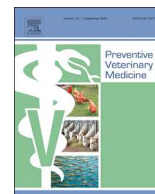




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Antibiotic dry cow therapy, somatic cell count, and milk production: Retrospective analysis of the associations in dairy herd recording data using multilevel growth models

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ABSTRACT

Antibiotic dry cow therapy (DCT) is an important part of most mastitis control programs. Updating DCT recommendations is an ongoing topic due to the global problem of antimicrobial resistance. Finland, along with other Nordic countries, has implemented selective DCT for decades. Our study analyzed Dairy Herd Improvement (DHI) information from 241 Finnish farmers who participated in a survey about their drying-off practices. The aim was to evaluate herd-level associations between milk somatic cell count (SCC), milk production, and various antimicrobial DCT approaches both cross-sectionally in 2016 and longitudinally in 2012–2016. The three DCT approaches in the study were selective, blanket, and no DCT use. An additional aim was to evaluate whether dynamic changes occurred in herd-average SCC and annual milk production over five years, and whether these potential changes differed between different DCT approaches. The method for the longitudinal analyses was growth modeling with random coefficient models. Differences in SCC and milk production between farms with different DCT approaches were minor. Regardless of the farm's DCT approach, annual milk production increased over the years, while average SCC was reasonably constant. The variability in SCC and milk production across all DCT groups was low between years, and most of the variability was between farms. Compared to other milking systems, farms with automatic milking system (AMS) had higher SCC, and in 2016 higher milk production. The results of this study suggest that it is possible to maintain low herd-average SCC and good milk production when using selective DCT and following the guidelines for prudent antimicrobial use. Average SCC and milk production varied across the herds, suggesting that advice on DCT practices should be herd-specific. The methodology of growth modeling using random coefficient models was applicable in analyzing longitudinal data, in which the time frame was relatively short and the number of herds was limited.

1. Introduction

Various studies show the importance of dry cow management and the dry period to dairy cow health (Dingwell et al., 2003; Bradley and Green, 2004). Mastitis remains the most costly disease for the dairy industry worldwide, and dairy cows are particularly susceptible to new intramammary infections (IMI) at the beginning and the end of the dry period (Dingwell et al., 2003; Bradley and Green, 2004). Antibiotic dry cow therapy (DCT) is efficient in reducing IMI prevalence and raising milk yield at subsequent lactation (Bradley and Green, 2004). DCT can be administered at dry-off either to all cows (blanket DCT), or only to infected cows or quarters (selective DCT). Some countries have recommended blanket DCT for decades as a part of the 5-point plan for

mastitis control (Neave et al., 1969). These recommendations emerged at a time when the most common causes of mastitis were contagious pathogens. The relative importance of different pathogens has changed, however, and now the most significant causes of new IMI during the dry period are environmental pathogens (Klaas and Zadoks, 2018).

Antimicrobial resistance is one of the most serious global public health threats (WHO, 2014). Although antibiotic resistance is a natural phenomenon, the use of antimicrobials has contributed to the dissemination and evolution of antibiotic resistance (Davies and Davies, 2010; Perry and Wright, 2013; Surette and Wright, 2017). Prudent use of antimicrobials is emphasized in human and veterinary medicine, as well as in agriculture (Laxminarayan et al., 2013; EMA and EFSA, 2017). The European commission recommends avoiding routine

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antimicrobial treatment of cows at dry-off (European Commission, 2015). Consequently, some countries have restricted the use of antibiotics by legislation (Santman-Berends et al., 2016; Gussmann et al., 2018). Finland and other Nordic countries have always recommended selective DCT as part of their national mastitis control programs (Ekman and Østerås, 2003; Rajala-Schultz et al., 2019). According to an online survey, only 13% of the responding Finnish dairy farmers applied blanket DCT (Vilar et al., 2018). In some other countries, blanket DCT is a common practice (Bertulat et al., 2015; USDA, 2016; More et al., 2017).

The use of selective DCT may become more widespread, if it is economically feasible and maintains the same udder health and milk production as blanket DCT. Recent results suggest that economics is not an argument against reducing DCT use, but the optimal decisions can vary considerably among herds (Huijps and Hogeveen, 2007; Halasa et al., 2010; Down et al., 2016; Scherpenzeel et al., 2018). In addition to DCT, other farm characteristics and dry cow management practices affect udder health. Although cow-level and quarter-level research exists (Rajala-Schultz et al., 2011; Cameron et al., 2014; Scherpenzeel et al., 2014; Cameron et al., 2015; Vasquez et al., 2018), longitudinal studies over years focusing on within-herd dynamics of udder health and DCT seem to be few (Vanhoudt et al., 2018).

The goal in longitudinal data analysis may be a combination of examining both the mean differences over time and patterns of change over time. Because the collection of longitudinal data is from single animals, groups, or herds over time, its observations are likely to show a high degree of non-independence. Observations that are closer in time will be more closely correlated than observations occurring farther apart. The pattern of change tends to vary over time. All of these methodological issues need to be taken into account. Longitudinal analyses called growth modeling (growth curve modeling, trend modeling) using random coefficient models is a more common method in organizational and psychological science than in veterinary science. This model-building strategy is, however, a useful and accessible approach and can help to extract more information from the data (Bliese and Ployhart, 2002; Raudenbush and Bryk, 2002; Twisk, 2006; Ployhart and Vandenberg, 2010).

