MANAGING BIOLOGICAL RESISTANCE IN AGRICULTURE: INVESTIGATING THE ROLES OF INFORMATION AND DATA ANALYSIS IN DECISION MAKING

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ABSTRACT

MANAGING BIOLOGICAL RESISTANCE IN AGRICULTURE: INVESTIGATING THE ROLES OF INFORMATION AND DATA ANALYSIS IN DECISION MAKING

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Damage control tactics have been widely applied to control organisms that are detrimental to agriculture. Due to natural selection, the targeted organisms will inevitably become less susceptible and in time develop resistance to these control tactics. Resistance development is a widespread problem and has had large adverse consequences for agricultural productivity and even for human health. My dissertation investigates damage control input decisions in agricultural production which have important implications for biological resistance management. The dissertation consists of three essays on the consequences of and management approaches to decisions regarding an infection control input in livestock and a pest control input in crop production.

Essay One presents a decision model of a farmer's disease management decision problem under uncertainty. In response to the concerns about antibiotic resistance development, prescriptions are now required in the USA for medically important antibiotic use in animals. We investigate determinants of farmers' demand for tests, veterinary services, and antibiotics and how they will change in light of increasing oversight. We show that although the prescription requirement (PR) may reduce farmer therapeutic antibiotic use it may not achieve the social optimum. PR may cause knock-on distortions in test and service markets such as excessive demand for veterinary services.

Essay Two develops on the work in Essay One. PR places stewardship of antibiotics susceptibility largely into the hands of veterinarians. We investigate how effectively veterinarians manage information when making diagnostic and antibiotic treatment decisions. In a survey sent to

veterinarians in practice across the United States, we asked for probabilistic assessments in stylized disease diagnosis settings. Combining the findings that information management biases exist in diagnosis decisions and that diagnosis affects treatment choices, we conclude that the veterinary oversight requirement as an approach to relying on veterinarians for promoting judicious antibiotic use may fail to manage on-farm antibiotic consumption efficiently. Training programs for veterinarians to improve their information management capabilities may complement the veterinary oversight requirement.

Essay Three investigates the impact of Bt corn adoption on substituting out applied insecticide use as well as the seed trait's environmental and health implications in the United States. Bt resistance management policies have expanded across countries over years, aiming at conserving the effectiveness of Bt crops. However, optimal regulation of Bt crops should also consider the external benefits of Bt crops when compared to other control tactics. Therefore it is important to justify and evaluate externalities associated with Bt crops. Using a panel dataset, we investigate how Bt corn can affect insecticide use by adopters and non-adopters over years in a generalized difference-in-difference framework. We found insecticide use reduction among both adopters and non-adopters as a result of Bt adoption.

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1.1. INTRODUCTION

Since the 1950s antibiotics have been widely applied in food animal production to prevent and control disease and to promote growth (Marshall and Levy 2011; Finlay 2004; Kirchhelle 2018). Globally, food-producing animals consume the lion's share of antibiotics, and consumption in this sector has been projected to increase significantly through to 2030 (van Boeckel et al. 2015; Tiseo et al. 2020). For example, over 10 million kilograms of antibiotics are sold or distributed for use among food-producing animals in the United States (U.S. Food and Drug Administration [US FDA] 2021b). These drugs have drawn attention because of consequences external to the business administering them.

Microbe selection pressure from antibiotic use in one environment is considered to be the major contributor to emergence and development of antibiotic resistance within that environment (Chang et al. 2015). While, to date, no consistent quantitative assessments of how antibiotic use in agriculture production impact human health have emerged (Marshall and Levy 2011; Hollis and Ahmed 2013; Hoelzer et al. 2017; Koch, Hungate and Price 2017; Chatterjee et al. 2018) and some research even suggests that the channel may not be important (Adda 2020), the fact that the largest fraction of antibiotics is consumed in livestock production generates a variety of concerns about threats posed for human health. Resistance arising in animals might transmit to humans directly through food or animal contact, or indirectly through environment routes, such as contaminated water, soil, or wildlife (Marshall and Levy 2011; Laxminarayan et al. 2013; Robinson et al. 2016; Chatterjee et al. 2018). Researchers estimate that more than 35,000 deaths in the United States (U.S. Center for Disease Control and Prevention [US CDC] 2019) and about 33,000 deaths in European Union (EU) countries ((European Centre for Disease Prevention and Control

[ECDC] and Organisation for Economic Co-operation and Development [OECD] 2019) are caused by antibiotic-resistant infections annually.

In addition to external effects, poor historical incentive structures have led to wasteful antibiotic treatment. From food animal producers' perspective, these medications have historically been inexpensive in comparison with expected benefits from use. In many contexts, benefits are uncertain, and especially so for those untrained in disease management as similar symptoms can have a wide variety of alternative causes. Farmers may use antibiotics abundantly regardless of whether antibiotic treatment brings benefits, i.e., use antibiotics precautiously with respect to achieving profit goals. This is because the additional private cost of precautious applications may be lower than that of clarification through expensive professional advice. Information that lessens uncertainty may reduce wasteful antibiotic use and therefore promote antibiotic stewardship. How disease management is complicated by uncertainty and how a regulation mandating information purchase impacts therapeutic antibiotic use are our paper's main research questions.

In response to apprehensions about external effects caused by inappropriate antibiotic administrations, across much of the world regulations promoting antibiotic stewardship have expanded over recent decades, where pressure for regulatory oversight dates as far back as the U.K. Parliament's Swann Committee (1969) report. EU countries have placed the most stringent controls in use, having proposed a ban on using penicillin and tetracycline as growth promoters in the early 1970s and having banned all antibiotics used as growth promoters in 2006. In the EU all antibiotic use for therapeutic purposes is on prescription only. The Netherlands mandated a 50 percent reduction in livestock antibiotic use during 2009-2013 (Sneeringer, Bowman and Clancy 2019). Introduced in 2010, Denmark's Yellow Card initiative requires that antibiotic consumption by food-producing animals be by prescription only and that usage be reported to the Danish system for surveillance of veterinary drug consumption. In addition, cattle and pork producers

whose herds consume antibiotics at a per animal level above twice the sector average will receive a yellow card (Sneeringer et al. 2019; Belay and Jensen 2021). These recipients will be fined and placed under additional supervision. Circumscribing on-farm antibiotic use in EU countries is an ongoing process and, commencing in 2022, all forms of routine antibiotic use will be banned in the area. Since 2020, and with intent to reduce antibiotic use for promoting growth, China, the largest antibiotic consuming country, has prohibited antibiotic inclusions into animal feed. In addition, China has initiated endeavors to bring antibiotic used for food producing animals under veterinary oversight.

While U.S. government agencies try to promote public health through multi-layered protections, such as adhering to a rigorous process of antibiotic approvals for use in animal agriculture, monitoring antibiotic residue and antibiotic resistance in meat and milk and requiring the labeling of antibiotic use in meat and dairy product, the U.S. has not engaged as enthusiastically in regulatory curtailing of antibiotic use. That said, starting from 1997, the U.S. restricted use of some antibiotics classes as growth promoters and restrictions expanded over subsequent years. In 2012, the U.S. Food and Drug Administration proposed principles of "judicious use of medically important antibiotics in food-producing animals" and issued a series of command-and-control (CAC) judicious use policies (JUP) including Veterinary Feed Directive (VFD) and prescription regulation (PR). Effective since 2017, the U.S. VFD regulation bans medically important[1] antibiotic use for growth promotion purposes and requires veterinarian oversight of use for disease treatment and prevention through feed or water (U.S. Food and Drug Administration [US FDA] 2013). Initiated in 2021, PR requires veterinary prescriptions for the remaining approved over-the-counter (OTC) medically important antibiotics that are used in the other forms (e.g., injectable)

[1] All antibiotics and their associated classes listed in Appendix A of FDA's Guidance for Industry #152 are considered to be "medically important" in human medical therapy.

(U.S. Food and Drug Administration [US FDA] 2021a). When PR is fully launched in 2023, all medically important antibiotics applied to animals will be under veterinary oversight.

Concerns related to inappropriate antibiotic use and antibiotic resistance have also generated extensive discussions on policy options intended to achieve optimal antibiotic use. The crux of the regulatory problem is that regulators lack knowledge about case-specific needs for the drug. As optimal policy on antibiotic use is inconclusive due to the complicated dynamics involved (Herrmann and Gaudet 2009), various CAC and incentive-based regulations have been proposed. CAC regulatory instruments have been proposed, such as simultaneous use of multiple antibiotics (Laxminarayan and Weitzman 2002) and using antibiotics with greater effectiveness before those with lesser effectiveness (Laxminarayan and Brown 2001). Secchi and Babcock (2020) specify conditions under which a ban on sub-therapeutic antibiotic use in animals is justified. Others favor incentive policy tools, such as Pigouvian taxes, that are intended to correct for overuse by introducing the external marginal cost of antibiotic resistance into the use cost. These policy tools have the advantage of requiring limited resources for implementation and can result in a significant reduction in antibiotic use (Hollis and Ahmed 2013; van Boeckel et al. 2017). Belay, Abate, and Jensen (2020) propose an efficient, incentive-compatible policy for antibiotic use in the livestock sector based on the Montero auction mechanism. They argue that this mechanism outperforms Pigouvian taxes since it does not require regulators to have full information about antibiotic abatement costs. Rather it incentivizes individual farmers to truthfully reveal their abatement cost.

There is a growing empirical research literature on assessments of implemented policies. While bans on growth promoters may result in a short-run increase in therapeutic use, long-term lasting negative effects have not been detected (Marshall and Levy 2011). This is consistent with findings that antibiotic use for growth promotion in the United States has a small positive impact on hog and broiler farmers' economic performances (Key and Mcbride 2014; Sneeringer et al.

2015), suggesting that improved farm practices and feeding programs may compensate for the absence of growth promoters (Marshall and Levy 2011). Dennis et al. (2018) point out that a ban on antibiotic use that directly impacts animal mortality risk is costlier than a ban on antibiotic use that targets production efficiency, implying that purpose-specific understandings of the tradeoffs arising from eliminating antibiotic use are essential for making informed policy decisions. Belay and Jensen (2021) argue that the Yellow Card initiative reduces gross profit and increases farmers' operating expenses. On the other hand, disclosure of high-consumption farms by media outlets during the preparation period preceding the Yellow Card initiative may have nudged farmers towards better compliance with the public standards (Belay and Jensen 2020), replacing antibiotics with substitutes such as vaccines. Empirical evidence to evaluate the impact of VFD on antibiotic consumption is only beginning to emerge (Rademacher, Pudenz and Schulz 2019; Dillon and Jackson-Smith 2021). These findings suggest that the impact of VFD on antibiotic use and other knock-on effects of VFD vary with industries and farm practices. Väänänen, Pietilä, and Airaksinen (2006) argued that prescription requirement changes antibiotic use behavior but its impact on total consumption is inconclusive. Another study suggests that prescription requirement reduces analgesics use in Australia and overdose cases (Elphinston et al. 2021).

Our research addresses disease management decisions, especially antibiotic administrations on an individual basis, under farm-level uncertainty about their effectiveness. When a disease is suspected, the farmer is uncertain about whether antibiotics will be effective. On-farm self-testing or purchasing veterinary services can reveal information about the suspected disease as well as the susceptibility of any causative bacteria to antibiotic treatment. Herd owners can be viewed as countenancing several linked decision problems: they choose whether to administer without information, to purchase more certainty by way of a self-test, or to procure both additional

certainty and reduced loss by way of a veterinary visit. This paper works through a decision model to examine this nexus of decisions and their interactions.

Furthermore, we examine the impact of various policy tools on the farmer's choices, with a focus on JUP. VFD mainly regulates antibiotic use for growth promotion and disease prevention while PR mainly targets therapeutic use. This study assesses the impact of PR on antibiotic administrations for disease treatment. By increasing to infinity the cost of antibiotics when used without prescriptions, we study how PR, through mandating a prescription for antibiotic use, has changed the farmer's disease management decisions. We show that PR can reduce antibiotic demand; however, it does not guarantee that farmers apply antibiotics at socially optimal levels. In particular, when the resistance cost is large then antibiotic treatment under veterinary oversight may increase farmer profits but fail to improve social welfare. When resistance cost is not high relative to veterinary service cost, PR may over-reduce antibiotic use compared with social optimum. In addition, PR may cause knock-on distortions in test choices since antibiotic administrations and testing choices interact. PR-constrained farmers demand excessive veterinary services while there may be overuse or underuse of self-tests depending on context. Our simulations suggest that PR results in excessive veterinary service demand but no reduction in antibiotic use among typical U.S. dairy farms. In practice, antibiotic treatment comes with a great loss in the form of discarded milk but also, if effective, brings great benefits. Since self-testing is inexpensive relative to costs and benefits associated with antibiotic treatment, using antibiotics according to test information is in the best interest of dairy farmers. For the same reason, while PR does not reduce antibiotic use it does substitute veterinary services for less expensive self-tests in obtaining information. Of course simulation results may differ in other livestock industry settings, where parameters take different values.

