shown for the groups that tended to deviate in figure 3 and figure 4. The proportion of working time serving as a pig practitioner and the extent of antimicrobial sensitivity testing usage were revealed as the characteristics that most often caused a tendency to score differently. Only two of the q values were very low (0.013 and 0.029), and only the p values corresponding to these two q values can be deemed significant with great confidence. Thus, the remaining 14 comparisons that resulted in low (<0.01) p values are of some risk of being false positives if counted as significant.

**Answers to the open-ended question**

In the open-ended question, 28.6 per cent of the respondents (n=30) stated that at least one additional factor influenced their choice of antimicrobial. After categorising the answers, some tendencies were found. Most remarkable was that eight respondents counted ‘Construction and condition of the piggery or pen’ influential, and another four did so for ‘The ease of administration’. Twenty-seven answers contained additional factors stated by less than four respondents, or the authors were unable to interpret the sense of the answer.

**Discussion**

The present study attempted to provide an overview of the factors influencing the choice of antimicrobials for intestinal diseases in Danish weaners. The findings indicate that multiple factors influence the clinical decision making. The most important factors are summarised in figure 5 with a suggestion for how they might exert their influence in the clinical decision-making. In general, experiences with clinical efficacy in the specific herd were scored highest among the 29 factors investigated, but other factors were reported to influence their choice of antimicrobials. These factors related to both the information available, own experience as pig practitioner and properties of the antimicrobials. The latter probably represents the demand for oral administration, as 98 per cent of all antimicrobials are administered through this route to Danish weaners. External factors such as TYCI were also deemed highly influential by the veterinarians.

**Strengths and limitations**

Danish farmers must enter into a VAC in order to legally store antimicrobials and execute treatments on own initiative. According to the Danish authorities, illegal Obtainment of antimicrobials is most probably very
Figure 2 Proportions (per cent) of Danish pig practitioners scoring a certain level (1–5) of influence by a given factor when choosing which antimicrobial to prescribe for intestinal diseases in weaners (n=105).

Figure 3 Proportions (per cent) of scored influence level (1–5) on antimicrobial choice for factors scored different by two groups of Danish pig practitioners (p<0.01).
Therefore, being the accountable veterinarian for at least one VAC was a well-chosen criterion of inclusion. Other studies obtained their study population based on membership of Veterinarian Societies, but the risk of selection bias cannot be ruled out for these methods. Veterinarians serving as pig practitioners in a small proportion of their working time proved important to include, since they tended to deviate when scoring certain factors. However, Danish law allows assistance from veterinarians other than the accountable for up to 50 per cent of the on-farm consultancies. Hence, there is a possibility of veterinarians, not accountable for any VAC themselves, prescribing antimicrobials. Therefore, a few relevant practitioners could have been overlooked by the used method. The authors believe such practitioners probably would be characterised by working as assistants and/or only have few years of veterinary experience.

In comparison with similar studies, this study achieved a very high response rate of 83.3 per cent (n=105). Gibbons and others and Busani and others reached 66 per cent (n=118) and 63 per cent (n=106) of their target population. Other studies had lower response rates between 1.5 per cent and 40 per cent. Dupont and others surveyed antimicrobial reduction strategies among Danish pig practitioners and achieved a response rate of 79.4 per cent (n=58).

The open-ended question answers could reasonably indicate the quality of the questionnaire design. As 71.4 per cent of the respondents felt the suggested factors were adequate to describe their clinical decision making, the most important factors must have been included. When the open answers were categorised, most answers were only stated by a few or a single respondent. However a few tendencies indicated missing factors: the solubility of the antimicrobial suits water administration, more than one disease is present at the same time, the ease of administration and the construction and condition of the piggery or pen. Adding these four factors, the designed questionnaire is suitable for reuse in similar studies.

Although several precautions were taken to minimise this, the present study, like other behavioural research studies, cannot be carried out without the risk of a variety of possible biases. The pig practitioners that reported to have obtained antimicrobial sensitivity tests more frequently (≥25 per cent of herds) in the past year were also scoring antimicrobial sensitivity testing more influential (p=0.00014, q=0.029) than the practitioners that used antimicrobial sensitivity tests less frequently (<25% of herds). This is indicative of an accordance between stated clinical decision-making and actual behaviour, although the finding could alternatively be explained by a consistency motif bias. Visschers and others made 215 farmers from four European countries estimate their antimicrobial usage compared to other farmers in their country. The farmers’ actual antimicrobial treatment incidence was accessed by on-farm visits. The study found that the estimated antimicrobial usage correlated to the actual intensity of antimicrobial usage. Furthermore, an overall tendency to estimate a low antimicrobial usage in comparison

### Figure 4
Proportions (per cent) of scored influence level (1–5) on antimicrobial choice for factors scored different by to groups of Danish pig practitioners (p<0.01).
to countrymen was revealed among the farmers. Accordingly, a questionnaire-based behavioural study is a valid method for studying the present subject, but multiple biases, for example, social desirability or demand characteristics, should reasonably be assumed to affect the results.