Our primary objective was to evaluate herd-level associations between somatic cell count (SCC), milk production, and different farm characteristics with a special focus on antimicrobial dry cow therapy. The secondary objective was to examine whether dynamic changes occurred in herd-average SCC and milk production over five years, and whether these potential changes differed between various DCT approaches.

2. Materials and methods

2.1. Data

The information on farm characteristics and dry cow management practices came from an online questionnaire conducted in 2017. The questionnaire was accessible to all approximately 5400 dairy farmers who belonged to the Finnish dairy herd recording system in 2016. The responding farms amounted to 715. Vilar et al. (2018) described the detailed information of the questionnaire. The farm characteristics indicated that the responding farms were representative of current Finnish dairy industry. The information included the herd level DCT approach in three categories, which were no DCT, selective DCT and blanket DCT. Information additionally included the length of the DCT approach in use (<1 year, from 1 to 5 years, >5 years). Furthermore, information comprised the milking system, use of intramammary teat sealants (ITS), desired milk yield at dry-off (<10 kg, between 10 and 15 kg, >15 kg), and average dry period length (≤ 8 weeks or >8 weeks). Information at the herd-level included the approximate proportion of DCT-treated cows, and proportion of cows with microbiological analysis of milk samples at dry-off.

The source of the Dairy Herd Improvement (DHI) data was the Finnish Milk Recording database (MTech Digital Solutions, Vantaa, Finland). From the farms that responded to the online questionnaire, those who granted permission to use their DHI data for research purposes totaled 271. DHI data from 2012 to 2016 comprised herd-level annual average milk SCC and herd-level annual milk production per cow. The DHI Association calculates these measures as annual herd-averages of usually monthly or bimonthly milk SCC and milk production measurements of the individual cows. Later in the text, these will be referred briefly as herd-average SCC and herd-average milk production. Additionally data included herd-average parity, culling rate, and herd size. The DHI data for every farm were combined with the above-mentioned questionnaire data from the farm.

Excluded farms were organic farms ($n = 9$) and conventional farms with an average number of cows less than 10 ($n = 4$). The farms that reported the length of the DCT approach being <1 year ($n = 11$) were excluded from the study. Furthermore, we excluded farms with less than 3 years of complete DHI data and farms without data from 2016 and 2015 ($n = 6$). The final data set comprised 241 farms.

2.2. Descriptive statistics, unconditional associations and multiple linear regression for 2016

The following steps describe the process of the statistical analyses for two models, where herd-average of individual cow SCC ($\times 1000$ cells/mL) measurements and herd-average milk production per cow ($\times 1000$ kg) were the continuous outcomes. The standard descriptive statistics were calculated from the data. The SCC and milk production data were normally distributed. The analysis of unconditional associations (main effects and first-order interactions) was performed between the explanatory variables and the outcome variables. The variables that were associated (p -value < 0.2) with herd-average SCC were herd size ($\times 10$ cows, continuous, centered on a median), herd-average milk production and milking system (categorical with three levels: pipeline, parlor, automatic milking system). The variables that were associated (p -value < 0.2) with herd-average milk production were herd size, herd-average SCC, milking system, herd-average parity (categorical with two levels: <2.5, ≥ 2.5), and the use of ITS (categorical with two levels: yes, no).

Multiple linear regression was used for the 2016 analysis with manual backward elimination model-building procedure to identify statistically significant explanatory variables (F -test, p -value < 0.05). DCT approach was kept in the final models, even though not significant, because it was the main variable of interest. Milking system and herd size were included in the final models as confounding variables. The interaction between milking system and herd size was tested in the models for the following reasons. First was to control the confounding effect of these variables in the best possible way. Second, it provided the opportunity to retain two highly correlated predictors in the models. Third, it is biologically plausible that the effect of increasing herd size in one type of milking system might have a different effect than in another. Model assumptions were checked by plotting residuals versus fitted values, and model validation indicated no violations against the assumptions. Analyses were done with R version 3.5.1 (R Core Team, 2018) using R Studio Version 1.1.463 (RStudio Team, 2016).

The variability between geographical areas was analyzed with linear mixed model for the 2016 data with the province as a random effect. There was no evidence of geographical dependency structure with either of the outcomes, and therefore geographic region was not considered in any of the analyses. Analyses were done with R version 3.5.1 (R Core Team, 2018) using R Studio Version 1.1.463 (RStudio Team, 2016) with the package lme4 (Bates et al., 2015).

2.3. Growth modeling using random coefficient models for 2012–2016

Growth modeling framework was done with R version 3.5.1 (R Core Team, 2018) using R Studio Version 1.1.463 (RStudio Team, 2016) with the package nlme (Pinheiro et al., 2018). To ensure that the effect over time was linear instead of discontinuous or nonlinear, outcomes SCC and milk production were plotted against time with a regression line. Both outcomes were analyzed using multilevel growth modeling. The effect of DCT approach over the time (continuous) was analyzed with linear mixed model. To aid the interpretation, time was centered so that the intercept represented the predicted herd-average SCC and milk production in 2012. In order to determine the most appropriate model structure, the following four models were fit for both SCC and milk production:

Model 1 – fixed effects: DCT and time, random effects: random intercept (herd).

Model 2 – fixed effects: DCT and time, random effects: random intercept and slope (time).

Model 3 – Model 2 with DCT*time interaction added as a fixed effect.