Our analytical framework highlights the interlinked nature of diagnostic testing decisions and antibiotic use decisions and the critical role of the costs in each decision type. Such interlinkages not only affect the impact of PR, but also the impact of other policies such as testing subsidies. We explain why the way in which a self-test subsidy affects antibiotic consumption should depend on antibiotic cost. Antibiotic demand decreases (increases) with a self-test subsidy given low (high) antibiotic cost. This is because inexpensive antibiotics incentivize farmers' precautionary antibiotic use without purchasing costly information. A self-test subsidy encourages more information acquisition and therefore reduces inappropriate antibiotic use. Conversely, expensive antibiotics may prevent any antibiotic use under uncertainty about antibiotic effectiveness. A self-test subsidy removes this uncertainty and therefore supports antibiotic use when needed. The context-dependent effect of this subsidy arises because tests are information goods, and the economics of such goods are not trivial. For example, although veterinary services are also information goods, we show that because veterinary services comprise a bundle of goods a subsidy will unambiguously decrease antibiotic demand.

The main body of this paper is organized into six sections. Section 2 introduces detailed background information on the research question. The basic model, which is preparatory for but does not address PR, and optimal solutions are provided in Section 3. Section 1.4 discusses social-economic efficient outcomes and also several policy tools. Section 5 analyzes the effect of PR on farmers' choices and it is followed by a brief concluding section.

1.2. BACKGROUND TO THE RESEARCH QUESTION

US FDA (2012) recommended two principles for promoting "judicious use" of antibiotics in livestock production:

"Principle 1: The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that are considered necessary for assuring animal health.

Principle 2: The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that include veterinary oversight or consultation."

Commencing 2017, VFD regulation has been enforced with intent to meet these principles of judicious use. It has eliminated medically important antibiotic use for growth promotion and requires veterinarian oversight of medically important antibiotic administrations in feed or water. Starting from June 2021, the PR complements VFD by changing from OTC to prescription the market status of remaining medically important antibiotics that are used in the other forms. VFD and PR outline a framework within which veterinarians prescribe medically important antibiotic administrations when needed. The authorization should always be made in the context of a veterinarian-client-patient-relationship (VCPR), ensuring that veterinarians have sufficient knowledge of the herd and assume responsibility for treatment recommendations.

JUP are very important for promoting antibiotic stewardship. In addition to avoiding completely inappropriate antibiotic use (Krömker and Leimbach 2017), by requiring veterinary oversight, the regulations promote "judicious use" through in effect placing stewardship of food animal antibiotic inputs largely into the hands of veterinarians who are trained and experienced in understanding animal disease, resistance biology and implications for animal welfare. The regulations also seek to foster holistic approaches to disease management so that antibiotics become an infrequent recourse of last resort. The intent is that more informed decisions and an emphasis on stewardship will lower overall use.

In this paper, we focus on farmer's disease management decision-making in the context of a dairy farm, which we consider an ideal setting for studying the impacts of PR. Cattle production consumes 41% of medically important antibiotics used by U.S. food-producing animals (U.S. Food and Drug Administration [US FDA] 2021b). On dairy farms, in contrast with the aquaculture, swine, poultry and beef sectors, most uses are therapeutic. As with humans, there are many

reasons why antibiotic therapy in the dairy industry can arise. Although lameness and respiratory problems are important reasons for treatment with antibiotics, the primary ailment treated with antibiotics is clinical mastitis (Laxminarayan et al. 2013; Ruegg 2019; Redding, Bender and Baker 2019). The antibiotics are used to restore, as best as possible, milk yield and quality by eliminating bacterial infections of mammary tissue. Antibiotics can be injected directly into the teat when the cow is not lactating so as to reduce the risk of udder inflammation. Alternatively, a lactating cow suspected of having mastitis may be treated with intramammary antibiotic tubes or systemic antibiotics and the milk discarded until it is free of antibiotics. Without effective antibiotic treatment, the infections may lead to further pain and permanently scarred, non-producing tissue as well as possible slaughter and infection of other animals.

The benefits of antibiotic treatment are uncertain for a livestock producer, but can be potentially very large. First of all, separate from the cause, inflammation can be difficult to detect so that inexperienced personnel may perceive a potential issue when one does not exist. Besides bacterial infections, inflammation can be caused by chemical, thermal or mechanical injury, where antibiotic treatment won't improve the condition. Even for bacterial infections, antibiotic effectiveness depends on how the bacteria respond to the administered antibiotics, the clinical manifestations, the cow's gestation status and the treatment program (Amer et al. 2018). It has been argued that a high proportion of cows with mastitis do not respond to antibiotic treatment (Cecchini, Langer and Slawomirski 2015; Krömker and Leimbach 2017). Finally, bacteria-originated mastitis is contagious where antibiotics can serve the purposes of reducing the rate of contagion and securing earlier eradication at the herd level.

Imperfect on-farm self-tests to detect mastitis are available at a cost (Merriman et al. 2014), where the California test (CT), a simple indicator of Somatic Cell Count (SCC) in milk, is perhaps the best known. High SCC suggests a bacterial infection. More accurate laboratory tests are also

available and all tests can be conducted at udder quarter, cow, or herd levels. Table 1 lists intramammary antibiotic tubes that are approved for mastitis treatment in the U.S. market (Ruegg 2020; U.S. Department of Agriculture [USDA] 2016). OTC antibiotic drugs are available for dairy farmers to use with or without self-test information. Once PR is fully implemented, farmers need to call a veterinarian for permission before antibiotic administrations.

Table 1 Intramammary antibiotic tubes that approved for mastitis treatment in the U.S. market[2]

Product name	Label claims for efficacy	Prescription status	Percentage operations
Amoxi-Mast™ 62.5 mg amoxicillin	Str. agalactiae, Sta. aureus	Prescription	1.4
DairClox™ 200 mg cloxacillin	Str. agalactiae, Sta. aureus	Prescription	0.0
Msti-Clear™ 100,000 IU Penicillin G	Str. agalactiae, Str. Dysgalactiae, Str. uberis	OTC→Prescription	0.8
Pirsue™ 50 mg pirlimycin	Sta. aureus, Str. Dysgalactiae, Str. uberis	Prescription	6.5
Polymast™ 62.5 mg ampicillin	Str. agalactiae, Str. Dysgalactiae, Sta. aureus, E. coli	Prescription	0.8
SpectramastLC™ 125 mg ceftiofur	CNS, Str. Dysgalactiae, E. coli	Prescription	34.4

[2] Notes: (1) The status of Msti-ClearTM 100,000 IU Penicillin G and TodayTM 200 mg cephapirin will change from OTC to prescription when PR is fully implemented in Jun. 2023.
(2) The data for Product name, Label claims for efficacy and Prescription status are from "Understanding the economic impact of mastitis. The role of duration and drug selection," by Ruegg, Pamela L, 2020, in: Third Am Assoc Bov Pract Annual Recent Graduate Conference, Columbus OH: American Association of Bovine Practitioners Proceedings 53(1): 84–91. https://doi.org/10.21423/aabppro20207976
(3) The data for percentage of operations using intramammary antibiotic tubes (Percentage operation) are from "Milk Quality, Milking Procedures, and Mastitis on U.S. Dairies," United States Department of Agriculture, 2016. https://www.aphis.usda.gov/animal_health/nahms/dairy/downloads/dairy14/Dairy14_dr_Mastitis.pdf

Table 1 (cont'd)

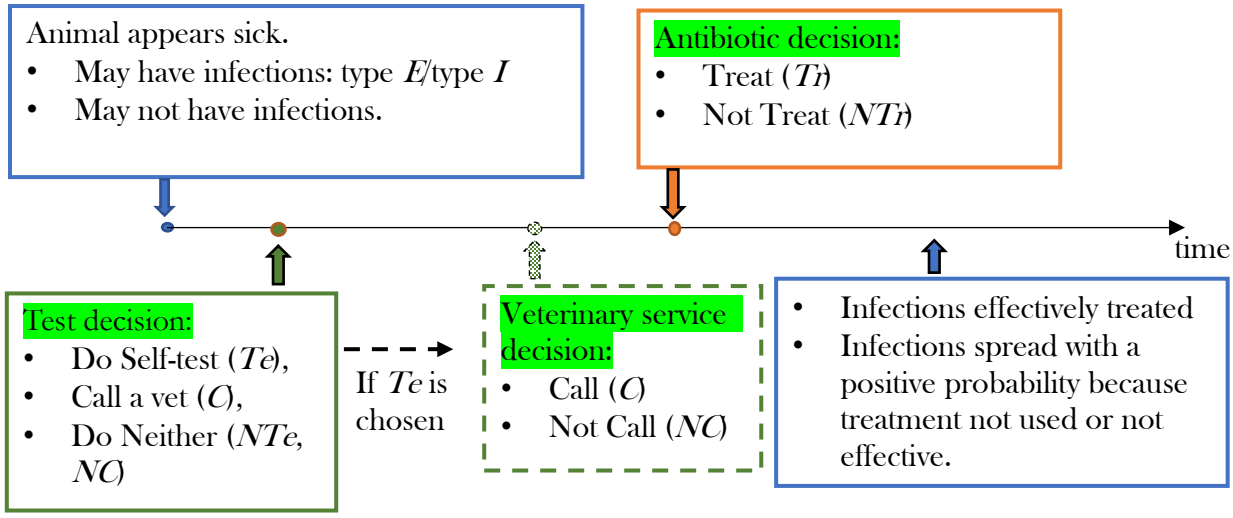
Today™ 200 mg cephapirin	Str. agalactiae, Sta. aureus	OTC→Prescription	32.2

Compared with self-tests, veterinary services provide more accurate diagnoses and reduce loss through professional advice. Veterinarians can use bacteriological diagnostics which help identify the causative pathogens. They may culture the milk sample at their own laboratory and then send the sample to an external laboratory if needed (Persson Waller et al. 2016). Identification of the pathogen would facilitate "judicious" antibiotic use (Merriman et al. 2014). When antibiotic treatment is preferable, a veterinarian could prescribe antibiotic regimes that are most effective for treating the mastitis case at hand. In addition to antibiotic treatment, veterinarians can recommend alternative courses of action. Common alternative treatment strategies include frequent milking, fluid therapy, massage and heat therapy, as well as drug courses with Oxytocin, Nonsteroidal anti-inflammatory drugs, Corticosteroids or intravenous Calcium (Persson Waller et al. 2016).

1.3. THEORETICAL MODEL AND OPTIMAL STRATEGIES WITHOUT POLICY INTERVENTIONS

Figure 1 shows the sequence of events in infection management that incorporates antibiotic use and related testing and veterinary call decisions. We assume two types of infections, namely where antibiotic treatment is *i*) effective, denoted as *E*; and *ii*) ineffective, denoted as *I*.

Figure 1 The sequence of events in infection management



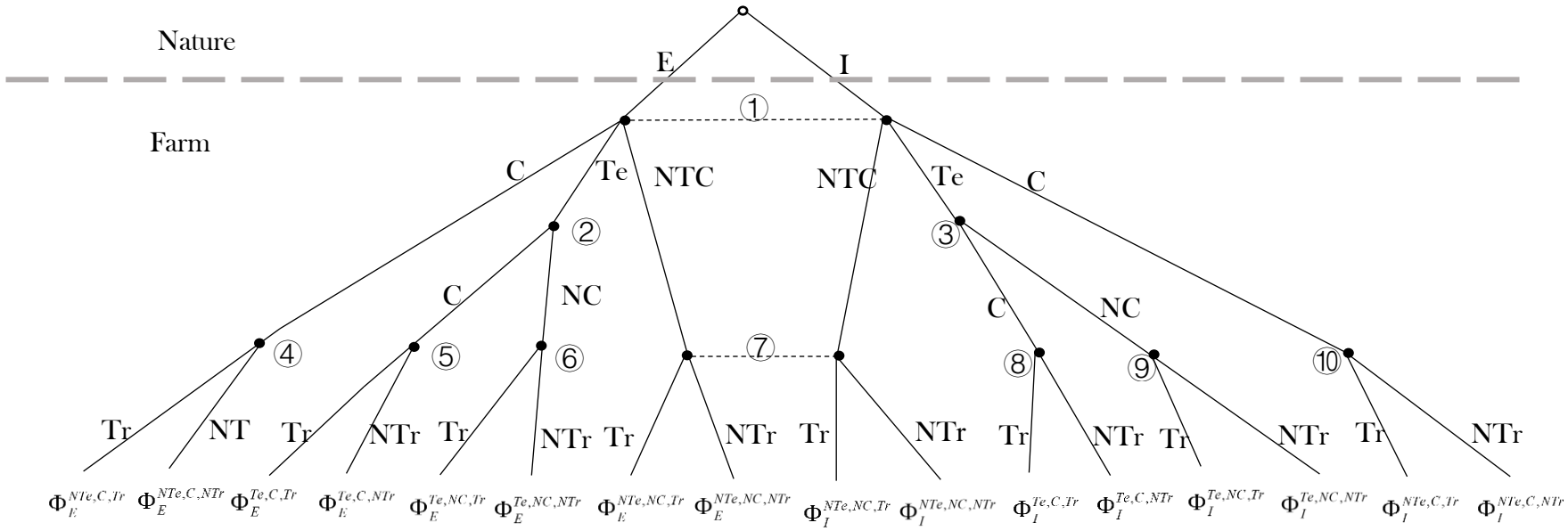
The farmer can be viewed as facing three sequentially linked decisions:

1) whether to self-test (denoted as *Te*) on farm or call a veterinarian (denoted as *C*) at some cost and receive full information about infection types. The farmer can choose neither approach (denoted as *NTe, NC*) and receive no information;

2) if a self-test is chosen in the first decision, whether or not to call a veterinarian (denoted as *C*) to acquire extra services (denoted as *NC*);

3) whether to treat (denoted as *Ti*) with antibiotics or not (denoted as *NTi*). Note that calling a veterinarian after self-testing, instead of before, is a strategy available to the farmer since we assume that veterinary services provide both the information that can be obtained from a self-test and additionally reduce loss through pertinent professional advice. In practice, the farmer thinks through the linked decisions before taking any actions. For analytic reasons, we regard the three decisions in sequence. The overall problem is characterized as a game against nature where the extensive form game tree is provided in Figure 2.

