Does differentiated restriction of antibiotic classes influence farm economic outcomes?

Yechale Getu Endalew, Dagim Belay, and Jørgen Dejgård Jensen

Abstract

As animal agriculture represents the primary sector for antibiotic consumption, there is a growing call for regulating their use to mitigate the increasing threat of antimicrobial resistance. In this context, current arguments for regulating the therapeutic application of antibiotics are shifting away from blanket restrictions towards more precise, class-specific restrictions. This paper presents the first empirical estimates regarding the effects of a differentiated restriction of antibiotic classes on farm antibiotic use and economic outcomes. We exploit the variations in the intensity/stringency of the restrictions under the latest Danish differentiated-yellow card scheme, which assigns varying weights for different classes in the existing yellow card antibiotic quota, as a quasi-policy experiment and use state-of-the-art econometric methods. Our findings indicate that the targeted restriction significantly reduces overall antibiotic use, particularly a threefold reduction in tetracycline (a class with largest weight), with smaller reductions in other classes. Furthermore, the differentiated restriction has led to increased farmers' operational costs and decreased profit. Higher rate of substitution to vaccination, higher veterinary and medical expenses and higher labor hours and costs are identified as the main pathways the restriction influenced farmers' production behavior. Results also show heterogenous responses across different age groups, with weaners and finishers displaying significant reductions in tetracycline use and more pronounced declines in profitability, characterized by higher operating costs.

Antibiotics, Antimicrobial Resistance, Yellow Card Initiative, Denmark, Difference-in-Differences

1. Introduction

Recently, there is a growing call for a shift from blanket restriction on (therapeutic use of) antibiotics towards more precise, class-specific restrictions (Belay et al., 2020). However, interventions in the livestock sector need various considerations including farm economic outcomes (Redding et al., 2020). Reducing antibiotic use among farmers is expected to yield significant societal benefits, in terms of a decrease in antibiotic-resistant infections. However, farmers may face the challenge of preventing animal infections through alternative methods, which could entail additional costs. This shift could influence their overall cost structure and economic outcomes.

In this study, we examine the effectiveness and costs of a sophisticated quantitative regulation on the therapeutic use of antibiotics in livestock production. In particular, the paper uses a unique policy experiment and dataset from Denmark to present the first empirical estimates regarding the effects of a differentiated restriction of antibiotic classes on pig farms' antibiotic use and economic outcomes.

In Denmark, around two-thirds of the total antibiotic consumption goes to the livestock sector, and the pig industry is the main driver as it accounts for 75% of the sector's contribution (Van Boeckel et al., 2015). In response, several interventions have been implemented in recent decades, particularly in pig production, though empirical studies on the impact of such interventions are scant (Belay & Jensen, 2022a). The Yellow Card initiative established from 2010 is such an intervention designed to monitor the highest users of antibiotics and impose a quantitative restriction on antibiotic use on those pig farms (DVFA, 2017). Although rigorous studies on the impact of such interventions on antibiotic use and economic outcomes are limited, a couple of studies (Belay & Jensen, 2022a, 2022b) investigated the impact of the initiative on the economic performance and efficiency of pig farms. However, the Yellow Card scheme was revised in 2016[1], where varying weights were assigned for different classes in the existing yellow card antibiotic quota, which henceforth we refer to as "Differentiated Yellow Card scheme (DYC)". In this study, we exploit variations in the intensity/stringency of the restrictions under the latest 2016 Differentiated Yellow Card scheme as a quasi-policy experiment. We combine datasets of veterinary drug use and economic accounts for the population of Danish pig farms and use state-of-the-art econometric methods, such as difference-in-differences and event studies combined with synthetic controls, to estimate the effects of class-differentiated restrictions of antibiotics for therapeutic use on farmers' antibiotic use and economic outcomes.