Model 4 – Model 3 with ar (1) correlation structure added to residuals.

Models were compared using a likelihood ratio test based on a maximum likelihood estimation.

The equations of Raudenbush and Bryk (2002) represent the two-level longitudinal random coefficient model structure:

$$\text{Level 1: } Y_{it} = \pi_{0i} + \pi_{1i}T_{it} + e_{it}$$

$$\text{Level 2: } \pi_{0i} = \beta_{00} + \beta_{01}X_i + r_{0i}$$

$$\pi_{1i} = \beta_{10} + \beta_{11}X_i + r_{1i}$$

Different intercept and slope parameters are possible for each herd, and this is why there are t (time) and i (herd) subscripts for the intercept (π_{0i}) and slope (π_{1i}). T_{it} in the model refers to the coding for time (linear). Y_{it} is the response variable related to the herd i at time t . X_i represents the explanatory variable related to the herd i . β_{00} represents the average intercept (fixed effect) and r_{0i} represents the variability in intercepts across the herds. β_{10} represents the average slope (fixed effect), and r_{1i} represents the variability in slopes across herds. Therefore, the Level 1 equation models the within-herd variability and the Level 2 equations model the between-herd variability in change over time.

Explanatory variables used in the 2016 data analysis were introduced to Model 2 with manual backward elimination model-building procedure to identify statistically significant explanatory variables ($p < 0.05$) thus forming the final models. The interaction effect between DCT approach and time was analyzed during the model comparison (Model 3). The effect of DCT on the change of SCC or milk production over time was insignificant and small, and the interaction

was omitted from the final models. In order to take into account the reported change in DCT approach in some of the farms, we evaluated the stability of DCT approach over time as a two-level categorical variable (approach in use 1–5 years, approach in use over 5 years). This variable was omitted, because it was not statistically significant for either of the outcome variables. As in the previously described multiple linear regression models for 2016, milking system and herd size were both included in the final models as confounding variables, and the interaction between milking system and herd size was tested in the final models. There was a reported change in milking system in 30 farms during 2012–2016 either to parlor or to automatic milking system. We analyzed the effect of this change as two-level categorical variable (same milking system during 2012–2016, change in the milking system during 2012–2016). In all longitudinal analyses, the farms with a change in their milking system were placed in the milking system category where they were at least three years during the study period. All model assumptions were checked by plotting residuals versus fitted values and model validation indicated no violations against model assumptions. Parameter estimation was based on the restricted maximum likelihood (REML).

After fitting the final models for both outcomes, the variance function in MLwiN (Rasbash et al., 2009) was used for calculation of the intercept variance, the slope variance, and the intercept-slope covariance for each year. The sum of these three was the total herd level variance for that year. Combining the herd level variance to the residual variance resulted in the total variance. The ratio of herd level variance to total variance resulted in the intra-class correlation coefficients (ICC) for each year.

3. Results

3.1. Descriptive statistics and multiple linear regression for 2016

Selective DCT was the most common approach (79.7%, 192/241) followed by blanket DCT (14.5%, 35/241) and no DCT (5.8%, 14/241). A high percentage of the farmers using selective DCT (73.4%) reported treating only up to one-fourth of their cows at dry-off, and only 9.4% of the farmers treated more than half of their cows at dry-off. The length of the DCT approach in use was 1–5 years in 51 farms and over 5 years in 190 farms. Table 1 presents descriptive statistics of farm characteristics in 2016. The target population of the questionnaire was all dairy farmers in the Finnish dairy herd recording system in 2016. That year, approximately 70% of Finnish herds and 80% of Finnish cows belong to this recording system. The sample seemed representative of Finnish herds, although the studied farms had slightly larger herd size, higher milk production, and lower SCC than the average Finnish dairy herds at that time. Based on postal zip codes, the farms were geographically distributed to 17 different Finnish provinces. Although the data showed

Table 1
Annual Dairy Herd Improvement (DHI) information presented from 241 dairy herds in 2016.

	Blanket DCT ^a (n = 35)			Selective DCT (n = 192)			No DCT (n = 14)			National database ^b
	Mean (median)	Min	Max	Mean (median)	Min	Max	Mean (median)	Min	Max	Mean
Herd size	77.9 (62.4)	15.4	254.7	49.5 (37.6)	13	314.7	46.1 (30.4)	15.7	153.7	41.5
SCC ^c (× 1000 cell/mL)	162.9 (157.0)	49	316	160.7 (163.0)	36	336	155.8 (166.5)	82.0	260.0	178
Milk production (kg)	10091.4 (9944.0)	7797	11,600	9693.9 (9664.5)	6693	12,486	10094.1 (10083.0)	7788	12,367	9542
Parity	2.4 (2.4)	1.8	3.4	2.5 (2.5)	1.7	4.3	2.2 (2.3)	1.8	2.8	2.4
Milking system	Number (%)			Number (%)			Number (%)			
Pipeline	10 (28.6)			97 (50.5)			11 (78.6)			
AMS ^d	16 (45.7)			40 (20.8)			1 (7.1)			
Parlor	9 (25.7)			55 (28.7)			2 (14.3)			

^a Dry cow therapy.

^b Finnish Milk Recording System (2016).

^c Somatic cell count.

^d Automatic milking system.