Figure 2 Decision tree for the test and treatment decisions



Nature plays first and determines the infection types, *E* or *I*. Then the farmer makes the three linked decisions where the decisions taken can enrich the information sets available for subsequent choices. First, the farmer decides whether to purchase information about infection type at information set ①. She can self-test (*Te*) to obtain information, call a veterinarian (*C*) to obtain information and other services, or do neither (*NTe*, *NC*). Second, whenever a self-test is chosen to reveal information then the farmer decides whether to purchase other services from a veterinarian at information sets ②-③ knowing the infection type. Third, treatment decisions are made at information sets ④-⑩. After obtaining information, antibiotic treatment decisions at information sets ④, ⑤, ⑧ and ⑩ are made under veterinarian oversight while those at information sets ⑥ and ⑨ are made without veterinarian oversight. At information set ⑦, the antibiotic treatment decision is made under total uncertainty about antibiotic effectiveness.

Consider an instance where nature chooses a type *E* infection. Information set ① involves information acquisition. Supposing that a self-test (*Te*) is chosen, the farmer learns that the infection is curable by antibiotics and then decides whether to call a veterinarian to acquire extra services at information set ②. At subsequent information sets, knowing that antibiotics are effective, the farmer makes antibiotic administration decisions under veterinarian oversight at information set ⑤ but without veterinarian oversight at information set ⑥. Supposing that the farmer calls a veterinarian for information and other services at information set ①, the farmer then faces antibiotic treatment decisions under veterinarian oversight at information set ④. However, the farmer won't acquire information about infection type when she does not purchase any information (through *C* or *Te*) at information set ①. The farmer then faces antibiotic administration decisions under uncertainty about the infection type at information set ⑦. The decision tree's type *E* side is symmetric with the type *I* side and explanations about the farmer's decisions in type *I* infection cases are similar.

The farmer's payoff Φ is determined both by infection types and the farmer's actions. Subscripts on Φ denote infection types and superscripts denote farmer's actions. For example, $\Phi_E^{NTe,C,Tr}$ is the payoff when the farmer does not self-test (*NTe*), but calls a veterinarian (*C*) instead and treats (*Tr*) with antibiotics in a type *E* infection case.

The farmer maximizes expected payoff by making decisions related to purchasing information and antibiotic administrations. The standard approach to deriving optimal strategies for the game in Figure 2 is backward induction. First, we solve for optimal decisions pertaining to antibiotic administrations. There are essentially seven problems, ④-⑩, to solve where different types of infections occur, and different self-test and veterinary service choices have been made. Then we solve for optimal veterinary service decisions where a self-test has revealed *E* and where a self-test has revealed converse results, information sets ②-③. Finally, we solve for optimal testing decisions just after observing suspected infection cases, information set ①. See formulated optimization problem in Supplemental Materials (SM) A1.

1.3.1. KEY FACTORS FOR DECISION-MAKING

Any factor that affects one decision has indirect impacts on the other two decisions. In this study, we especially focus on how self-test, veterinary service and antibiotic cost parameters affect choices. Using two examples we will first show how one cost parameter affects multiple choices. In one example we will remove the self-test choice from consideration while in the other example we will remove the veterinary service call choice.

Example 1 (Extremely high self-test cost): The farmer does not perform a self-test given an extremely high self-test cost. This example can be regarded as an application of our theoretical model where self-tests are banned or are very inaccurate. Veterinary services are the only eligible or reliable source of information about infections. In this situation the farmer's problem simplifies

to two linked decisions. She has to decide whether to 1) call a veterinarian at information set ①, and 2) use antibiotics when the veterinarian reveals *E* (information set ④), when the veterinarian reveals *I* (information set ⑩) and when no veterinarian is called (information set ⑦).

When antibiotics are inexpensive compared with veterinary services, the farmer does not call her veterinarian. Instead she uses antibiotics directly since the benefit from precautious use exceeds judicious use under veterinarian oversight. As veterinary service cost decreases, situations may exist in which the farmer substitutes information acquisition, through a veterinary visit, for a precautionary course of antibiotics. In that case, the farmer's optimal strategy changes to judicious use according to professional advice. Another possible outcome as a result of a decrease in veterinary service cost is that the farmer substitutes alternative treatments from a veterinarian for antibiotic treatment. That is, the farmer's optimal strategy changes to calling a veterinarian and then not administering antibiotics at all. Thus a decrease in veterinary service cost may not only increase veterinary service demand but also reduce the expected antibiotic use, i.e., veterinary services and antibiotics can substitute.

Example 2 (Extremely high veterinary service cost): This example can be regarded as an application of our theoretical model where the veterinary service resource is scarce. Lacking veterinary service supply, the only approach to acquiring infection information is by performing a self-test. As the farmer does not call a veterinarian given an extremely high veterinary service cost, she faces two linked decisions, namely whether to 1) self-test on farm at information set ①, and then 2) use antibiotics when the self-test reveals *E* (information set ⑥), when the self-test reveals *I* (information set ⑨), and when no self-tests reveal information (information set ⑦).

When antibiotics and self-tests are both sufficiently expensive then of course the farmer prefers to apply neither. As self-tests become less expensive, the farmer may prefer to test at little cost and then administer antibiotics according to test results. However, when the antibiotics cost is

too high then the farmer won't change her initial decisions regarding self-tests and antibiotics even when self-tests become cheaper. Thus a decrease in self-test cost may increase demand for both self-tests and antibiotics, i.e., the inputs can complement.

These two examples show that every cost parameter is essential for determining the farmer's optimal strategies. In addition, the various possible outcomes associated with changes in cost parameters suggest complex interactions between the three linked choices. To address those interactions but also not render the problem intractable, we assume a linear payoff function for further investigation. The payoff consists of three parts: payoff without infections (a), costs related to managing infections including self-tests, veterinary services and antibiotic administrations (d, v, b) and losses incurred by infections ($l(\cdot)$);

$$\Phi = a - 1_{\text{self-t}}\, d - 1_{\text{vet}}\, v - 1_{\text{antib}}\, b - l(\cdot). \tag{1.1}$$

In a suspected infection case, indicator variable 1_{antib} equals one whenever the farmer uses antibiotics and zero otherwise. We also include indicator variables $1_{\text{self-t}}$ and 1_{vet} to represent choices regarding self-tests and veterinary services. The loss incurred, $l(\cdot)$, is a function of farmer's actions and infection types. To define these losses we need assumptions about self-tests and veterinary services. Self-tests and veterinarians are assumed to be able to reveal full information about infection types, i.e., whether antibiotic treatment is effective for infections. In addition, a veterinarian can reduce loss incurred by alternative means (Persson Waller et al. 2016).

Let functions $l_E(\cdot)$ and $l_I(\cdot)$ denote the losses incurred in type E and type I infection cases as:

$$l_E(y,z) = \begin{cases} l_1 & \text{whenever } z = 1; \\ l_2 & \text{whenever both } y = 1 \text{ and } z = 0; \\ l_3 & \text{whenever both } y = 0 \text{ and } z = 0; \end{cases} \tag{1.2}$$

$$l_I(y) = \begin{cases} l_2 & \text{whenever } y = 1; \\ l_3 & \text{whenever } y = 0. \end{cases} \tag{1.3}$$

Let l_1 be a relatively small loss incurred in type E infection cases when treated with antibiotics, l_2 be a moderate loss incurred under veterinarian oversight but in the absence of effective antibiotic treatment, and l_3 be a large loss in the absence of veterinarian oversight and effective antibiotic treatment. "The absence of effective antibiotic treatment" refers to two scenarios: 1) type E infection cases without antibiotic treatment, and 2) type I infection cases regardless of antibiotic administration choices. The large loss l_3 includes not only loss incurred through the sick animal but also expected loss incurred by potential in-herd infection spread. Note that $l_1 < l_2 < l_3$. Therefore, $l_E(\cdot)$ is a function of veterinary service (y) and antibiotic administration (z) decisions, while l_I is a function of veterinary service decisions only since type I infections do not respond to antibiotic treatment. SM A2 specifies each payoff in Figure 2.

To simplify[3] the optimal strategies, we make an additional assumption, namely $l_2 - l_1 < \beta(l_3 - l_1)$. We can rewrite this assumption as

$$\frac{l_2 - l_1}{l_3 - l_2} < \frac{\beta}{1-\beta} = \text{odds of type } E \text{ against type } I. \tag{1.4}$$

The left-side numerator measures how much antibiotic treatment outperforms alternative treatments in type E infection while the left-side denominator measures how much alternative treatments outperform antibiotic treatment in type I infection. Since infection contagion in herds can result in a large expected economic loss, l_3 is much greater than the economic loss incurred on the sick animal under other strategies, l_2 and l_1. Therefore, the left-side ratio being smaller

[3] This assumption allows us to focus on the issue at hand which is the nexus of decisions on antibiotic administration and information purchase and their interactions.

than the comparative prevalence ratio is a reasonable assumption. Table 2 summarizes the notations that appear in the model setup.

Table 2 Notations in model setup

Notation	Explanation
a	Default payoff without infections
d	Self-test cost per case
b	Antibiotic cost per case
v	Veterinary service cost per case
β	Probability of the occurrence of infection for which antibiotics are effective
l_1	Loss per case when antibiotics are effective and applied regardless of veterinary service decisions.
l_2	Given that a veterinarian is called, loss per case when antibiotics are either ineffective or not used

Our research interests focus on how antibiotic cost, b, self-test cost, d, and veterinary service cost, v, affect disease (e.g., mastitis) management decisions and therefore antibiotic use and testing demand. Thus, we treat the maximum expected payoff V as a function of (b,d,v) and other factors as parameters when solving for optimal strategies.

1.3.2. FARMER'S OPTIMAL STRATEGIES WITHOUT POLICY INTERVENTIONS

We present the problem solution process step by step in SM A3. To facilitate further explanation and analysis of outcomes, we graph the optimal strategies, holding one cost parameter among (b,d,v) fixed. The farmer's optimal strategy varies with cost parameters. For each optimal strategy, $E(A)$ is the expected antibiotic use. Expected antibiotic use is one when the farmer always administers antibiotics, β when the farmer only administers antibiotics in a type E infection case, and 0 when the farmer does not use antibiotics. Figure 3-Figure 5 are sample outputs. [4]

[4] Detailed explanations about Figure 3-Figure 5 are in SM A4

Figure 3 The farmer's optimal strategies in the *b*-*d* plane given high veterinary service cost $v > l_3 - l_2$

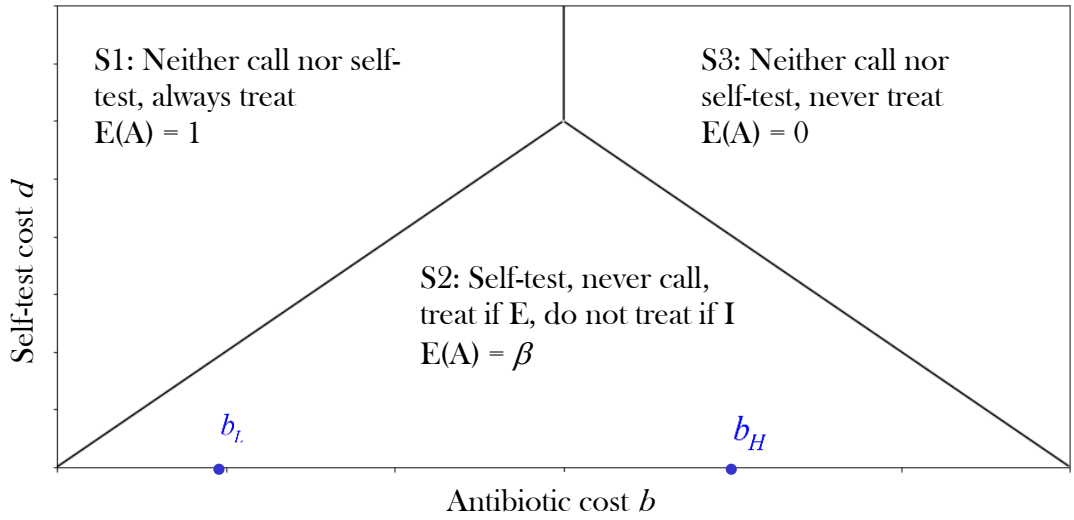


Figure 4 The farmer's optimal strategies in the *b*-*v* plane given high self-test cost $d > \beta(1-\beta)(l_3 - l_1)$