The paper contributes to the literature in several ways. By empirically estimating the effect of differentiated restrictions on overall antibiotic use and specific antibiotic classes that have been assigned different weights, the study contributes to the literature on impacts of restrictions on antibiotic use and to the debate surrounding the blanket vs targeted restriction on antibiotic use (Claeys et al., 2018; Tamma et al., 2017). The study provides first estimates on the effects of class-differentiated antibiotic restrictions on antibiotic use and farm economic outcomes, which adds to previous corresponding studies of the effect of blanket restriction (Belay & Jensen, 2022a, 2022b). Unlike Belay and Jensen (2022b), our study uses actual measures of antibiotics and vaccines to study farm-level mechanisms triggered by the regulation. Furthermore, our findings from a Danish setting can contribute to ongoing policy discussions in other countries

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[1] Note: While the policy was introduced in July 2016, for our analysis, we consider the intervention to have effectively started in 2017. Thus, 2016 is treated as a pre-intervention year.

contemplating similar initiatives.

2. Regulatory context and rationale

Veterinary antimicrobials were first introduced in the 1950s, followed by the development of antimicrobial growth promoters (AGPs) and the license by the EU to use antimicrobials as feed additives in the 1970s. While the EU permission regarding the use of antimicrobials for food animals included measures to prevent harm to animal and human health, these precautions failed to consider the evolutionary pathways that result in the emergence of antimicrobial resistant bacteria in livestock, which can then be transmitted to humans. These advancements result in the introduction and execution of diverse initiatives in various nations mainly within the European Union. Denmark leads the way in adopting and implementing such policies that curb the level of antimicrobial use in the livestock sector. Over the last three decades several reforms have been enacted regarding the use of antibiotics in the livestock sector, leading to significant advancements in curbing the incidence of resistant bacteria (Jensen & Hayes, 2014; Levy, 2014). Efforts to restrict antibiotic use first started in the 1990s and ranged from establishment of financial constraints on veterinarians' earnings from antibiotic sales to the prohibition of antimicrobial growth promoters (AGP) and non-therapeutic antibiotics. For ease of exposition, we summarize the main antimicrobial stewardship interventions implemented in Denmark in **Error! Reference source not found.**[2].

In 1997, the Copenhagen Recommendations were introduced by the Chief Medical Officers of the European Union. These recommendations primarily addressed five key areas: the impact on

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[2] **Note:** This figure is produced by the help of BioRender and the information is collected from reports and scientific works, including (Aarestrup, 2004; Aarestrup et al., 2010; Laxminarayan et al., 2015).

human health, the monitoring of resistant microorganisms, the tracking of antimicrobial agent usage, the promotion of proper practices in using antimicrobial agents, and the establishment of a framework for developing research program guidelines (Becquet, 2003). Subsequently, nontherapeutic antibiotic use has been prohibited in the pig industry in 1999. One year later, the Danish Veterinary Medicines Statistic Program (VETSTAT) was created. VETSTAT is a comprehensive database that stores information on all medications given by veterinarians for animals. This includes details such as active substances, quantities, target species, age groups, diagnosis groups, and farm identification numbers. In 2010, the Danish Veterinary and Food Administration (DVFA) introduced a quantitative restriction known as the "Yellow Card Scheme" to specifically target pig farms that excessively use antibiotics. The implementation of this strategy involved establishing national threshold limitations for the utilization of antimicrobials based on the age groups of pigs. In 2013, another intervention was implemented which imposed restrictions on the use of broad-spectrum antimicrobial drugs and flock treatment. This intervention required verification before prescribing group treatments for intestinal and respiratory infections. Additionally, it imposed a differentiated tax on the active antimicrobial compound. This was followed by the implementation of the DYC in 2016 (Andersen & Hald, 2017; Becquet, 2003; Emborg et al., 2001).

3. Data and methods

3.1. Data

The study combines two unique and big panel datasets from VETSTAT and SEGES. VETSTAT is a national database monitoring antibiotic application in livestock, where the herd-level veterinary antimicrobial use (AMU) prescription data has been recorded since 2000 (Kruse et al., 2019; Stege et al., 2003a), including information on herd-level consumption of prescription medicines across different animal species, age groups, and diagnoses, combined with data on drug sales from pharmacies transferred to VETSTAT by the Danish Health Data Authority (Dupont et al., 2017). The VETSTAT database contains information on all prescription drugs sold to animals all over the country, that originate from pharmacies, veterinarians, and feed mills (Stege et al., 2003b). VETSTAT presents antibiotic use in terms of total doses and animal daily doses (ADD). For our analysis, we use ADD as it is used to set thresholds for the Yellow Card quantitative restriction and provide comparable figures across different species. ADD is also defined as "the assumed average maintenance dose per day for the main indication in a specified species" (Doe, 2015; Jensen et al., 2004). Although VETSTAT contains data on several species, we extract the data for pig farms only as this study focuses on the pig sector, the largest consumer of antibiotics in Danish livestock production. Data on antibiotic use by pig farms is also further segregated by age groups, i.e., sows, weaners, and finishers. We also extracted vaccination data from VETSTAT.