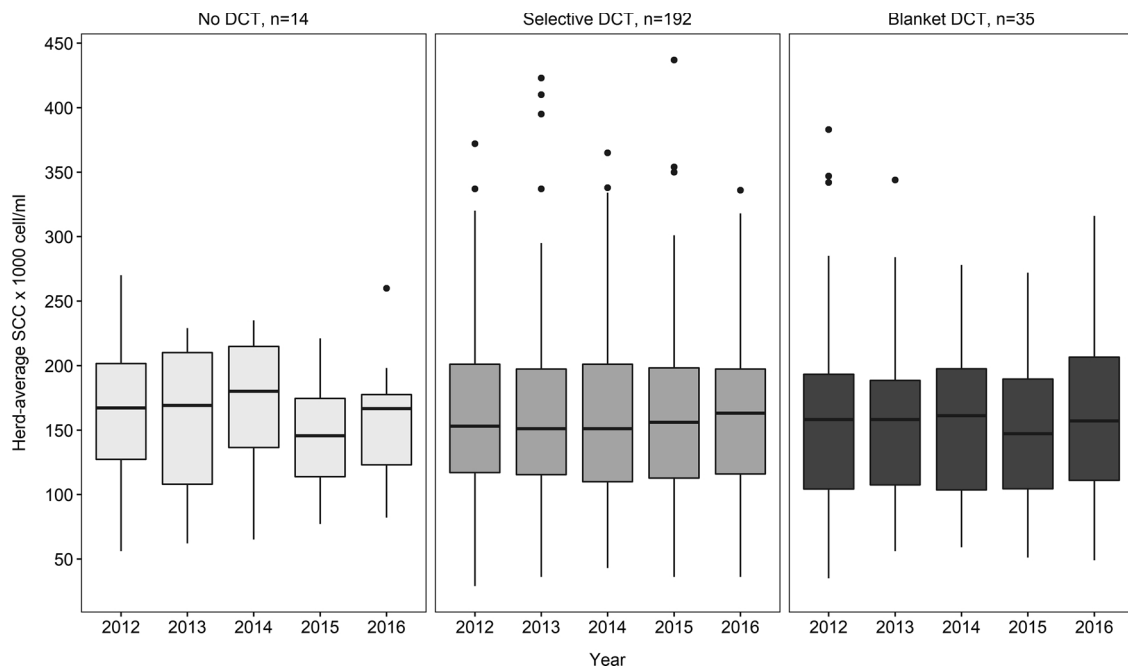


Fig. 1. Tukey boxplot of herd-average milk somatic cell count (SCC) ($\times 1000$ cell/mL) over five years in three dry cow therapy (DCT) approach groups, based on 1195 recordings from 241 dairy herds.

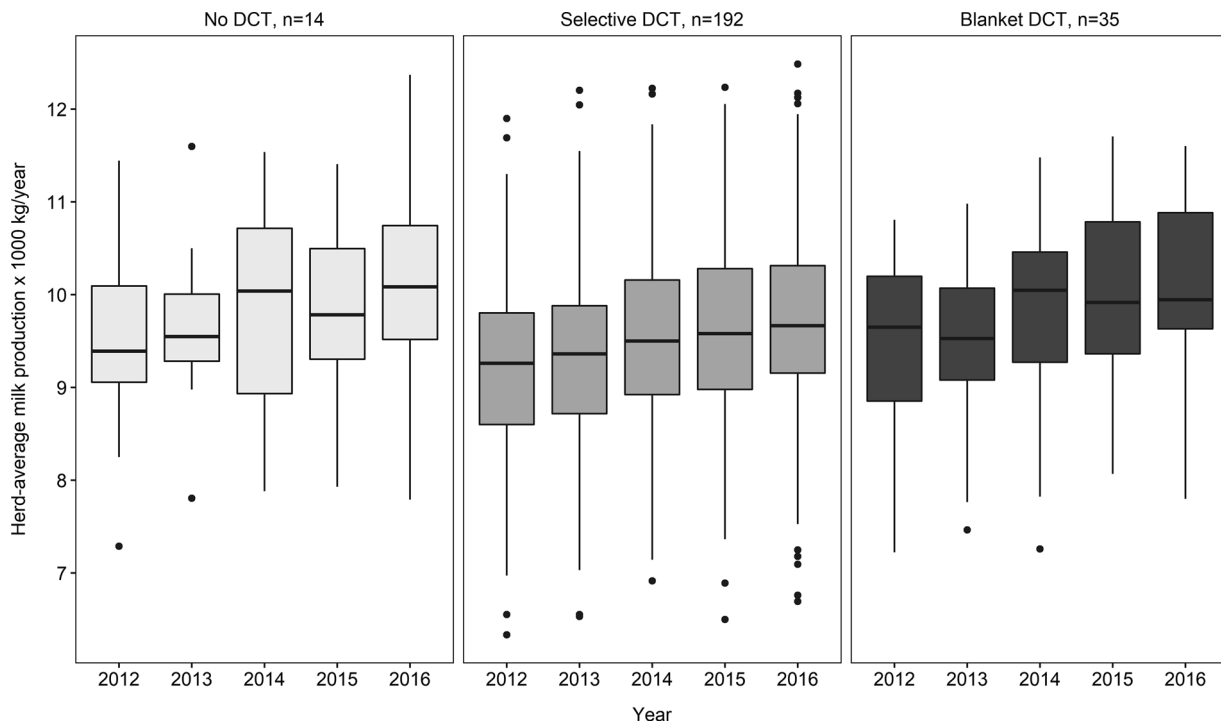


Fig. 2. Tukey boxplot of herd-average milk production ($\times 1000$ kg) over five years in three dry cow therapy (DCT) approach groups, based on 1195 recordings from 241 dairy herds.