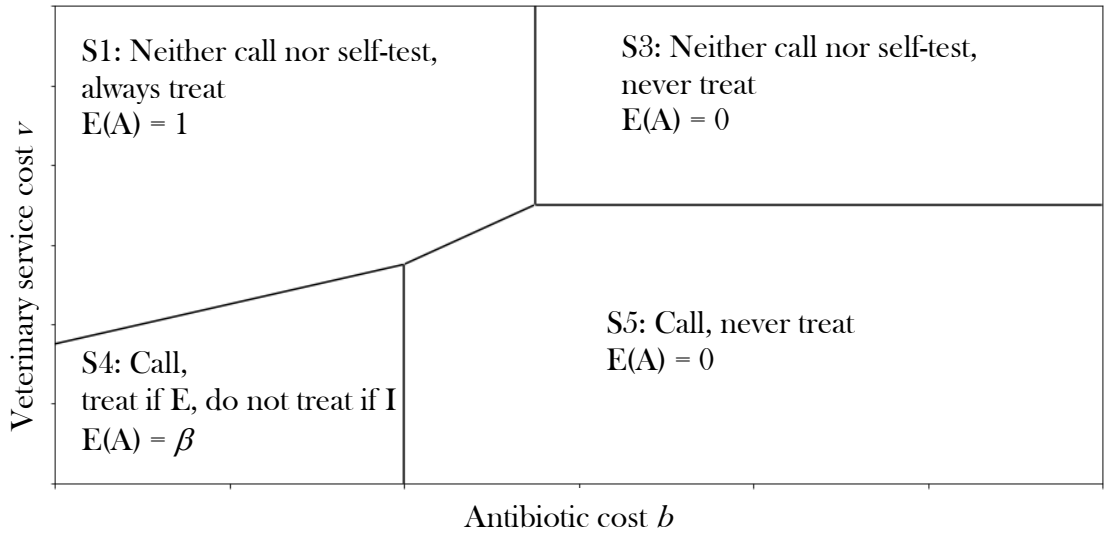


Figure 5 The farmer's optimal strategies in the d-v plane given lower medium antibiotic cost $b < l_2 - l_1$

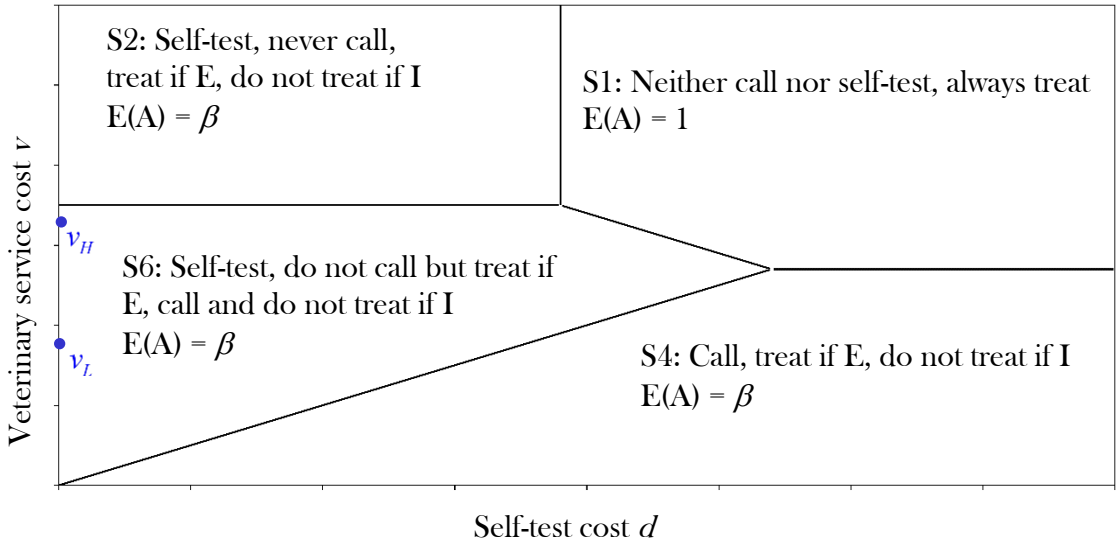


Figure 3 illustrates the farmer's optimal strategies in the b-d plane when veterinary services are sufficiently expensive to outweigh the loss reduction from veterinary services (i.e., $v > l_3 - l_2$). Under this condition, it is straightforward to show that the farmer does not prefer veterinary services. Figure 3 presents optimal choices regarding self-tests and antibiotic administrations as considered in Example 1, Section 1.3.1. Strategy S1 denotes farmer's precautionary antibiotic use without information, strategy S2 denotes judicious antibiotic use according to self-test results, and strategy S3 denotes neither antibiotic use nor information purchase.

Figure 4 presents the farmer's optimal strategies in the b-v plane when self-testing costs too much. Thus our discussion focuses on veterinary service and antibiotic choices. Two new strategies become possible: strategy S4 describes judicious antibiotic use according to veterinarians' professional advice, and strategy S5 describes information acquisition and alternative treatment application through a veterinarian. Figure 5 illustrates the farmer's optimal strategies in the d-v plane when antibiotics are sufficiently inexpensive that it is profit-increasing to use antibiotics in type E infection cases under veterinarian oversight. One further strategy becomes possible: strategy

S6 denotes heterogeneous treatment in different types of infection cases after a self-test reveals information. The farmer uses antibiotics whenever the self-test reveals *E* but otherwise uses alternative treatments through a veterinarian.

We summarize optimal strategies including those not presented in Figure 3-Figure 5. In our analysis of optimal strategies, we use backward induction. Therefore we will also present optimal choice summaries in temporally reversed order. Detailed explanations about Summary 1-3 are in SM A4.

Summary 1. (Optimal antibiotic choices) When purchasing no information is optimal, the farmer prefers precautious antibiotic use whenever antibiotics are inexpensive. When purchasing information through a self-test is optimal, the farmer prefers to use antibiotics for type E infections and to not use for type I infections. When purchasing information through a veterinarian is optimal, i) in type E infection cases, the farmer prefers to use antibiotic treatment given a low antibiotic cost while replacing antibiotic treatment with alternative treatments given a high antibiotic cost, ii) in type I infection cases, the farmer unambiguously prefers to not use antibiotics.

Summary 2. (Optimal choices regarding veterinarian visits and alternative treatments) When purchasing information through a self-test is optimal and the self-test has revealed I, i) the farmer will call a veterinarian to seek alternative treatments and eliminate contagion risk in the herd whenever the cost is low; ii) otherwise, calling a veterinarian cannot be the optimal choice. When purchasing information through a self-test is optimal and the self-test has revealed E, the farmer prefers to not call a veterinarian.

Summary 3. (Optimal information acquisition decisions) Self-tests and veterinary services substitute in information acquisition decision-making except when antibiotics are too expensive. When antibiotics are too expensive, then information is useless since the farmer

does not use antibiotics regardless of infection type. In that case, the farmer does not perform self-tests, while the farmer calls a veterinarian in order to obtain alternative treatments whenever veterinary services are inexpensive.

1.4. SOCIAL OPTIMUM AND POLICY TOOLS

In a farmer's optimal strategy, a social cost that is caused by the use of antibiotics, namely the development of resistance to antibiotics and the consequent cost, ω, may not be considered by a farmer seeking to remain competitive. Therefore we can obtain social payoffs by replacing private antibiotic cost b in the farmer's payoffs with social antibiotic cost $b+\omega$. Similar to the farmer's problem, the social planner can either make antibiotic decisions without information or purchase certainty at a cost and make antibiotic decisions after that. We derive the socially optimal disease management strategies using the same approach as in the farmer's problem. Here is the summary about biases in privately optimal choices relative to social optimum. We explain Summary 4 in detail in SM A5.

Summary 4. (Biases in privately optimal choices) Absent government interventions the farmer over-uses antibiotics but under-uses veterinary services compared to the social optimum. Whether the farmer demands fewer self-tests depends on antibiotic cost. Given low (high) antibiotic cost the farmer underuse (overuse) self-tests compared to the social optimum.

Divergences from social optimum point to the need for regulations to relieve or eliminate distortions in actions. In this subsection we investigate the farmers' responses to different policies, such as *i*) antibiotic tax, *ii*) subsidies on self-tests and *iii*) veterinary services and PR regulation.

1.4.1. ANTIBIOTIC TAXES

In theory, the Pigouvian tax $\tau=\omega$ restores the farmer's problem to that of the social planner. The taxed farmer faces antibiotic cost $b+\omega$, instead of b, and therefore internalizes the resistance cost. However, obtaining an estimate of ω is challenging in practice given how little is

known about the risk posed to human health. Discrepancies exist in the estimate of resistance cost associated with antibiotic use in agriculture on human health (Hollis and Ahmed 2013; Marshall and Levy 2011; Hoelzer et al. 2017; Koch et al. 2017; Chatterjee et al. 2018). There is insufficient understanding of two key linkages in cost estimation (Hoelzer et al. 2017). These are 1) linkage between on-farm antibiotic use and the emergence of resistance among pathogens, and 2) linkage between how farm-sourced resistant bacteria affect human infections. The first linkage is complex since antibiotic drug and treatment regimens can be confounded with other external factors, such as feed type used on a given operation, in affecting the emergence of resistance (Hoelzer et al. 2017). The emergence rate may vary with bacteria species. It is difficult to exactly quantify the resistance emergence attributed to on-farm antibiotic use because, for example, resistance genes can transfer across bacteria in different reservoirs. Failings in the second linkage can arise from our limited ability to trace resistance genes back to first breakout (Marshall and Levy 2011). Technological advances toward allowing for accurate tracing will likely offset this weak link over time (Hoelzer et al. 2017; Koch et al. 2017; Wee, Muloi and van Bunnik 2020).

1.4.2. SUBSIDIES ON SELF-TESTS/VETERINARY SERVICES

To assess the impact of testing subsidies on expected antibiotic use, it is essential to understand the interactions between antibiotics and self-tests/veterinary services. Summary 5 characterizes interactions among farmer's interlinked decisions. Details are in SM 4.

Summary 5. (Interactions between choices) Antibiotics and veterinary services substitute, while the interaction between antibiotics and self-tests varies with antibiotic cost. Antibiotics and self-tests complement (substitute) given a high (low) antibiotic cost. The interaction between self-tests and veterinary services varies with veterinary service cost: when veterinary service cost is i) low then self-tests and veterinary services substitute in regard to purchasing

information; ii) high then they complement since veterinary services function as alternative treatments.

Since the interaction between antibiotics and self-tests varies, the effect of self-test information on antibiotic demand depends on context. When antibiotics are sufficiently cheap to purchase and administer then the farmer without information may over-apply in order to avoid the risk of incurring losses due to infections. In this case, more self-test information about whether the suspected disease is an antibiotic treatable infection will decrease the expected antibiotic use. Alternatively, when antibiotics are sufficiently expensive, then the farmer with low information may under-apply. In this case, more self-test information will increase the expected antibiotic use. In contrast, when the farmer purchases information through a veterinarian, the expected antibiotic use decreases unambiguously since a veterinarian provides alternative treatments bundled with information services. Hence,

Summary 6. (The impact of incentive-based policies) A Pigouvian tax can restore the farmer's private best choices to the social optimum. Deciding the optimal tax rate is difficult in practice due to insufficient understanding on the resistance cost associated with antibiotic use in agriculture on human health.

A self-test subsidy potentially decreases (increases) expected antibiotic use when treatment cost is low (high). A veterinary service subsidy can only decrease expected antibiotic use.

1.4.3. PRESCRIPTION REGULATION (PR)

Following VFD regulating medically important antibiotic use in feed or water, PR changes from OTC to prescription the market status of remaining medically important antibiotics that are used in other forms. Thus the farmer is not allowed to use antibiotics without a veterinary visit, i.e., at information sets ⑥, ⑦ or ⑨, or with veterinary visit but no prescription allowing antibiotic use, i.e., at information sets ⑧ and ⑩. There are two antibiotic decisions remaining: 1) when a

veterinarian reveals E at information set ④; 2) when a self-test reveals E and a veterinarian is called at information set ⑤. Figure 6-Figure 8 are sample outcomes of the optimal strategies under PR and are counterparts to the unregulated privately optimal strategies depicted in Figure 3-Figure 5.