The data concerning additional components in farms' profit function is obtained from SEGES, the knowledge center of the Danish agricultural sector. The database from SEGES comprises annual financial information of the agriculture sector including pig farms. The dataset contains detailed information on farm characteristics and economic accounts. For our analysis, we extracted data on farms' profit, revenues, cost components, labor hours; and covariates such as number of animal units, age of the farm manager, and an indicator of whether the farm is organic or not. The data used in this analysis spans from 2006 to 2020.

3.2. Estimation Strategy

Despite having identified plausible counterfactuals, there could still remain observable and unobservable confounders potentially correlated with the outcome variables (antibiotic use and profit, etc.), and ensuring unbiased causal effects requires the proper consideration of these confounders.

Difference-in-differences estimators offer a powerful tool to evaluate causal effects in such settings by accounting for unobservables due to the non-random assignment (Abadie & Cattaneo, 2018; Athey & Imbens, 2017). However, it relies on an identifying assumption that the farms affected by the DYC restrictions and (always) low-user farms not affected by the restriction would have followed a similar trend in the absence of the DYC. In addition, we assume that there are no anticipation effects before the intervention. We test for these assumptions and results are provided under section 4.5 for robustness checks. Together with other falsification tests, the results support that our model fulfills the indicated identifying assumptions.

For our main analyses, we specify our difference-in-differences model using fixed effects as follows:

$$Y_{it} = \alpha_0 + \beta \text{ post }_{it} * \text{ DYC }_{it} + \phi X_{it} + \omega_i + \tau_t + \varepsilon_{it} \tag{6}$$

where Y_{it} stands for main outcome variables in the study given in logarithms such as antibiotic use, total operating cost, vaccinations, feed cost, veterinary medical cost, labor cost, and hired labor hour, and IHS (inverse hyperbolic sine) transformed values of profit and revenue of farm i at year t. β is the parameter estimate of the policy variable (the class-differentiated yellow card (DYC)), ϕ the vector of estimates for covariates (Xs) such as livestock units, being organic or not, farm manager age and age group of farms. ω_i stands for farm fixed effects, τ_t stands for year-fixed effects and ε_{it} is an idiosyncratic random error term to capture unobserved random variables affecting farm outcomes. In our estimations, we cluster the standard errors at municipality level to capture random shocks correlated at municipality level.

4. Results

This section presents the main results of the empirical analysis. We first present the impact of the DYC intervention on antibiotic use, followed by its effect on farm economic indicators such as profit, revenue, and variable costs. Next, we analyze potential mechanisms driving the effects of the regulation, including vaccination, feed cost, labor cost, labor hours, and veterinary and medical costs. Subsequently, the impact of the regulation on antibiotic use, vaccination and veterinary medical expenses is examined in relation to heterogeneity among age groups. Ultimately, we examine robustness and validity checks of the main regression findings.

4.1. Antibiotic use

Table 1[3] presents the estimates for the impact of the DYC regulation on antibiotic use in three sections. Results in the first two columns show the effects of the regulation on overall antibiotic use, regardless of antibiotic classes. The third and fourth columns of the table present estimates on tetracycline usage, while the fifth and sixth columns address all other antibiotic classes, excluding tetracycline. The first columns in each of these categories indicate the effects of the regulation without controlling for other covariates, while the second columns indicate the effects with the inclusion of covariates. The results indicate that, on average, the class-differentiated yellow card intervention has reduced overall antibiotic use on pig farms in the treatment group by around 10% compared to those in the comparison group. Examining the sub-samples reveals that the policy has led to a significant decline in tetracycline use by approximately 28%, whereas there has been a reduction of approximately 5% in classes other than tetracycline due to the