clear regional clustering into three provinces with the highest dairy livestock density in Finland, the regional variance was very small (< 0.0001) between areas across all DCT approaches with both outcomes. The overall proportion of farms in 2016 with pipeline milking system, parlor milking system and automatic milking systems (AMS) was 49%, 27%, 24%, respectively. The corresponding numbers were 50%, 29% and 21% during 2012–2016, reflecting the change in the milking system in some farms. DCT approaches were implemented in different frequency among farms with different milking systems;

blanket DCT was most commonly used in the AMS farms (Table 1). Microbiological analysis of milk samples at dry-off was carried out in 54.3% of the blanket DCT farms and in 83.9% of the selective DCT farms. Farms that did not use DCT did not analyze milk samples either. Although some of the farm characteristics were different, SCC and milk production did not differ between selective DCT, blanket DCT and no DCT farms. Figs. 1 and 2 show Tukey boxplots representing herd-average SCC and herd-average milk production of the DCT groups.

Table 2 presents the results of the multiple linear regression for SCC

Table 2Model estimates from multiple linear regression for annual herd-average milk somatic cell count ($\times 1000$ cells/mL) from 241 dairy herds in 2016.

Variable	Category	Coefficient	S.E.	t-value	p-value	95% CI ^a	
Intercept		203.582	35.851	5.679	<0.0001	132.947	274.216
DCT ^b approach					0.679 ^e		
	No DCT	7.831	15.521	0.505	0.614	-22.748	38.411
	Blanket DCT	-7.171	10.608	-0.676	0.500	-28.071	13.729
	Selective DCT	Ref.					
Milk production ($\times 1000$ kg)		-9.691	3.617	-2.679	0.008	-16.819	-2.564
Herd size ($\times 10$ cows) ^c		10.971	3.976	2.759	0.006	3.137	18.805
Milking system					0.0007 ^e		
	Parlor	48.188	17.167	2.807	0.005	14.364	82.012
	AMS ^d	90.625	22.005	4.118	<0.0001	47.269	133.980
	Pipeline	Ref.					
Milking system \times herd size ($\times 10$ cows)					0.028 ^e		
	Parlor	-9.376	4.187	-2.239	0.026	-17.626	-1.127
	AMS	-11.691	4.356	-2.684	0.008	-20.273	-3.108
	Pipeline	Ref.					

^a Confidence interval.^b Dry cow therapy.^c Centered on a median herd size of 40 cows.^d Automatic milking system.^e Wald test.**Table 3**Model estimates from multiple linear regression for annual herd-average milk production per cow ($\times 1000$ kg) from 241 dairy herds in 2016.

Variable	Category	Coefficient	S.E.	t-value	p-value	95% CI ^a	
Intercept		9.567	0.271	35.367	<0.0001	9.034	10.100
DCT ^b approach					0.160 ^f		
	No DCT	0.454	0.276	1.644	0.101	-0.090	0.998
	Blanket DCT	0.211	0.189	1.119	0.264	-0.161	0.585
	Selective DCT	Ref.					
SCC ^c ($\times 1000$ cell/mL)		-0.003	0.001	-2.679	0.008	-0.005	-0.001
Herd size ($\times 10$ cows) ^d		0.165	0.071	2.316	0.021	0.025	0.306
Milking system					0.0002 ^f		
	Parlor	0.325	0.311	1.045	0.297	-0.288	0.939
	AMS ^e	1.345	0.398	3.382	0.0008	0.561	2.129
	Pipeline	Ref.					
Milking system \times herd size ($\times 10$ cows)					0.073 ^f		
	Parlor	-0.153	0.075	-2.042	0.042	-0.301	-0.005
	AMS	-0.180	0.078	-2.297	0.022	-0.334	-0.026
	Pipeline	Ref.					

^a Confidence interval.^b Dry cow therapy.^c Somatic cell count.^d Centered on a median herd size of 40 cows.^e Automatic milking system.^f Wald test.

and Table 3 for milk production in 2016. There were no statistically significant differences in SCC or milk production predictions, when no DCT and blanket DCT farms were compared to selective DCT farms. Compared to the farms with pipeline milking system, AMS and parlor farms had significantly higher herd-average SCC. This difference was noteworthy from the practical point of view especially on farms with AMS. Difference in estimated herd-average milk production between AMS farms and pipeline farms was 1345 kg. Taking into account the interaction between milking system and herd size, the effect of increasing herd size on SCC and milk production was significantly different in AMS and parlor farms compared to pipeline farms. Increase in herd size by 10 cows above 40 cows seem not to have any meaningful effect on SCC or milk production in AMS and parlor farms.