Figure 6 The farmer's optimal strategies under PR in the b-d plane given veterinary service cost $l_3 - l_2 < v < l_3 - \beta l_1 - (1-\beta) l_2$

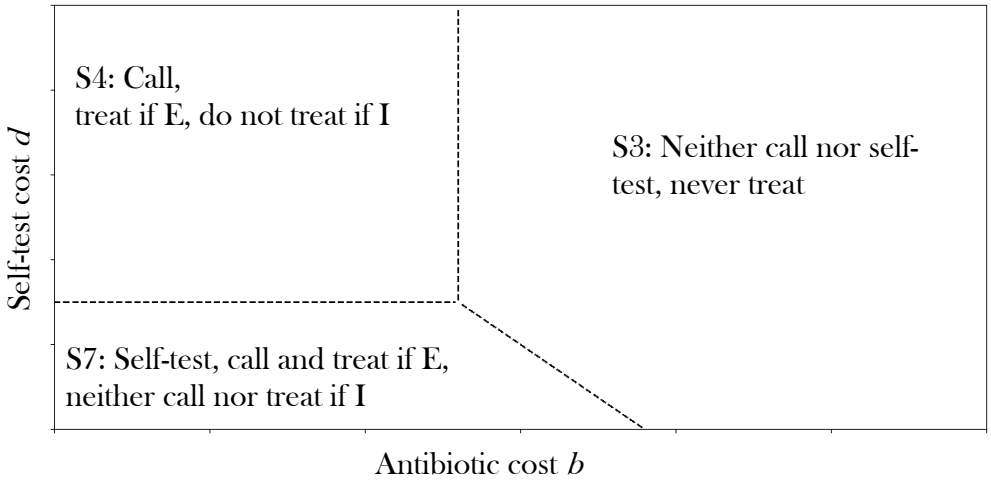


Figure 7 The farmer's optimal strategies under PR in the b-v plane given high self-test cost $d > \beta(1-\beta)(l_2 - l_1)$

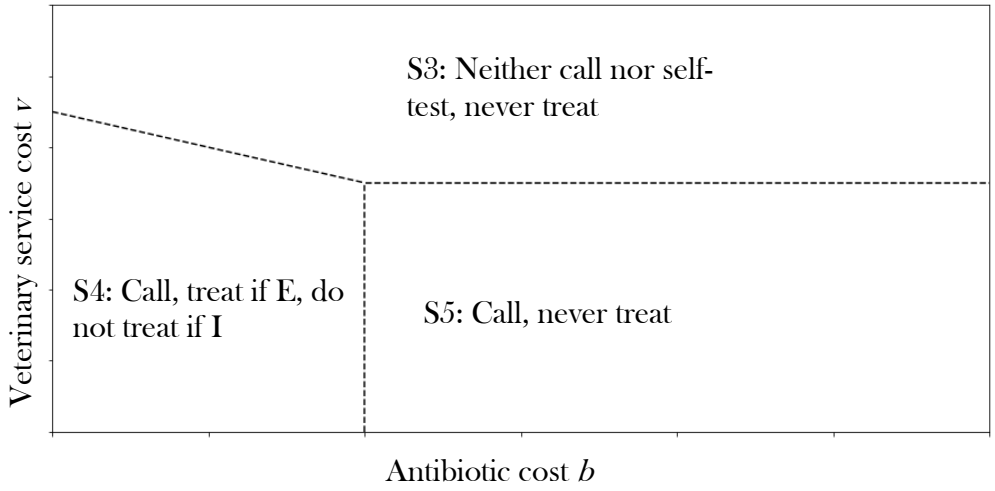


Figure 8 The farmer's optimal strategies under PR in the *d*-*v* plane given low antibiotic cost $b < l_2 - l_1$

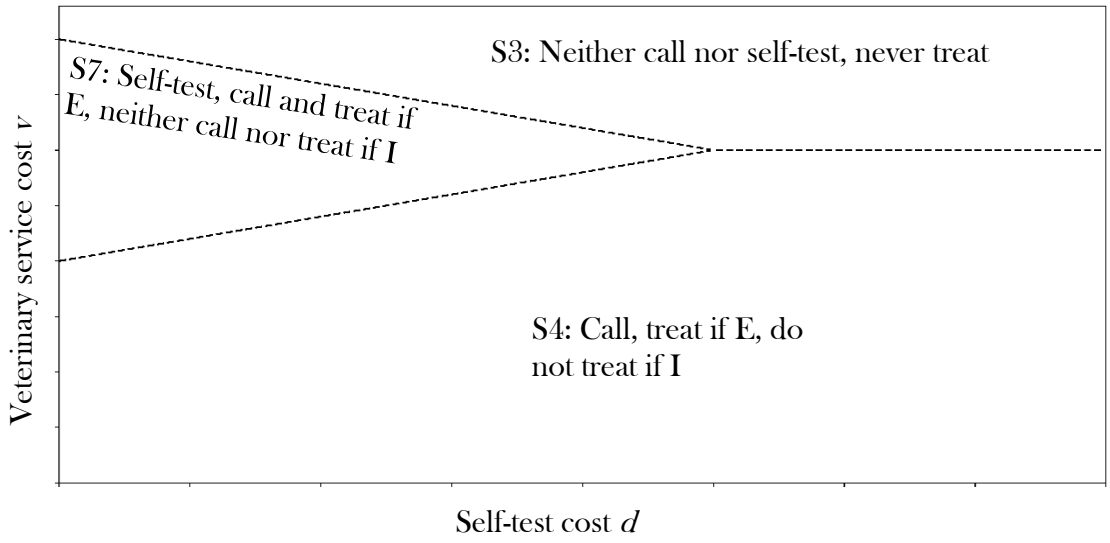


Figure 6 illustrates the farmer's optimal strategies under PR when the veterinary cost is sufficiently high that veterinary services are not preferred before PR implementation. However, under the same cost parameters the PR-constrained farmer may prefer veterinary services since PR favors information through a veterinarian and leads farmers to substitute away from self-test information. For a similar reason, in Figure 7 self-testing is sufficiently expensive that it is not preferred under PR even though it can be optimal absent constraints. Figure 8 illustrates the farmer's optimal choices under PR given low antibiotic cost. The triangle area illustrates how the interaction between veterinary services and self-tests can vary with cost parameters. Similar to optimal choices without regulations, when the veterinary service cost is relatively low then self-tests and veterinary services substitute in regard to purchasing information. When veterinary service cost is relatively high, however, then these actions complement.

In general, consistent with "prudent use" principles, PR removes from the farmer's optimal strategy choices the possibility of precautiously applying antibiotics without information. Also antibiotic administrations based on self-test information are not allowed. A strategy now emerges

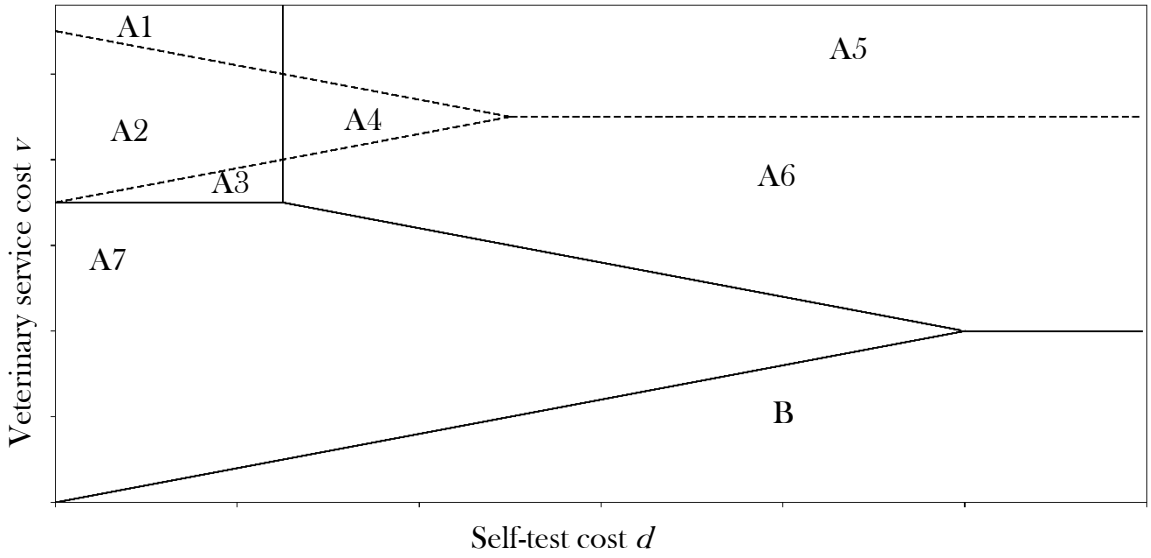
that never appeared without regulations. Strategy S7 describes where the farmer self-tests, and then calls a veterinarian and administers antibiotics whenever the infection type is found to be *E*. The new optimal strategy S7 is a costly choice where the veterinarian's only function is to sign the prescriptions. Unless compensation is provided, PR cannot increase and may decrease farmer welfare. In the next section we evaluate PR in regard to actions and efficiency.

1.5. ASSESSMENT OF PR

In this section, we investigate whether and, if so, how PR drives farmer decisions towards social optimum.[5] Since farmer's decisions on testing, veterinarian use and antibiotic use depend on context, the impacts of PR also vary with context. To better illustrate the consequences of PR, we compare the farmer's optimal strategies with and without PR in the same figure. Figure 9 is a sample output given low antibiotic cost $b < l_2 - l_1$, where we combine the farmer's optimal strategies without PR in Figure 5 and the optimal strategies under PR in Figure 8. Solid lines and dashed lines indicate optimal strategies for unregulated farmers and constrained-farmers respectively. Those lines divide the d-v plane into 8 areas, named A1-A7 and B. Noteworthy is area B. Given high self-test cost but low veterinary service cost, the farmer uses veterinary services without government interventions, a strategy that completely complies with the standard performance required by PR and so PR has no impact on her disease management. In the A areas, PR can either change antibiotic administration decisions or testing decisions. In the sub-sections that follow we discuss these changes in different cost parameters scenarios, i.e., different A areas of Figure 9.

[5] Optimal solutions are given in SM B.

Figure 9 Comparison between farmer's optimal strategies concerning antibiotic use without and with PR in the d-v plane given low antibiotic cost $b < l_2 - l_1$



	Without PR	Under PR
A1	Self-tests, never call, treat if E, do not treat if I	Neither, never treat
A2	Self-tests, never call, treat if E, do not treat if I	Self-test, call and treat if E, neither call nor treat if I
A3	Self-tests, never call, treat if E, do not treat if I	Call, treat if E, do not treat if I
A4	Neither, always treat	Self-test, call and treat if E, neither call nor treat if I
A5	Neither, always treat	Neither, never treat
A6	Neither, always treat	Call, treat if E, do not treat if I
A7	Self-tests, do not call but treat if E, call but not treat if I	Call, treat if E, do not treat if I
B	Call, treat if E, do not treat if I	Same

Notes: Solid lines and dashed lines indicate optimal strategies for farmers without and with constraints respectively. Each area represents an optimal strategy given the values of (d, v) either with or without the PR constraint.

1.5.1. PR'S IMPACTS ON ANTIBIOTIC ADMINISTRATION DECISIONS

Except for A2, A3 and A7, where PR has no impact on antibiotic administrations, PR decreases expected antibiotic use in other A areas. As is required by "Principle 1 of judicious use" (U.S. Food and Drug Administration [US FDA] 2012), PR eliminates any antibiotic use for type *I* infections. For example in areas A4 and A6, given high testing cost and low antibiotic cost, without PR, the farmer would prefer to remain uninformed and apply antibiotics regardless. PR requires the farmer to call a veterinarian before antibiotic administrations. The veterinarian won't prescribe antibiotics for type *I* infections and therefore no antibiotics are administered in type *I* cases. For these areas PR reduces needless antibiotic use when type *I* infection occurs.

PR may, however, eliminate antibiotic use in *E* type infection cases due to the additional cost associated with antibiotic use imposed by PR. OTC antibiotics are no longer available under PR. In order to administer antibiotics, the farmer must pay for not only antibiotics but also veterinary services. The additional economic burden is the main reason for a reduction in antibiotic use for *E* type infections. Area A1 provides one example of this outcome. Without PR, the farmer applies antibiotics in type *E* infection cases based on self-test information, while under PR the farmer does not use antibiotics regardless of drug effectiveness. This is because antibiotic administration costs have become too high. These costs consist of two components 1) veterinary service cost to obtain a prescription, and 2) antibiotic cost. Another example is area A5. Absent regulations, the farmer prefers to use antibiotics without testing. This is because precautious antibiotic use is more profitable for the farmer than informed antibiotic use given high testing costs and low antibiotic cost. PR prevents antibiotic use since the farmer would rather not call a veterinarian at a high cost for a prescription when OTC antibiotics are not allowed.

Summary 7. PR may have no impact on farmer's optimal strategies (e.g., when self-tests are expensive but veterinary services are cheap). However, PR will not increase antibiotic use

and may decrease antibiotic use (e.g., when infection is of the type that cannot be treated with antibiotics). By mandating costly veterinary services in order to obtain antibiotics PR may prevent antibiotic use for infections that can be cured by antibiotics.

1.5.2. PR'S IMPACT ON TESTING DECISIONS

We next examine situations where PR results in some knock-on effects on testing choices. These effects arise because, as we showed earlier, decisions regarding antibiotic use are closely related to decisions regarding self-testing and veterinary services. PR changes both the de facto cost of applying antibiotics and the comparative prices of alternative infection status information sources.

PR may decrease demand for self-testing since self-test information can no longer be applied directly to guide antibiotic administrations. For example, in area A3, the unregulated farmer self-tests to obtain information while the PR-constrained farmer purchases information through a veterinarian since a prescription is required for antibiotic purchases under PR. In area A7, the unregulated farmer prefers to purchase information through a self-test; in type E infection cases she administers antibiotics while in type I infection cases she calls a veterinarian for alternative treatments. The PR-constrained farmer has to call a veterinarian for a prescription in type E infection cases. In that case, self-tests become redundant and are never performed given the fact that the farmer under constraints calls a veterinarian in both infection types. In area A1, absent PR the farmer performs a cheap self-test to obtain information. Under PR the high cost of veterinary services required for antibiotic administrations makes it less profitable to administer antibiotics for type E infections. The farmer with cost parameters located in this area would rather save on veterinary service and antibiotic expenditures by leaving the suspected infection untreated. As well as reducing demand for self-tests, in areas A3 and A7 PR increases veterinary service demand while in A1 PR does not promote veterinary service use due to its high cost.