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[3] The same analysis is conducted using the quarterly data on antibiotic use and results which are not significantly different from the yearly data analysis are found.

regulation, when controlling for covariates. As the use of tetracycline decreases more than the use of other classes of antibiotics, these results indicate a substitution between tetracycline and other antibiotics. The results are not surprising as the restriction assigns a multiplication factor where tetracycline is given a higher weight (1.5) compared to other antibiotic classes, and this could be expected to encourage some substitution of tetracycline with other types of antibiotics, to the extent that their effects on infections are comparable.

Holding other variables including the treatment status constant, the number of livestock units has a positive effect (approximately 0.4%) on antibiotic use. However, this does not apply to tetracycline, and the fact that tetracycline has been assigned a higher weight than other classes might discourage farms from modifying their tetracycline use in correlation with their livestock units to not reach the quota limits with a small amount of use. Meanwhile, antibiotic use in organic pig farms has decreased by around 50% compared to conventional ones. Sow farms utilize a lesser amount of animal daily doses, whereas being weaner or finisher farm results in antibiotic use of three and two times the amount used by sows, respectively. This finding is consistent with a recent cross-sectional study by Moura et al. (2023), which found that weaners take a substantial proportion of antibiotic use in the pig sector.

Due to series of revisions to the quota limit values under the Yellow Card scheme, we re-estimate our models controlling for both the actual quota limit values and their changes over the years in our study period. This accounts for changes in the stringency of the quantitative restrictions (due to the decline in quota values over time) in our analysis for estimating the impact of DYC on antibiotic use. Nevertheless, we find that the impact of DYC is robust to changes in quota limit values.

Table 1 Antibiotic use

	All antibiotics		Only tetracycline		Other than tetracycline	
	(1)	(2)	(3)	(4)	(5)	(6)
DYC × post	-0.099***	-0.114***	-0.384***	-0.283***	-0.014	-0.048***
	(0.027)	(0.016)	(0.103)	(0.058)	(0.026)	(0.017)
Livestock units		0.004***		0.004		0.003**
		(0.001)		(0.006)		(0.001)
Organic farm		-0.492***		-0.720***		-0.388**
		(0.168)		(0.255)		(0.178)
Weaner farm		2.161***		2.193***		2.047***
		(0.032)		(0.095)		(0.039)
Finisher farm		0.916***		1.021***		0.861***
		(0.027)		(0.094)		(0.033)
Constant	1.409***	0.603***	2.025***	0.765***	1.259***	0.593***
	(0.006)	(0.018)	(0.023)	(0.082)	(0.006)	(0.019)
R^2	0.488	0.592	0.610	0.687	0.511	0.604
Observations	57255	57255	11158	11158	45463	45463

Note: All dependent variables are in logs. All estimations control for year and farm fixed effects. Clustered standard errors at municipality level in parenthesis. Significance levels: 1%***, 5%**, and 10%*.

4.2.Economic outcomes

Table 2 provides the estimation results for the effects of the class-differentiated yellow card intervention on revenue, costs and profit. Overall, the results reveal that the intervention has increased total farm operating costs and decreased profits, whereas the effect on revenue is insignificant.

The Differentiated Yellow Card intervention has not had a significant effect on revenue, as illustrated in columns (3) and (4)[4]. This indicates that overall, the substitution of tetracycline treatments with other treatment strategies has been sufficient to preserve the output levels on the

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[4] We checked the revenue effect of the DYC for different farm age groups and the in all cases the result is found insignificant.

Danish pig farms.

Columns (1) and (2) show that operating costs increased by approximately 7% due to the DYC intervention. This outcome aligns with the findings of Belay and Jensen (2022b), who reported a 5% increase in farm operating costs due to the blanket Yellow Card initiative. More details regarding DYC's effects are discussed below.