3.2. Growth modeling using random coefficient models for 2012–2016

3.2.1. Model comparison

Table 4 shows the random effect components and the summary of the model comparison for the herd-average SCC and Table 5 for the

herd-average milk production. Including the random slope (Model 2) improved the model fit statistically significantly for both outcomes (p -value < 0.0001). DCT was forced into the models, because it was the main explanatory variable of interest. In Model 3, the DCT*time interaction term was forced into the models in order to evaluate the effect of DCT over time. Adding the autoregressive, ar(1) correlation structure to the models reduced the log likelihood only slightly. The Log likelihood reduction was about 10 in milk production model (from -1063 to -1054) and under 10 in SCC model (from -6317 to -6314). In the milk production model, the addition of ar(1) structure had a noticeable influence on the correlation between intercepts and slopes and changed the random effect variance structure to resemble what it was in the random intercept-only model (Table 5). Thus, it seemed that random coefficient modeling removed the need for adding correlated residuals, even though the fit of the model was best when using both. Because of the risk of overfitting the model, the final models were build up without ar(1) autocorrelation structure.

Table 4
Multilevel growth modeling for annual herd-average milk somatic cell count ($\times 1000$ cell/mL), based on 1195 recordings from 241 dairy herds (2012–2016).

	Model 1 ^a		Model 2 ^a		Model 3 ^a			Model 4 ^a						
<i>Random effects</i>														
	Variance	SD ^b	Variance	SD	Corr. ^c		Variance	SD	Corr.	Variance	SD	Corr.		
Herd (intercept)	2452.752	49.525	3505.512	59.207			3515.513	59.292		3190.277	56.483			
Time (slope)			135.093	11.623	−0.553		136.808	11.696	−0.555	91.848	9.584	−0.540		
Residual	1553.888	39.419	1217.966	34.899			1217.982	34.900		1428.464	37.795			
<i>Model comparison</i>														
					Model 1 versus 2						Model 2 versus 3		Model 3 versus 4	
	LogL ^d	df ^e	LogL	df	L. ratio ^f	p-value	LogL	df	L. ratio	p-value	LogL	df	L. ratio	p-value
	−6346.626	6	−6317.076	8	59.100	<0.0001	−6316.864	10	0.424	0.809	−6314.441	11	4.847	0.0277

^a Model 1: fixed effects DCT and time, random intercept (herd); Model 2: fixed effects DCT and time, random intercept and slope (time); Model 3: Model 2 with DCT**time* interaction added as a fixed effect; Model 4: Model 3 with ar (1) correlation structure added to residuals.

^b Standard deviation of random effect variance component.

^c Correlation between intercepts and slopes.

^d Log likelihood value.

^e Degrees of freedom.

^f Likelihood ratio.

3.2.2. Associations between antimicrobial dry cow therapy, SCC, and milk production 2012–2016

Table 6 presents the results of the final model for herd-average SCC and Table 7 for herd-average milk production. There were no statistically significant differences in SCC or milk production predictions, when no DCT and blanket DCT farms were compared to selective DCT farms. The herd-average SCC did not change over the five years. Milk production increased about 127 kg for each additional year from 2012 onwards. The SCC in farms with AMS was 50 000 cells/mL higher compared to the pipeline milking system and 39 000 cells/mL higher compared to the farms with parlor milking facility. The variable reflecting a change in the farm’s milking system during 2012–2016 was statistically significant explanatory variable only for milk production, but not for SCC. Milk production estimate for 2012 was about 451 kg higher for farms that changed their milking system in 2012–2016 compared to the farms maintaining the same milking system.

3.2.3. Variance components

The variability in SCC and milk production across all DCT groups was low between years, and most of the variability was between farms (Tables 6 and 7). Annual ICC values ranged from 0.61 to 0.70 when modeling SCC and from 0.83 to 0.85 when modeling milk production. When the outcome was SCC, there was a negative correlation of −0.56 between intercepts and slopes (Table 6) showing that herds with low intercept (SCC in 2012) had steeper slope than herds with high

intercept. When the outcome was milk production, the negative correlation between intercepts and slopes was −0.35 (Table 7) showing that herds that had low intercept (milk production in 2012) had steeper slope (i.e. gained more) than herds with high intercept.

4. Discussion

Selective DCT has been widely implemented in Finland (Vilar et al., 2018), and therefore the Finnish DHI data enabled us to test the study objective. Although the use of DCT may have an effect on herd-level SCC or milk production, this study found no significant differences between various DCT approaches. Based on these results, what is impossible to know is whether udder health or milk production would change, if DCT approach changed. These results show, however, that Finnish farms implementing selective DCT can maintain low SCC and high milk production. In the data, some blanket-DCT farms had average SCC under 100–150,000 cell/mL and, based on SCC-measures, apparently good udder health (Fig. 1). On those farms, switching to selective DCT could be worth trying for economic reasons and for promoting prudent antibiotic use. Although the group of farms using no DCT was too small to allow firm conclusions, our data suggest that it is possible to achieve low herd-level SCC and high milk production even without DCT. Based on the variance components and interquartile ranges, annual average SCC and milk production varied across the herds. This suggests that advice on DCT practices should be herd-specific, as has

Table 5
Multilevel growth modeling for annual herd-average milk production ($\times 1000$ kg), based on 1195 recordings from 241 dairy herds (2012–2016).