PR may increase veterinary service demand. For example, in area A2, the farmer used to administer antibiotics according to self-test information. Under the PR restriction, the farmer has to call a veterinarian after a self-test reveals E in order to administer antibiotics. In area A6, the unregulated farmer does not purchase any information and substitutes precautious antibiotic use for information input. As PR mandates veterinarian use before antibiotic administrations, the regulated farmer purchases veterinary services in order to obtain a prescription allowing antibiotic use. George Stigler (1971) might be skeptical about veterinary profession advocacy in shaping PR and other judicious use policies (U.S. American Veterinary Medical Association 2018).

Strikingly, PR can raise demands for both self-tests and veterinary services. This outcome will occur in situations where self-tests and veterinary services complement. In area A4, without PR the farmer performs no tests since precautious antibiotic use is more beneficial than informed antibiotic use given low antibiotic cost compared with testing cost. Under PR constraints, antibiotic administrations for type E infections are allowed and profitable even when the cost of compulsory veterinary services before administrations is taken into account. Therefore farmer uses antibiotics under veterinarian oversight in type E infection cases. However, in type I infection cases, it is not profit-increasing to use veterinary services. Facing a relatively high veterinary service cost compared with self-test cost, the farmer uses veterinary services and self-tests as regulation-induced complements. In light of self-test information, the farmer makes distinct veterinary service decisions. She calls a veterinarian for type E infections so as to obtain prescriptions. That explains why, in favoring veterinary services, PR pushes up both demands for self-tests and veterinary services.

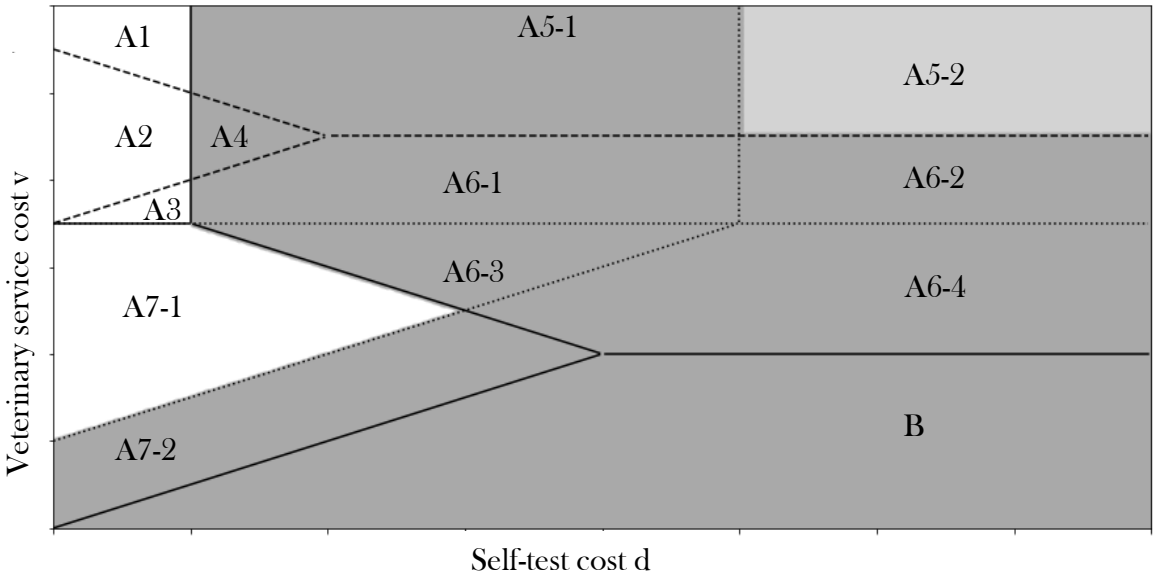
Summary 8. PR may produce knock-on effects which vary by context. On the one hand, PR can reduce demand for self-tests since self-test information is no longer sufficient to guide antibiotic administrations. However, PR can increase the use of self-tests because self-tests can

provide information on the benefit from antibiotic use and so from veterinary services. PR will not decrease veterinary service demand for information acquisition or for obtaining a prescription to permit antibiotic use.

1.5.3. COMPARISON OF PR'S OUTCOMES WITH SOCIAL OPTIMUM

We compare the farmer's optimal strategies under PR and socially optimal strategies so as to better illustrate how PR performs from the perspective of social welfare. For example, Figure 10 depicts a comparison given low antibiotic cost $b < l_2 - l_1$ and some level of antibiotic resistance cost. In addition to solid lines and dashed lines indicating optimal strategies for unregulated farmers and constrained-farmers respectively, dotted lines indicate how the social optimum varies with cost parameters. Thus in Figure 10 the d-v plane is further partitioned relative to Figure 9. For example, area A6 is divided into four subareas, namely A6-1, A6-2, A6-3 and A6-4. Although the regulated farmer's choices are common across subareas, social optimum varies and therefore assessment of PR efficiency varies. Note that social optimum not only varies with cost parameters b, d, and v, but also with antibiotic resistance cost ω. Despite the fact that Figure 10 presents an example comparison between the farmer's optimal choices under PR and social optimum, the findings showcase how food animal production distortions may arise due to PR.

Figure 10 Comparison between farmer's optimal strategies concerning antibiotic use under PR and social optimum in the d-v plane given low antibiotic cost $b < l_2 - l_1$.



	Social optimum
A1	Self-tests, never call, treat if E, do not treat if I
A2	Self-tests, never call, treat if E, do not treat if I
A3	Self-tests, never call, treat if E, do not treat if I
A4	Self-tests, never call, treat if E, do not treat if I
A5-1	Self-tests, never call, treat if E, do not treat if I
A5-2	Same
A6-1	Self-tests, never call, treat if E, do not treat if I
A6-2	Neither, never treat
A6-3	Self-tests, do not call but treat if E, call but do not treat if I
A6-4	Call, never treat
A7-1	Self-tests, do not call but treat if E, call but do not treat if I
A7-2	Call, never treat
B	Call, never treat

Notes: (1) Solid lines and dashed lines indicate optimal strategies for farmers without and with constraints respectively. Dotted lines indicate social optimum. Each area represents an optimal strategy given the values of (d, v) either with or without the PR constraint.
(2) In the white areas, the unregulated farmer's choices realize social optimum while PR changes the wedge between actual choices and socially optimal choices. In dark grey areas, PR may change sub-optimal private choices but does not produce social optimum. In light grey area, PR improves the farmer's choices and produces social optimum. The farmer's optimal strategy in each area is listed in the table below Figure 9.

We use colors to illustrate an assessment of PR efficiency. In the white areas, PR worsens outcomes: the unregulated farmer's choices realize social optimum while PR creates a wedge between actual choices and socially optimal choices. In dark grey areas, PR may change sub-optimal private choices and either improve or worsen welfare but does not produce social optimum. Neither farmer's choices without PR nor choices under PR attain social optimum. In the light grey area, PR improves the farmer's choices and produces social optimum. This is because, given high testing cost the regulated farmer would rather not call a veterinarian and therefore antibiotic use is not allowed. However it is socially optimal to not use antibiotics due to a large antibiotic resistance cost. Were a higher antibiotic resistance cost posited then the light grey area expands and could even cover areas A5-1 and A1 while the white areas shrink and could disappear. PR may improve upon privately optimal choices given inexpensive antibiotics and expensive tests, especially when a large cost of antibiotic resistance to society has been proved by science. The table below Figure 10 provides detailed information about farmer's choices under PR and social optimum. We also use different colors shading to match with the figure.

In the analysis to follow we will focus on how PR causes distortions. These distortions vary with antibiotic cost and testing cost as well as expected damage that antibiotics resistance will incur. To do so, in the subsections that follow we take white and dark grey areas in Figure 10 as examples and discuss the biases in choices regarding antibiotics and tests that these areas support.

1.5.3.1. Biases in antibiotic decisions

Except in areas A2-A4, A6-1, and A6-3 where PR attains socially optimal antibiotic use, PR biases antibiotic decisions in other white and dark grey areas compared to social optimum. PR may result in underuse of antibiotics. One example is where veterinary service cost is high but self-tests are inexpensive (e.g., areas A1 and A5-1). In that case, it is socially optimal to purchase information through a self-test and then use antibiotics according to the self-test result, while the

PR-constrained farmer would rather not call a veterinarian and so leaves the infection without antibiotic treatment. However, in reducing antibiotic use for type *E* infections, PR may give rise to more antibiotic use as the infection progresses or spreads to herds. This is a consequence of the law of unintended consequences (Hayes and Jensen 2003). Another example is where social cost of antibiotic use is low and so is outweighed by testing cost (see areas A4 and A6 in SM Figure C-32). In that case, it is socially optimal to use antibiotics without purchasing information. However, the regulated farmer is not allowed to substitute precautious antibiotic use for information input even if the substitution is more cost-effective, and therefore avoids antibiotic use in type *I* infection cases. Interestingly, when we assume a higher antibiotic resistance cost associated with antibiotic use, PR outcomes in these examples may become consistent with social optimum since a greater antibiotic resistance cost incentivizes the social planner to reduce antibiotic use even further. This is likely the implicit assumption underlying the policy of placing tighter restrictions on antibiotics viewed as being more important to human medicine (World Health Organization [WHO] 2019; European Medicines Agency 2020).

Conversely, PR may result in overuse of antibiotics compared to social optimum. Given low antibiotic and veterinary service costs but high self-test cost, the PR-constrained farmer prefers to call a veterinarian and then administer antibiotics according to any ensuing prescription. However, the social planner facing an extra resistance cost for antibiotic use does not see any benefit from antibiotic treatment for type *E* infections. That is, it is not socially optimal to use antibiotics regardless where areas A6-2, A6-4, A7-2 and B are examples in the d-v plane. PR fails to sufficiently restrict antibiotic use since it does not address the antibiotic resistance from antibiotic administrations to type *E* infections. Recall that PR does not even reduce farmer's antibiotic demand in areas A7-2 and B. In area A6-2 PR does restrict antibiotic use, but the reduction is socially insufficient. When we posit a higher social cost of antibiotic resistance then the areas where

PR results in overuse of antibiotics can expand to everywhere in the d-v plane excluding areas A1 and A5. Were a large antibiotic resistance cost of on-farm antibiotic use to society demonstrated, then more attention should be paid to the possibility that PR may fail to restrict antibiotic demand sufficiently. In such situations, just requiring a prescription for antibiotics may be inadequate. More stringent policies might be needed.

Summary 9. The magnitude of the social cost of antibiotic resistance is a key factor in determining the social efficiency of PR. If the social cost is low, then PR can cause socially excessive reduction of antibiotic use and thus farmers may face a higher operation cost (e.g., where social cost of precautious antibiotic use is outweighed by testing cost) or a greater risk of infection spread (e.g., where veterinary service cost is sufficiently high to prevent antibiotic use even when effective). On the other hand, if the scientific basis for assuming a high antibiotic resistance cost is strong then PR may not sufficiently restrict antibiotic use.

1.5.3.2. Biases in testing decisions

Except in areas A6-4, A7-2 and B where PR achieves socially optimal testing choices, PR results in testing decision biases. PR may result in insufficient self-testing since self-test information is insufficient to guide antibiotic administrations. For example in areas A3, A6-1, A6-3 and A7-1, calling a veterinarian is the best choice under PR since the veterinarian not only provides information but also issues a prescription whenever antibiotics provide effective treatment for the case at hand. However there exist more cost-effective choices from the perspective of social welfare. In these areas, where the self-test cost is low, it is socially optimal to obtain information through a self-test instead of a veterinary visit and then use self-test information to guide the follow-up decisions. In areas A1 and A5-1, it is socially optimal to obtain information through a self-test and then use antibiotics accordingly, while the PR-constrained farmer would rather leave the infection untreated since mandatory veterinary services before antibiotic administrations are

expensive. In that case, information is useless so that the farmer does not self-test. In addition to insufficient self-test use, PR elicits excessive veterinarian use in areas A3, A6-1, A6-3 and A7-1 since self-tests and veterinary services substitute in information acquisition. Veterinarian use distortions do not occur in areas A1 and A5-1.

PR may cause excessive veterinarian use for information acquisition or for obtaining a prescription. Area A6-2 exemplifies the first case. When both self-test and veterinary service costs are high, social benefit from informed antibiotic use is lower than information cost. Therefore, it is socially optimal to neither use antibiotics nor purchase information. However, informed antibiotic use is a profit-increasing choice for the PR-constrained farmer who does not take the resistance cost into consideration. Therefore, in area A6-2 the farmer under constraints prefers to call a veterinarian and make informed antibiotic treatment decisions. Note that A6-2 is an instance of the law of unintended consequences where PR restricts antibiotic demand insufficiently but causes excessive veterinary service demand. Areas A2 and A4 exemplify the second case. The farmer under PR will call a veterinarian primarily for permission to use antibiotics. Calling a veterinarian is not socially optimal; self-testing is sufficient to guide antibiotic use.