The insignificant impact of the policy on farm revenue, combined with the policy effects on profit and operating costs exhibiting approximately equal magnitudes but opposite signs, suggests that the policy's influence on farm profit is primarily attributed to the increase in operating costs. Estimates from columns (5) and (6) reveal that the DYC intervention has exerted a significant 7% negative effect on farm profit. This result supports the findings of Belay and Jensen (2022b), who identified a significant negative effect of the blanket Yellow Card Initiative on farm profit. At the same time, the result contrasts with findings by Bergevoet (2019), Rojo-Gimeno et al. (2016) and van Asseldonk et al. (2020) , where antibiotic reduction measures in all cases result in a positive or insignificant effect on farm performance. These discrepancy/contrasting findings might be attributed to the small sample size and softer interventions, such as biosecurity measures considered by these studies.

Farm manager's age, number of livestock units, and being a weaner farm are significant covariates affecting farm profit and operating costs. Compared to sow farms, being a weaner farm is associated with approximately 9% higher operating costs, and a one-unit increase in the number of livestock units increases operating costs by 1.3% - also corresponding to a decrease in profit of roughly the same magnitude. Conversely, with every one-year increase in the age of the farm manager, operating costs decrease by about 0.5%, which, in turn, increases profit by an approximately equal percentage.

Table 2 Economic Outcomes

	Revenue		Cost		Profit	
	(1)	(2)	(3)	(4)	(5)	(6)
DYC × post	-0.030	-0.024	0.070***	0.070***	-0.070***	-0.070***
	(0.130)	(0.130)	(0.019)	(0.019)	(0.020)	(0.019)
Farm manager age		-0.000		-0.005***		0.005***
		(0.004)		(0.001)		(0.001)
Livestock units		0.003		0.013***		-0.014***
		(0.009)		(0.002)		(0.002)
Organic farm		0.009		0.010		-0.011
		(0.075)		(0.008)		(0.008)
Weaner farm		0.318**		0.088***		-0.088***
		(0.160)		(0.024)		(0.024)
Finisher farm		0.192		0.026		-0.026
		(0.155)		(0.027)		(0.027)
Constant	0.973***	0.826***	15.173***	15.299***	-15.863***	-15.985***
	(0.025)	(0.234)	(0.004)	(0.059)	(0.004)	(0.059)
R^2	0.601	0.601	0.889	0.892	0.889	0.892
Observations	21403	21403	21403	21403	21403	21403

Note: Cost is given in logs, while revenue and profit are in inverse hyperbolic sine transformations. All estimations control for year and farm fixed effects. Clustered standard errors at municipality level in parenthesis. Significance levels: 1%***, 5%**, and 10%*. The data on revenue and profit have significant numbers of observations with zero and negative values respectively. Though it is possible to overcome the issue of skewed distribution with log transformation it results in loss of observations with negative and zero values and thus we use an alternative transformation, the inverse hyperbolic sine (IHS) transformation to simultaneously deal with skewness and account for the observation that could be lost with the log transformation. Mathematically: $sinh^{-1}(V) = \log(V + (V^2 + 1)^{1/2})$, where V is the variable to be transformed (Bellemare & Wichman, 2020; Burbidge et al., 1988; De Brauw & Herskowitz, 2021).

4.3.Mechanisms

We also estimate potential pathways through which the DYC intervention could affect antibiotic use and farm economic outcomes. The estimates show that the intervention has resulted in an approximately 6-10% increase in vaccine use on farms, regardless of controlling for covariates. This is likely due to farms' use of more vaccines to substitute for the reduction in antibiotic use. Existing vaccines that are effective against certain bacteria[5] have already played a significant role in combating antimicrobial resistance by reducing both disease prevalence and antibiotic use (Hoelzer et al., 2017; Jansen et al., 2019).On the other hand, replacing antibiotics with vaccines could lead farms to incur additional costs, as vaccines are often more expensive than antibiotics, affecting farm profit.

Feed costs have increased by around 7% due to the implementation of the Differentiated Yellow Card intervention. This result aligns with the findings of (Belay & Jensen, 2022b) where an approximate 8% increase in feed cost is found following the implementation of the blanket Yellow Card initiative. A possible explanation for this could be the role of antibiotics in improving the efficiency of feed conversion, but with the reduced or limited use of antibiotics, higher-quality and nutrient-dense feed might also be required to maintain the health of pigs, thereby increasing feed costs.