	Model 1 ^a		Model 2 ^a		Model 3 ^a			Model 4 ^a						
<i>Random effects</i>														
	Variance	SD ^b	Variance	SD	Corr. ^c		Variance	SD	Corr.	Variance	SD	Corr.		
Herd (Intercept)	0.759	0.871	0.824	0.908			0.824	0.908		0.738	0.859			
Year (Slope)			0.026	0.161	−0.266		0.026	0.161	−0.266	0.015	0.121	−0.157		
Residual	0.210	0.459	0.147	0.383			0.147	0.383		0.210	0.459			
<i>Model comparison</i>														
					Model 1 versus 2						Model 2 versus 3		Model 3 versus 4	
	LogL ^d	df ^e	LogL	df	L. ratio ^f	p-value	LogL	df	L. ratio	p-value	LogL	df	L. ratio	p-value
	−1116.115	6	−1064.332	8	103.567	<0.0001	−1063.491	10	1.681	0.432	−1054.056	11	18.870	<0.0001

^a Model 1: fixed effects DCT and time, random intercept (herd); Model 2: fixed effects DCT and time, random intercept and slope (time); Model 3: Model 2 with DCT**time* interaction added as a fixed effect; Model 4: Model 3 with ar (1) correlation structure added to residuals.

^b Standard deviation of random effect variance component.

^c Correlation between intercepts and slopes.

^d Log likelihood value.

^e Degrees of freedom.

^f Likelihood ratio.

Table 6

Model estimates from multilevel growth modeling for annual herd-average milk somatic cell count ($\times 1000$ cell/mL), based on 1195 recordings from 241 dairy herds (2012–2016).

Variable	Variance	S.D.	Corr. ^a		
<i>Random effects</i>					
Herd (Intercept)	2803.658	52.950			
Year (Slope)	133.666	11.561	−0.561		
Residual	1226.504	35.021			
Variable	Category	Coeff.	S.E.	t-value	p-value
<i>Fixed effects</i>					
Intercept		220.447	21.434	10.285	<0.0001
DCT ^b approach					0.127 ^f
	No DCT	9.865	13.119	0.752	0.453
	Blanket DCT	−16.408	8.973	−1.829	0.069
	Selective DCT	Ref.			
Year ^c		0.371	1.100	0.338	0.736
Milk production ($\times 1000$ kg)		−7.772	2.204	−3.526	0.0004
Herd size ($\times 10$ cows) ^d		3.024	2.895	1.044	0.297
Milking system					<0.0001 ^f
	Parlor	10.864	8.084	1.344	0.180
	AMS ^e	50.290	10.625	4.733	<0.0001
	Pipeline	Ref.			
Milking system \times herd size ($\times 10$ cows)					0.648 ^f
	Parlor	−0.682	3.119	−0.219	0.827
	AMS	−2.228	3.124	−0.693	0.488
	Pipeline	Ref.			

^a Correlation between intercepts and slopes.

^b Dry cow therapy.

^c Centered on year 2012.

^d Centered on a median herd size of 40 cows.

^e Automatic milking system.

^f Wald test.

been stated also in other studies (Rajala-Schultz et al., 2011; Gussmann et al., 2018). Farms will choose selective DCT over blanket DCT, if it maintains similar udder health and milk production level in herds, and if it proves to be an economically profitable solution. Optimal economic decisions about DCT use can vary greatly between herds, but several studies suggest that economics is not a reason for blanket use of DCT (Huijps and Hogeveen, 2007; Halasa et al., 2010; Down et al., 2016; Scherpenzeel et al., 2018).

Longitudinal studies focusing on within-herd dynamics of udder health and dry cow therapy practices are scarce. Vanhoudt et al. (2018) reported that transition from mainly blanket DCT to selective DCT in the Netherlands had no detrimental effect on udder health. Their study differed from ours, because they analyzed changes in average herd-level percentage of new IMI and cured IMI over the years as well as cow-level SCC dynamics over the dry period. In our study, annual DCT-treatment percentage of the herds was not available. Although the actual DCT-treatment percentage in the selective-DCT farms varies, based on the survey data, about 70% of the farmers in the current study reported treating up to one-fourth of their cows, and only 9% of the farmers treated more than half their cows at dry-off. According to this information, antibiotic DCT usage in most Finnish selective DCT herds was lower than in selective DCT herds in the Vanhoudt et al. (2018) study. Both of these results seem to indicate that selective treatment of only infected cows is not an obstacle to long-term good udder health or milk production, and based on our findings, the herd-level DCT-treatment percentage can safely be even fairly small.

Herd-level studies about the effect of DCT on udder health are lacking, but cow-level and quarter-level studies exist. Results are

Table 7

Model estimates from multilevel growth modeling for annual herd-average milk production per cow ($\times 1000$ kg), based on 1195 recordings from 241 dairy herds (2012–2016).

Variable	Variance	S.D.	Corr. ^a		
<i>Random effects</i>					
Herd (Intercept)	0.821	0.906			
Year (Slope)	0.025	0.158	−0.346		
Residual	0.147	0.383			
Variable	Category	Coeff.	S.E.	t-value	p-value
<i>Fixed effects</i>					
Intercept		9.416	0.114	82.946	<0.0001
DCT ^b approach					0.274 ^g
	No DCT	0.308	0.243	1.268	0.206
	Blanket DCT	0.179	0.166	1.078	0.283
	Selective DCT	Ref.			
Year ^c		0.127	0.013	9.479	<0.0001
SCC ^d ($\times 1000$ cell/mL)		−0.001	0.000	−2.173	0.030
Herd size ($\times 10$ cows) ^e		0.086	0.044	1.944	0.052
Milking system					0.023 ^g
	Parlor	−0.326	0.146	−2.229	0.027
	AMS ^f	−0.033	0.198	−0.168	0.867
	Pipeline	ref.			
Change in milking system in 2012–2016	Yes	0.451	0.191	2.355	0.019
	No	Ref.			
Milking system \times herd size ($\times 10$ cows)					0.200 ^g
	Parlor	−0.079	0.048	−1.648	0.100
	AMS	−0.045	0.049	−0.912	0.362
	Pipeline	Ref.			