PR may lead to excessive use of both self-tests and veterinary services. Although such cases do not arise in Figure 10, the intuition is quite straightforward. The farmer's privately optimal choices under PR in areas A2 and A4 do not change with antibiotic resistance cost, i.e., self-test information is used to confirm the need for veterinarian use. Consider now a much higher antibiotic resistance cost than depicted in Figure 10 (e.g., SM Figure C-34). It is then socially optimal to not use antibiotics due to the high social cost of doing so, thus no information purchase is needed. Alternatively, consider a situation where much lower antibiotic resistance cost is assumed than is depicted in Figure 10 (e.g., SM Figure C-32). In area A4, antibiotics precautious use without information becomes socially optimal due to the low social cost of antibiotic use. In

these two examples, the constrained-farmer over-uses veterinary services as well as self-tests since they complement.

Summary 10. The comparison between private choices regarding tests under PR and social optimum depends on context. PR can result in overuse of veterinary services compared to social optimum since a veterinarian prescription is required for antibiotic use. As self-tests and veterinary services can substitute or complement depending on cost parameters, the farmer under PR may under-use or over-use self-tests compared to social optimum.

1.5.4. EMPIRICALLY PARAMETERIZED MODEL AND BROADER RELEVANCE

Given the conclusion that assessment of PR depends on context, a follow-up question is which context best represents the current state of U.S. livestock production. We conduct a simulation in a dairy farm disease management setting where we assess the effectiveness and efficiency of PR on antibiotic use. A survey about antibiotic administration on dairy farms was sent to producers in three U.S. Great Lakes Region states (Wisconsin, Minnesota, Michigan) during Summer 2017. This survey asked about costs to producers' herds for a mastitis case (see descriptive statistics in SM D). We set parameters in our model from the survey data or follow values in extant literature (Cha et al. 2011; Pinzón-Sánchez, Cabrera and Ruegg 2011; U.S. Department of Agriculture [USDA] 2016; Liang et al. 2017; Kniesner and Viscusi 2019; Ruegg 2020; U.S. Center for Disease Control and Prevention [US CDC] 2019; U.S. Food and Drug Administration [US FDA] 2021b; U.S. Center for Disease Control and Prevention [US CDC] 2013). See detailed explanations about parameter set in SM E.

In the baseline scenario, we assume $b = \$10$, $d = \$5$, $v = \$27.5$, $l_1 = \$95$, $l_2 = \$150$, $l_3 = \$630$, $\beta = 0.35$, and ω is in the range \$2.2-\$3.9. Under these parameters and without any regulations, farmers self-test to obtain information. In revealed type E infection cases, they

administer OTC antibiotics, while in revealed type I infection cases, they call a veterinarian but do not use antibiotics. These outcomes are consistent with dairy farmers' perception that they use antibiotics only if needed (Wemette et al. 2020). Cephapirin, an OTC antibiotic, is the leading treatment for mastitis (U.S. Department of Agriculture [USDA] 2016; Redding et al. 2019). While the other OTC antibiotic Penicillin has been less frequently used in recent years (Redding et al. 2019; U.S. Department of Agriculture [USDA] 2016), well documented resistance to penicillin on dairy farms may explain its infrequent use and suggests frequent use before resistance developed (Mathew, Cissell and Liamthong 2007).

Our simulation results suggest that PR does not decrease antibiotic use. In practice, antibiotic treatment comes with great private cost in the form of discarded milk but, if effective, also brings great private benefits. When information cost is inexpensive relative to costs and benefits associated with antibiotic treatment, dairy farmers prefer informed antibiotic administrations. That also explains why PR does not reduce therapeutic antibiotic use but instead substitutes veterinary services for self-tests in obtaining information. Dairy farmers' optimal strategy without regulations attains the social optimum. Therefore, PR causes excessive demand for veterinary services but does not decrease antibiotic use among typical dairy farmers. According to our rough parameter estimates, PR moves dairy farmers' choices from social optimum. The findings are robust when we increase or decrease parameter values by 20%. Were accumulated scientific evidence to support a higher antibiotic resistance cost in future research, for example, $\omega = \$50$, then calling a veterinarian but not administer antibiotics becomes socially efficient. This is consistent with the underlying consideration behind the suggestion that antibiotics classified as critically important for human medicine should not be used for animal disease treatment (World Health Organization [WHO] 2017).

In analysis, we take dairy farm disease management as an example but the modeling framework and its analysis can also be applied to other livestock animal and companion animal settings. For example, in the poultry sector avian mycoplasmas is a leading cause of large economic losses (Elyazeed et al. 2020). Antibiotics can sometimes be effective and sometimes ineffective in treating avian mycoplasmas. Before applying antibiotics, poultry farmers can perform simple tests using point-of-care testing kits or they can call a veterinarian in order to identify the most effective course of treatment. PR also regulates medically important antibiotic use for all non-human animals. Absent PR, pet owners who suspect that their pets have infections can administer OTC antibiotics directly or use test information to guide their treatment choices. When PR becomes effective in 2023, medically important antibiotic use in companion animals also must be under veterinary oversight. Although pet owner disease management decisions are not motivated by production or profit considerations, our modeling framework also applies to pet owners' decisions by re-specifying payoff functions. The way we consider antibiotic administration in veterinary practice may also be extended to human medicine. For instance, people who observe symptoms and suspect a urinary tract infection can purchase and administer antibiotics without purchasing information, i.e., self-medication, or perform a home test and then use antibiotics whenever tests indicate antibiotics, or see a doctor for professional advice and then take treatment if needed. The underlying story is similar to that in the veterinary practice setting.

1.6. CONCLUSION

Animal agriculture consumes the greatest share of antibiotics while inappropriate use of antibiotics in food-producing animals can degrade antibiotic effectiveness and accelerate antibiotic resistance development. In light of this concern, various policies have been proposed to promote antibiotic stewardship. It is important that we understand the implications of policies aimed at promoting judicious use of antibiotics. To assess policy impacts on antibiotic use, we need to

understand how a policy will change decisions related to antibiotic use and whether such changes will lead us closer to the social optimum.

In this study, we examine the prescription regulation (PR) that requires prescriptions of medically important antibiotic use through non-feed forms in animal agriculture. We set up a modeling framework of farmers' disease management related decisions and show how antibiotic use decisions interact with decisions on testing and calling for veterinary services. PR does not change the farmer's choices in cases where farmers are not interested in administering antibiotics or where unregulated farmers do call a veterinarian before antibiotic administrations. However, PR will not increase, and may reduce, expected antibiotic use. PR prohibits precautious (in regard to protecting profits) use without information and eliminates antibiotic treatment for infections which can not be cured by antibiotics, realizing the "judicious use" intent of PR. An almost inevitable consequence of mandating that veterinary services precede any antibiotic therapy is prevented use under some circumstances on infections which can be cured by antibiotics.

PR can also produce unintended impacts on testing decisions. PR will not decrease veterinary service demand for information acquisition and for the right to use antibiotics. As self-tests and veterinary services can be substitutes or complements depending on context, PR can decrease or increase demand for self-tests. In other words, veterinary service demand for information acquisition substitutes for self-tests as a result of PR, while veterinary service demand for prescriptions complements self-testing to assess whether a veterinarian call is warranted. Situations exist where PR does not have any impact on antibiotic administrations but does change testing decisions.

Efficiency assessment of PR depends on cost parameters pertaining to antibiotics and tests as well as antibiotic resistance. PR can make things worse: specifically, when the farmer's laissez faire choices realize social optimum while PR generates action distortions. Situations also exist where

the PR changes sub-optimal private choices but still do not procure social optimum, i.e., farmer's choices are not socially optimal either without or with PR and there is no reason to believe that efficiency is improved by PR. PR can improve the farmer's choices and support social optimum given inexpensive antibiotics and expensive tests, especially when a large antibiotic resistance cost to society has been confirmed by science. To determine whether PR is an unduly stringent control on on-farm antibiotic use, further efforts to quantify the adverse effect of antibiotic use in animal agriculture on human health are warranted.

Despite the absence of evidence on an adverse impact on human health due to antibiotic used in agriculture production (Marshall and Levy 2011; Hollis and Ahmed 2013; Hoelzer et al. 2017; Koch et al. 2017; Chatterjee et al. 2018), concerns about the threats posed for human health arise from the fact that the largest fraction of all antibiotics consumed are consumed in livestock production. Similar to the belief that actions are needed to address climate change despite uncertainties associated with climate change mitigation and adaptation (Schelling 2007; Gray 2011), policy decisions have to be made notwithstanding the many uncertainties associated with antibiotic restrictions and regulations (Robinson et al. 2016; Larsson et al. 2018). We must weigh different policy options and make decisions even when we do not fully understand the benefits, costs, and probabilities of different outcomes (Jim O'Neill 2016). In this spirit, a variety of policy scenarios need to be considered. We have done so while we have also provided a rather speculative assessment of which policy scenarios are most relevant. We find that using antibiotics whenever needed in disease management is profit increasing for dairy farmers with and without PR. This is because information cost through either a self-test or a veterinarian is inexpensive relative to discarded milk cost and potential loss saving associated with antibiotic treatment. PR does not decrease therapeutic antibiotic use but raises excessive demand for veterinary services on typical

U.S. dairy farms. However, simulation results will likely differ for other livestock industries (e.g., swine), where parameters take different values.

The interlinked nature of diagnostic testing decisions and antibiotic use decisions highlighted in our framework will also affect the best choice of antibiotic incentive policy tools. A test subsidy's implications for antibiotic consumption will depend on context. When antibiotic cost is low (respectively, high) then expected antibiotic use decreases (increases) with a self-test subsidy. The context-dependent effect of this subsidy arises because self-tests are information goods, where the consequence of more information varies with context. The economics of such goods are not self-evident. For example, although veterinary services are also information goods, we show that a veterinary service subsidy will unambiguously decrease expected antibiotic use.

In practice, medically important antibiotics and non-medically important antibiotics are both applied in agricultural production. Under restrictions on medically important antibiotics, producers are likely to substitute in non-medically important antibiotics. Despite concerns that non-medically important antibiotics may also contribute to resistance, we should be cautious about expanding PR to non-medically important antibiotics. Regulations attaining social optimum regarding medically important antibiotics may be too stringent for non-medically important antibiotics which are prima facie accepted as producing lower resistance costs.

Regarding opportunities for model development, while tests are assumed to reveal perfect information in the model setup, in practice self-test information is less accurate than information obtained through a veterinarian. Were we to allow into our model heterogeneous accuracy of information obtained through tests, then the conclusions may become more favorable to PR. A further limitation is our model's omission of animal welfare effects. Any accounting for this effect will cast PR in a less favorable light as the prescription requirement sometimes leads to untreated cases where antibiotics would have been effective. If the benefit to society of avoiding animal pain

and suffering exceeds the expected cost to society of human health consequences due to additional antibiotic applications then emphasis might be placed on reducing transactions costs for obtaining a prescription.

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CHAPTER 2: ESSAY TWO: WILL TESTS LEAD TO MORE INFORMED ANTIBIOTIC USE? AN APPLICATION IN VETERINARIAN DIAGNOSTIC DECISIONS

2.1. INTRODUCTION

Antibiotic resistance, which degrades antibiotic effectiveness to kill bacteria, is one of major threats to public health (World Health Organisation [WHO] 2020). In addition to additional health care cost (Fullybright 2019), infections caused by resistant bacteria lead to staggering number of death. A recent study estimate that, in 2019, more than 4.95 million deaths are associated with antibiotic resistance around the world, among which 1.27 million deaths are direct results of antibiotic resistance (Murray et al. 2022). In other estimations, more than 35,000 deaths in the United States and about 33,000 deaths in European Union (EU) countries can be attributed to antibiotic resistance annually (U.S. Center for Disease Control and Prevention [US CDC] 2019; European Centre for Disease Prevention and Control [ECDC] and Organisation for Economic Co-operation and Development [OECD] 2019).

The wide spread antibiotic resistance problem is a result of millions of tons of antibiotics use in past 75 years (Laxminarayan and Herrmann 2015). Under the selection pressure imposed by antibiotics, bacteria can become resistant through mutation, inductive expression or genetic transferring (Neu 1992). Despite of the warning that antibiotic use inevitably contribute to antibiotic resistance, negligent antibiotic use is a leading reason of antibiotic resistance development (Chokshi et al. 2019). In developing countries, lack of proper oversight and diagnosis causes excessive antibiotic use in human and therefore accelerate antibiotic resistance development. It is common that physicians prescribe antibiotics without utilizing diagnostic methods, unskilled health workers prescribe antibiotics for patients, and patients purchase antibiotics easily and self-mediate. In developed countries, despite that inappropriate antibiotic use in human medicine exists (Cully 2014), overuse in animals is the main contributor to antibiotic

resistance(Chokshi et al. 2019). Antibiotics have been applied in food-producing animals mainly for growth promotion, disease prevention and disease treatment. Food-producing animal production accounts for the greatest share of global antibiotic use (van Boeckel et al. 2017) and antibiotic use in food animals has been expected to rise significantly through 2030 (Tiseo et al. 2020; Van Boeckel et al. 2015). In absence of regulation and oversight, low dose antibiotic use for non-therapeutic purpose, which creates a ideal condition for resistance development, were prevalence in animal agriculture production (Levy 2014). Most antibiotic administration for therapeutic purpose are made without proper oversight and diagnosis (Chan et al. 2020; De Briyne et al. 2013). For instance, mastits is the main ailment treated with antibiotics on dairy farms while it has been argued that up to 50% antibiotic treatment are needless or inappropriate (Krömker and Leimbach 2017). In this study we investigate how proper oversight and diagnosis affect antibiotic therapeutic use and its implication for antibiotic stewardship promotion. Specifically, we study antibiotic administration decisions in animal disease management in the United States as a special case to answer the research question.