Another potential mechanism is veterinary and medical costs, which we find positive and significant. Even though the quantity of antibiotics is restricted due to the DYC, veterinary and medical costs are expected to increase with the restriction, as farms could begin to rely more heavily on veterinarians for advice on antibiotic use and disease management, thereby incurring higher costs (Hallenberg et al., 2020). Furthermore, the restriction may incur a shift towards more costly medicines, which would also tend to increase these costs. Belay and Jensen (2022b) also found a significant increase in veterinary and medical expenses due to the implementation of the blanket Yellow Card.

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[5] These includes Streptococcus pneumoniae.

Whereas the magnitude of relative change in feed and veterinary/medical costs is similar, labor costs seems to change substantially more as a result of the intervention. Farms may need to adopt different management strategies, including biosecurity measures, which necessitate more labor hours and labor costs. A significant reduction in antibiotic use could potentially escalate morbidity and mortality rates, requiring more time and resources to care for sick animals (Lhermie et al., 2020). Hence, the intervention induces substitution effects that significantly influence the cost structure on the pig farms.

4.4. Heterogeneity between types of pig production

A nuanced policy evaluation requires identifying a specific segment of study units/groups where the effects of the intervention could be more pronounced and potentially induce substantial changes. To this end, we investigate whether the effects on antibiotic use, veterinary and medical costs, and vaccination vary among farms with different age groups of pigs (specifically, sow vs. weaner vs. finisher farms). We first estimate the effects on antibiotic use across three different groups of pig farms, both for total antibiotic use and tetracycline use, and we found that the DYC intervention significantly reduces antibiotic use in all age groups of pig farms. Nevertheless, the intervention-induced reduction for weaner farms on both total antibiotic and tetracycline use is much higher than reductions on finisher and sow farms, where sow farms registered the smallest reduction. Given the fact that weaners are using the most antibiotics (Fertner et al., 2015; Jensen et al., 2012), the highest reduction is expected to come from this group, as the initial high usage of antibiotics could imply a greater potential to reduce it. We also explore heterogeneous effects across the three groups on veterinary and medical costs and the results reveal that the Differentiated Yellow Card intervention significantly increases veterinary and medical costs at sow and weaner farms, with the increase being markedly higher for weaner farms. This result suggests that farms experiencing greater reductions in antibiotic use might to a larger extent move to other alternatives such as vaccines and more consultations with veterinarians, implying higher expenses.

4.5. Test for parallel trends and robustness checks

A key assumption for the validity of DID estimation is the presence of parallel trends between the treatment (DYC targeted) groups and the comparison group before the implementation of the DYC intervention. In other words, we assume the two groups would have followed similar patterns in the absence of DYC. To this end, we performed parallel trend analyses on all outcome variables of the study using pre-intervention data. This approach examines whether the treated and control groups exhibited similar trends before the intervention. The aim is to attribute any post-intervention trend differences between these groups directly to the intervention's impact. As the regulation's implementation period draws near, the absolute values of difference coefficients become nearly zero. This suggests that when considering covariates, there is not only a lack of statistical significance but also no substantial economic distinction in the outcomes of interest between the two groups before the intervention. This reinforces our identification approach, which utilizes the class-differentiated yellow card policy as a quasi-experimental framework for this study.

Moreveor, we conducted parallel trend tests for all potential mechanisms presented above. The results indicate that the two groups of farms would have exhibited common trends in the absence of DYC regulation, controlling for the confounding covariates.

So far, we use a static DID to estimate the effects of DYC on farm outcomes. However, the effects of the DYC could be different over the years, calling for the need to estimate dynamic treatment effects. To this end, we conducted an event study and a consistent result is found in regard with the effect of the DYC regulation on all of our main outcome variables.