^a Correlation between intercepts and slopes.

^b Dry cow therapy.

^c Centered on year 2012.

^d Somatic cell count.

^e Centered on a median herd size of 40 cows.

^f Automatic milking system.

^g Wald test.

somewhat contradictory. Although some studies found no major differences in udder health between selective DCT and blanket DCT treated cows (Rajala-Schultz et al., 2011; Cameron et al., 2014, 2015; Vasquez et al., 2018), one study reported an increase in clinical and subclinical mastitis after selective DCT among low-SCC cows (Scherpenzeel et al., 2014). In terms of milk yield, the effects of DCT during the following lactation of dry-treated and untreated low-SCC cows appears negligible, but there is variability between herds (Rajala-Schultz et al., 2011; Cameron et al., 2015). Overall, selective DCT approach appears to have little or no disadvantages, while the benefit of reducing the amount of used antibiotics is important.

To the best of our knowledge, there are no previous studies about the effect of DCT on the udder health or milk production together with the milking system information. The milking system and herd size were closely associated with each other in the study population, which reflects the situation in Finnish dairy farming. Based on herd size, herds with pipeline milking were the smallest followed by parlor herds and then AMS herds. A previous study showed that the DCT approach was associated with the milking system in Finland (Vilar et al., 2018). To sum up, the proportion of farms using blanket DCT was higher in larger AMS herds than in smaller pipeline or parlor farms. Consistent with earlier results from Finland, our study found that farms with AMS had higher SCC compared to the other milking systems (Hovinen et al., 2009; Hiitö et al., 2017). In the current study, in 2016, milk production in the AMS herds was significantly higher than in the other milking

facilities, but during 2012–2016, milk production of the AMS farms did not differ from that of the pipeline farms. Others report an increase in milk yield after introducing AMS into the farms (Tse et al., 2018), which is probably associated with the more frequent milking (Friggens and Rasmussen, 2001), or with the change towards improved overall barn environment. A portion of the farms updated their milking system during the study period and thus the milking system data for 2012–2016 differed slightly from the corresponding information for 2016. This is probably one explanation, why the effect of the milking system was not similar in the longitudinal analyses compared to cross-sectional analyses. Our results show that those farms, which updated their milking system 2012–2016, had higher milk production compared to the farms that did not change their milking system. The probable explanation is in part the fact that successful and progressive farms are more eager to expand and make improvements.

Studies show the preventive effect of ITS against IMI (Halasa et al., 2009; Rabiee and Lean, 2013). A recent study states that good udder health herds may use ITS alone in low-SCC cows without any large effects on herd-level SCC (McParland et al., 2019), and result seems to favor the use of selective DCT. In the unconditional analyses of our study, the use of ITS was related to higher milk production but not to SCC. This explanatory variable was left out from the final model for milk production, because it was non-significant. Only a small proportion of the farms use ITS in Finland (Vilar et al., 2018), and this lack of widely implemented use is probably the reason, why our study could not find the previously reported beneficial effects of ITS. There are no official recommendations in Nordic countries to administer ITS at drying-off to all cows. Although studies show the beneficial preventive effect, there is not enough scientific evidence to favor the economics of administering ITS to all cows on all farms (Rajala-Schultz et al., 2019).

The variability in the phenomenon at a given time can be different from the variability in the phenomenon over time, and thus longitudinal studies have their place alongside cross-sectional studies. When the time is relatively short and/or the number of observations is few, growth models can be a convenient way to model the information (Raudenbush and Bryk, 2002). One of the benefits of random coefficient models is that parameter estimates are based on all available information. The relatively high ICC, as in our results, is generally a more common finding in longitudinal analysis than in cross-sectional multi-level analysis (Twisk, 2006). As ICC is a measure of similarity between observations within a cluster, the ICC values of our data indicate that SCC and milk production observations within a herd across the years remain similar.

The main limitation in our study is the imbalance of DCT groups, but that simply reflects the Finnish dairy production. A considerably higher proportion of farms in Finland use selective DCT than blanket or no DCT. The imbalance of herds in the various DCT groups may have limited the power to identify significant differences between them. Some of the farms reported a change in their DCT approach during 2012–2016 potentially causing some misclassification bias in the longitudinal analyses. This was, however, taken into consideration in the longitudinal analyses by evaluating the change in DCT approach over time. Results showed that the effect of this variable on SCC and milk production was non-significant. The change did not affect the cross-sectional analyses, and yet the results did not differ for the DCT.

5. Conclusions

The results of this study suggest that it is possible to maintain low herd-average SCC and good milk production when using selective DCT and following the guidelines for prudent antimicrobial use. Regardless of the farm's DCT approach, annual milk production increased over the years, while herd-average SCC remained reasonably constant. Average SCC and milk production varied across the herds, suggesting that advice on DCT practices should be herd-specific. The methodology of growth modeling using random coefficient models was applicable in analyzing

longitudinal data, in which the time frame was relatively short and the number of herds was limited.

Declaration of competing interest

None.

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