A legitimate criticism of the used statistical method would be the lack of correlation analysis between the explanatory variables. Therefore, the results in figure 3 and figure 4 should be interpreted with the possibility of unrevealed confounders in mind.

**Reflections on results in perspective of Danish prudent use initiatives**

An evaluation of the Danish authorities’ initiatives to promote PAMU in pig production could be beneficial in order to identify functioning legislative interventions. The present study’s findings on TYCI, the SRLD, and EPUG made by DVFA are therefore discussed in this perspective.

**The Yellow Card Initiative**

Previous studies had shown that TYCI motivated and directed a reduction of antimicrobials used in Danish pig production. TYCI scored as having either great or decisive influence on the choice of antimicrobial by 78.1 per cent of the respondents. As such, the present study provides good evidence that TYCI reduces the used amount of antimicrobials and influences the choice of antimicrobials as well. With the introduction of the ‘differentiated’ TYCI, it seems that a tool for regulating the choice of antimicrobial has been developed. This assertion needs to be further confirmed.

**The statutory requirement of laboratory diagnostics**

MLD generally scored high (78.1 per cent scored ≥4). The influence of the MLD has been investigated in two other
studies. MLD was conducted in most Danish weaner herds in relation to the introduction of the SRLD in 2014. Jensen and others used VETSTAT data to determine the prescribed antimicrobial for intestinal diseases; the study compared the choices of antimicrobials in the three months preceding the time point where the MLD was conducted and two to five months after the MLD was conducted. It revealed a change of antimicrobial in 28 per cent of the 1653 studied herds. Fourteen per cent changed to an antimicrobial that complied better with the evidence-based guidelines defined in the study. This shows a tendency, but the study proves no causal relation. Pedersen and others performed MLD on faecal samples from diarrhoea outbreaks in 38 Danish weaner herds. The test result for each herd was presented to the accountable veterinarian. Four weeks later, the 24 participating veterinarians were asked if preventive strategies or the antimicrobial treatment were changed in the herd based on the MLD, and this was the case in 32 per cent of the herds.

The present investigation found that a small fraction (6.6 per cent) of respondents grades the MLD of no or small influence. This could possibly be understood by findings from other studies. Jensen and others found that more than one pathogen were demonstrated in moderate massive amount in 47.1 per cent (n=809) of bacteriological laboratory findings for intestinal diseases in Danish weaners. Assuming that Dutch and Danish veterinarians are somewhat alike, these results are of little use according to Speksnijder and others. Their investigations showed that Dutch farm animal practitioners often consider tests detecting multiple pathogens an insignificant diagnostic tool.

Taken together, the present and previous studies show that MLD is generally considered a useful tool. In the Netherlands, the farmers’ reluctance is a common reason not to have MLD performed. Thus, the SRLD ensures the veterinarian a helpful tool regardless of the farmer’s opinion.

It can be discussed whether SRLD at least once a year is sufficient. The findings of Pedersen and others indicate that MLD should be conducted more frequently. In this research, three consecutive quantitative PCR tests examined faecal samples for Escherichia coli (Fimbria type F4 and F18), Brachyspira pilosicoli and Lawsonia intracellularis in Danish weaner herds. This detected a change of infection within a two months period in 84 per cent (95 per cent CI 64 per cent 95 per cent) of the herds. However, this study showed that 68.6 per cent of Danish pig practitioners sometimes requests MLD beyond the SRLD on own initiative.

The EPUG made by DVFA Prudent use guidelines made by DVFA scored rather modest overall. However, figure 2A shows a tendency (p=0.0091, q=0.23) for a considerable fraction of veterinarians only serving as a pig practitioner in a small proportion of their working time. They state that this factor exerts great influence or decisive influence on their antimicrobial choice. It is reasonable to think that these practitioners could be in greater risk of making clinical decision errors, as they are manoeuvring outside their main field. This somewhat aligns with their slightly more reserved inclination (p=0.0079, q=0.23) to trust their tentative diagnosis based on clinical signs also seen in figure 2A. As it is essential to help these veterinarians reduce the risk of clinical decision errors, it seems that the EPUG made by DVFA serves a decent purpose. This conclusion is of great uncertainty as both of the mentioned q values were 0.23.

Conclusion This study provides an overview of to which extent different factors influenced the Danish pig veterinarians’ choice of antimicrobials prescribed for treatment of intestinal diseases in weaners. The veterinarian’s own experiences of clinical efficacy in a specific herd exerted the greatest influence overall. The investigation revealed that TYCI is a functioning intervention to affect the Danish pig practitioners’ choice of antimicrobials. Furthermore, the SRLD secures the pig practitioners a useful tool in order to make an appropriate choice of antimicrobial.

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Competing interests None declared.

Ethics approval No ethical approval was sought for the study, as it was not necessary for this type of study according to Danish legislation.

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