Synthetic difference-in-differences (SDID) is another strategy we use to estimate the effects of the DYC regulation on our main outcome variables, as part of the robustness check. Introduced by Arkhangelsky et al. (2021)Arkhangelsky et al. (2021)Arkhangelsky et al. (2021), the SDID estimator combines strengths of the SC and traditional DID to estimate causal effects by creating a synthetic control group that best mimics the treated group before an intervention, thus providing more accurate comparisons of changes over time. Unlike the DID method, the SDID estimation does not require the assumptions of a common trend or the exogeneity of the treatment to be upheld. Instead, it constructs a counterfactual by applying weights to pre-treatment periods and cross-sectional units. This method is particularly convenient for causal estimation, as it accommodates heterogeneity in outcomes, thereby enhancing the precision of the estimator (Porreca, 2022). The plots depicted in **Error! Reference source not found.** d emonstrate the results of our SDID analysis. The average treatment effects of the policy, along with the corresponding t-values, are annotated directly on the plots. Similar to the findings from our main analysis, which utilized the DID estimation method, the results indicate that the implementation of the policy leads to a reduction in antibiotic use. Additionally, the policy appears to cause an increase in farm operating costs and a decline in farm profit[6].

4.5.1. Alternative Counterfactuals

Our last robustness check is testing estimates with alternative counterfactuals. We first test

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[6] It should be noted that the SDID method works only if the data is a balanced panel. In our case, the analysis of antibiotic use is based on balanced data, making it possible to compare the results from the DID estimation and SDID methods. However, in the case of cost and profit analyses, the panel data used in the DID estimation is unbalanced. The SDID estimates are based on the balanced portion of the data, which constitutes no more than 15% of the data used in the main analysis. Therefore, any comparisons of the estimates should take this into consideration.

whether the results hold if treatment and comparison groups are constructed based on the threshold established during the Yellow Card initiative of 2010. As the setup is dynamic based on the threshold and farms' antibiotic use in the last nine months, treatment and comparison group observations change. This framework facilitates a rigorous examination of the sensitivity of the estimation results, particularly in relation to the shifts in the alternative comparison group, which now encompasses all those below the threshold, as opposed to solely focusing on the extremely low users, which constituted the main comparison group in the initial analysis.

The other analysis in relation to this is dividing the pre-DYC observations into two groups: those before and after the implementation of the blanket yellow card, which occurred 2011. In this regard, we perform two regressions for each of the antibiotic use and economic outcome variables – one regression including data for 2000-2010 and 2016-2020, and another regression including data for 2010-2020. The results indicate no significant variation with the results in our main analysis, which takes into account all observations.

4.5.2. Placebo tests

To further validate our results thus far, we conduct placebo tests, where we execute two falsification tests for the two main outcomes: antibiotic use and operating expenses. In the case of antibiotic use, we modified the time for the treatment period from 2017 to 2010, a period during which the class-differentiated yellow card intervention had not been implemented. We then conducted regressions for the sample data up until 2017 (the initial treatment period) to verify if the model still yields significant results.

For operating costs, we omitted certain components that are expected to be correlated with antibiotic use including feed, veterinarian services, medicine, and labor costs. We then ran the same DiD regression on the remaining operating costs[7], i.e., other operating costs, serving as a placebo outcome. The objective of this analysis is to demonstrate that the intervention does not significantly affect costs unrelated to antibiotic use.

5. Discussion and conclusions

In this study, we exploit variations in the intensity/stringency of the restrictions under the latest Danish differentiated-yellow card scheme, which assigns varying weights for different classes in the existing Yellow Card antibiotic quota as a quasi-policy experiment. Using state-of-the-art econometric methods, we examine the effects of differentiated restrictions of antibiotic classes on farms' antibiotic use and economic performance. The results show a substantial reduction in the overall use of antibiotics and tetracycline; a class of antibiotics facing greater weight. Moreover, we also observe a modest decrease in the use of other classes of antibiotics, potentially due to regulatory spillover effects. Our results align with the reports by DANMAP (2021) and with findings that investigated the efficacy of the blanket Yellow Card scheme in reducing antibiotic use (Lopes Antunes & Jensen, 2020; Speksnijder et al., 2015).

In regard to the economic performance of farms, results show a decline in the economic performance of farms, characterized by a reduction in profit mainly due to an increase in operating costs. Operating costs have surged due to a rise in the purchase of inputs including feed, labor, and veterinary and medical services, as well as alternative measures such as vaccination. Our findings of an increase in operating costs align with the findings by Belay and Jensen (2022b), who noted a reduction in farm performance brought about by an increased purchase of inputs after the implementation of the blanket Yellow Card regulation on Danish pig farms in 2011. Similarly, Mathews (2002) indicates that regulating antibiotic use in beef production would increase costs for producers. In contrast, Bergevoet (2019) found that, in

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[7] Livestock related costs that are not related with antibiotic use.

the long run, a reduction in antibiotic use did not negatively affect the economic performance of Dutch pig and broiler farms.

Our findings also demonstrate that the effects of the Differentiated Yellow Card scheme on antibiotic use, veterinary and medical costs, and vaccination utilization are heterogeneous across different age groups of pig farms. We observe that the reduction in antibiotic use is significantly higher in weaner farms compared to finisher and sow farms, with the reduction in finisher farms being more substantial than that in sow farms. The potential for a reduction in antibiotic use due to the policy seems greater among the already high user groups, which is particularly the case for weaners, as they are the primary consumers of antibiotics in the sector (Jensen et al., 2012). Moreover, the policy's effect on veterinary and medical costs is significant for both weaners and sows, with the effect being much more pronounced in weaner farms than in sow farms. This might be due to either more veterinarian hours after the reduction in antibiotic use or more expensive substitute inputs of the antibiotic use such as vaccines. The response of vaccination use to the policy appears to be roughly equivalent for finishers and weaners, but a slight increment in vaccination is also observed in sows. Groups that experienced a large increase in vaccination are the ones that witnessed a significant decrease in antibiotic use, implying that farms are using vaccination to offset the animal health effects from reduced use of antibiotics. Heterogeneous effects of antibiotic restriction policies were also found in some previous studies (Belay & Jensen, 2020; Faccin et al., 2019; Hemme et al., 2018).

Since research suggests that implementing antibiotic restriction regulations in food animals is critical for public health — as it can help diminish the development and spread of antibiotic-resistant bacteria — these regulations are designed and implemented to combat the spread of antibiotic resistance. Resistant bacteria can transfer from animals to humans through direct contact or the consumption of contaminated food or water. This can lead to treatment failures and severe illnesses, demonstrating the significant externalities associated with antibiotic use in livestock production (Goforth & Goforth, 2000; Massol, 2021; Mathew et al., 2007). Our findings show that the differentiated restrictions led to a substantial reduction in antibiotic use, which could potentially contribute to reductions in AMR. However, our study focuses solely on assessing the regulation's impact on farm outcomes, excluding consideration of its potential public health benefits. The effect of the regulation is anticipated to be positive if approached from a One Health perspective, taking into consideration the broad societal benefits and costs.

Our findings suggest that strict regulation of antibiotics, like the Differentiated Yellow Card, could negatively affect farms' economic performance, at least in the short run, as it increases operating costs through the augmented purchase of inputs. Given that antibiotic restriction regulations have a public health benefit by curbing antimicrobial resistance, it could be reasonable to find a way to distribute the additional costs incurred by livestock farms more fairly across the wider public, for instance through providing subsidies to farms, thereby helping to ensure that the livestock sector's export competitiveness remains unhindered.

Building upon the findings of the present study, future research might explore the following remaining issues. First, the present study examines the effects of the Differentiated Yellow Card intervention by applying a difference-in-differences approach, using (always) low users as a comparison group. Although we conducted a synthetic difference-in-differences analysis as one of our robustness checks, it would still be worthwhile to undertake a more rigorous synthetic control analysis, perhaps using data from neighboring countries. Second, given that the regulation resulted in an increased operating cost, research into efficient and sustainable farming methods that can maintain farm profitability by curbing operating costs amid reduced antibiotic use could be crucial. This might entail optimizing feed utilization, developing labor hour-minimizing technologies, and innovating more affordable vaccinations as substitutes for antibiotic use. Third, future studies could also look at the underlying reasons for the heterogeneous treatment effects and might consider analyzing other potential moderating variables, such as the size of the farms or geographical location, that could provide further insights into the regulation's effects. Lastly, an in-depth cost-benefit analysis that encompasses both the economic outcomes and the public health benefits arising from the regulation is worth investigating. This could involve constructing detailed economic models to gauge the net benefit of reduced antibiotic usage in pig farms, considering both the financial strains and the public health advantages.

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