Before 2017, most antibiotics for food-producing animals were available without veterinary prescription in the United States. To address concerns about antibiotic resistance arising from animals, the U.S. Food & Drug Administration (FDA) introduced principles of "judicious use" in animals (U.S. Food and Drug Administration [US FDA] 2012). "Judicious use" restricts antibiotic use to cases objectively assessed as being in real need and requires veterinary oversight before antibiotic administrations. Since 2017 the Veterinary Feed Directive (VFD), a command and control regulation, has enforced the "judicious use" requirement before medically important (i.e., important for human disease treatment) antibiotic application through feed in food producing animals. VFD mainly eliminates medicially antibiotic use for growth promotion purpose, successfully reducing the sale of antibiotics in food-producing animals by more than 30% (U.S.

Food and Drug Administration [US FDA] 2021b). Commencing 2021 veterinary oversight requirement was expanded to medically important antibiotic use in other forms (e.g., injection) and other animals (i.e., companion animals). Whether this requirement can secure optimal use depends on veterinarians' understanding of animal diseases, resistance biology, and implications for animal welfare and so the capacity in judgment about whether antibiotics are needed for disease treatment or prevention. Our concern is with better understanding an assumption underpinning the antibiotics stewardship governance approach that mandates veterinary oversight. Specifically, how effectively do veterinarians manage information when making antibiotic recommendations in suspected disease cases and how might effectiveness be improved?

In the literature on medical applications, "evidence-based medicine" (EBM) has attracted increasing attention. This approach defines a Bayesian approach to making good decisions in a medical context (Ashby and Smith 2000). The American Veterinary Medical Association (2015) also asserts that veterinary practices based on the best evidence available can improve animals' health conditions and contain antibiotic resistance as much as possible. In a suspected disease case, EBM requires veterinarians to assess the probability of the disease based on available evidence and incorporate possible benefits and costs as a result of treatment alternatives on animals with and without the disease. Therefore, veterinarians face three sequential decisions in a suspected disease case. The first is diagnostic decisions: how likely is the animal at hand to have a disease? In practice, veterinarians have priors about the diagnosis based on their knowledge, experience, observations, and disease history. After obtaining more information from tests, they may update their beliefs about animals' health conditions. The second is cost and benefits assessment: how to measure costs and benefits associated with treatment alternatives? Should private costs and benefits only be considered or should social costs and benefits also be considered? The third is the

treatment decision: do benefits outweigh costs of treatment and is this the best treatment alternative?

The three-step decision process implies three possible channels that may lead to different antibiotic recommendations. Veterinarians may make different antibiotic recommendations depending on how they update information, how they assess the benefits and cost associated with antibiotic use, and how they weigh the trade-offs of different treatment options. In this paper, we will focus on the first channel, i.e., the effect of information updating on antibiotic treatment decisions. We are curious about whether veterinarians are capable of managing test information efficiently following Bayes' theorem in diagnosis. If not, are their probability assessments upward biased or downward biased when compared with standard probability assessment? How do the errors in diagnosis affect assessments of treatment alternatives and final treatment decisions? The conclusion will shed light on an important channel affecting antibiotic demand and future regulations promoting antibiotic stewardship.

While various belief updating errors in diagnosis are well documented in literature of human medicine (Henriquez and Korpi-Steiner 2016; Elstein 1999; Blumenthal-Barby and Krieger 2015; Eddy 1982), economics studies in medical diagnosis setting is very few (Rottman 2017). In this study, we setup a framed field experiments which differs from standard lab experiments in subjects, incentives and task setting. Most behavioral economics studies on belief updating biases recruit university students to participant experiment (Benjamin 2019), while this study focuses on a specialized population, veterinarians who received professional training in managing evidence in a disease diagnosis context. In addition, instead of describing experiment tasks in an abstract setting (Grether 1980; Grether 1978; Benjamin 2019), such as games with balls and urns, we describe experiment tasks in veterinary clinical setting. Compared with providing fixed rewards to phycisians in diagnosis decision making (Rottman 2017), we incentivize veterinarians to process information

carefully and report their beliefs truthfully. Therefore empirical findings from such innovative experimental data can complement lab evidence (Grether 1980; Grether 1978; Benjamin 2019) in respect to understanding how people behave in the real world. This is because field experiments simulate real word and so enhance generalizability of experimental findings (Gangadharan et al. 2022). Our research disentangles biases due to inefficient use of priors from biases due to inefficient use of new information in clinical settings. We found that veterinarians do not use priors and new test information properly. They neglect prior information and treat new information as if they are less informative than that prescribed by Bayes' updating. With regard to new information underuse, we make novel empirical inquiries about the reason of underuse. In addition, veterinarians respond more strongly to test information that agrees with their priors than to test information that contradicts their priors. Disagreeing with the typical findings that experience can reduce information management biases (Benjamin 2019), we found that experienced veterinarians perform worse in managing priors and test information when compared with their less experienced colleagues.

Furthermore, we frame diagnosis as a context variable in discrete choice experiments and investigate the effect of diagnosis errors on veterinarian's treatment choices. The effect of context variables in discrete choice experiments have been examined in other fields (Molin and Timmermans 2010; Charoniti, Rasouli and Timmermans 2017; Bujosa, Torres and Riera 2018), we are unware of such studies in clinical settings. Our findings support the view that diagnosis biases affect treatment choices. We define disease likelihood in treatment decisions as the likelihood that the animal has disease. In the presence of lower disease likelihood, veterinarians are less likely to use treatment alternatives that comes with higher treatment cost. The disutility of treatment cost increases as disease likelihood decreases. The treatment cure rate has positive effect on utility and utility decreases as disease likelihood decreases. Economic loss avoided associated

with treatment has a similar effect on utility as cure rate. However, veterinarian's preference towards antibiotic resistance cost and animal welfare improvement does not depend on disease likelihood.

The paper unfolds as follows. Section 2 introduces the conceptual framework of diagnosis decisions. In section 3, we explain our research method and survey design. Section 4 discusses data used and reports descriptive statistics. Section 5 analyzes the respondents' probability belief updating behaviors in animal disease management practice. A conclusion section follows.

2.2. CONCEPTUAL FRAMEWORK

In animal disease management practice, veterinarians are faced with a sequence of decisions. The first involves making a diagnosis based on available information while the second decision requires assessing utilities of possible outcomes from treatment alternatives and selecting a socially efficient treatment. Therefore, we have two separate parts in the conceptual framework.

2.2.1. BELIEF UPDATING IN DIAGNOSIS DECISIONS

When making diagnostic decisions, veterinarians usually first inspect suspected disease cows, check their disease history, and learn their management procedures which help form a prior about the likelihood that the cow has some disease. To further examine suspected cases, veterinarians may conduct tests. Efficient management of test information and priors requires belief updating as prescribed by Bayes' theorem. Suppose that visual inspection of a cow suggests prior probability, $p(D)$, that the animal has a disease. Then a test generates new information $I \in \{I^-, I^+\}$ where $p(I \mid D)$ is the likelihood of observing I given the cow has a disease and $p(I \mid ND)$ is the likelihood of observing I given that the cow does not have a disease.[6] Test results can be positive

[6] It is naturally to assume that $p(I^+ \mid D) > 0.5$ and $p(I^- \mid ND) > 0.5$ and we make this assumption.

I^+ or negative I^-. Bayes' theorem then asserts that the posterior belief that the animal has a disease is

$$p^B(D \mid I) = \frac{p(I \mid D)}{p(I \mid D)p(D) + p(I \mid ND)p(ND)}, \tag{2.1}$$

where ND indicates that the cow does not have the disease and $p(ND) = 1 - p(D)$. A positive test result on disease pushes the updated probability up from $p(D)$ toward 1 and a negative test result pushes the probability down toward 0.

In clinical setting, diagnosis errors may result in asymmetric losses (Rottman 2017). Overprediction in diagnosis may lead to unnecessary treatment and so additional healthcare cost, while underprediction may rule out life-threatening disease and so cause larger losses than overprediction. Therefore following (Bora, Katchova and Kuethe 2021), we assume loss incurred when veterinarians' probabilistic estimate deviate from Bayesian posteriors as

$$L = (p^B - p)^2 + \tau \operatorname{sgn}(p^B - p)(p^B - p)^2, \tag{2.2}$$

where p^B is Bayesian posteriors, p is veterinarians' probabilistic estimates, τ $(\tau \geq 0)$ is asymmetry parameter, $\operatorname{sgn}(p^B - p)$ represent the sign of $p^B - p$. The relative loss ratio of underestimate can be defined as the ratio of loss incurred by underestimate and loss incurred by overestimate.

$$\textit{relative loss ratio} = \frac{L(p^B > p)}{L(p^B < p)} = \frac{(1+\tau)}{(1-\tau)}, \tag{2.3}$$

where $\textit{relative loss ratio} \in [1, +\infty)$. When veterinarians are certain about Bayesian posteriors p^B, it is optimal to estimate $p = p^B$. However, in most cases, veterinarians are uncertain about p^B but have rough estimates. Thus we assume veterinarians believe that Bayesian posteriors is uniform distributed with mean p^B and standard deviation $\frac{\sigma}{\sqrt{3}}$.

$$\tilde{p}^B \sim U(p^B - s, p^B + s). \tag{2.4}$$

As an expected loss minimizer, veterinarians' problem can be written as

$$\min_p E_{\tilde{p}^B}(L) = \min_p [\int_{p^B - s}^{p} (1-\tau)(p^B - p)^2 f(\tilde{p}^B) d\tilde{p}^B + \int_{p}^{p^B + s} (1+\tau)(p^B - p)^2 f(\tilde{p}^B) d\tilde{p}^B], \tag{2.5}$$

where $f(\tilde{p}^B)$ is density function of $\tilde{p}^B$.

$$f(\tilde{p}^B) = \frac{1}{2\sigma}. \tag{2.6}$$

Therefore, the optimal probabilistic estimate is

$$p = p^B + \frac{\sqrt{relative\ loss\ ratio} - 1}{\sqrt{relative\ loss\ ratio} + 1}\sigma. \tag{2.7}$$

Note that the second component in equation (2.7) is in the range of $[0, \sigma)$. When losses associated with diagnostic errors are asymmetric, veterinarians' optimal probabilistic estimate p deviate from Bayesian posteriors p^B. When underestimate causes greater losses ($\tau > 0$), veterinarians are incentivized to report probabilistic estimate p greater than Bayesian posteriors. That said, there are various types of biases in diagnosis, such as incentive induced baises and information management biases. It is important to first identify source of biases and then implement regulations to correct them. In this study, we provide symmetric incentives in our experiments and so incentive induced biases are not a concern. Whenever veterinarians updating belief efficiently, veterinarian's optimal probabilistic estimates and Bayesian posteriors are consistent. In symmetric incentive context, people may not use information efficiently in the sense that updated probabilistic beliefs do not follow Bayes' theorem. Figure 11 and Figure 12 provide schematics of two dominant biases: underinference and base rate neglect biases respectively. Note that solid red arrows indicate Bayesian posteriors while dashed purple arrows indicate biased posteriors.

Figure 11 Underinference bias

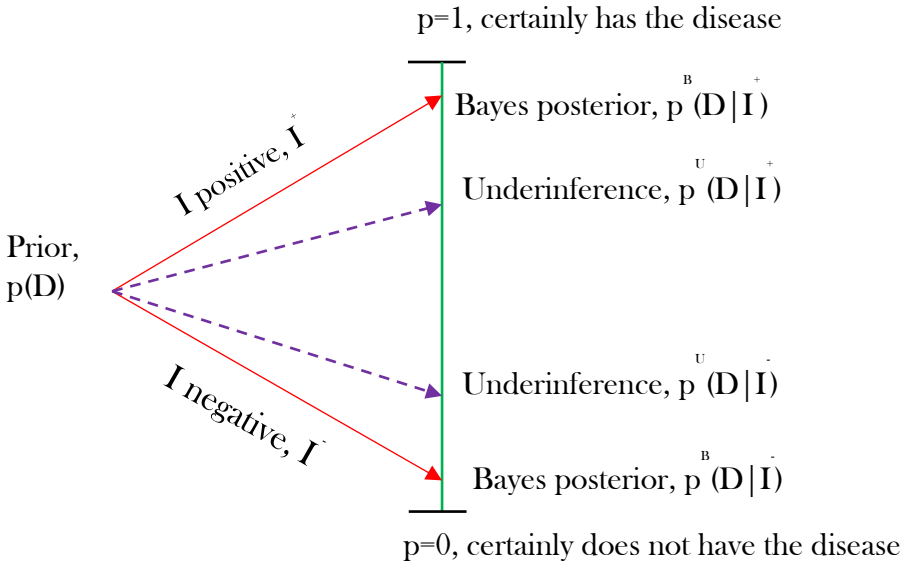
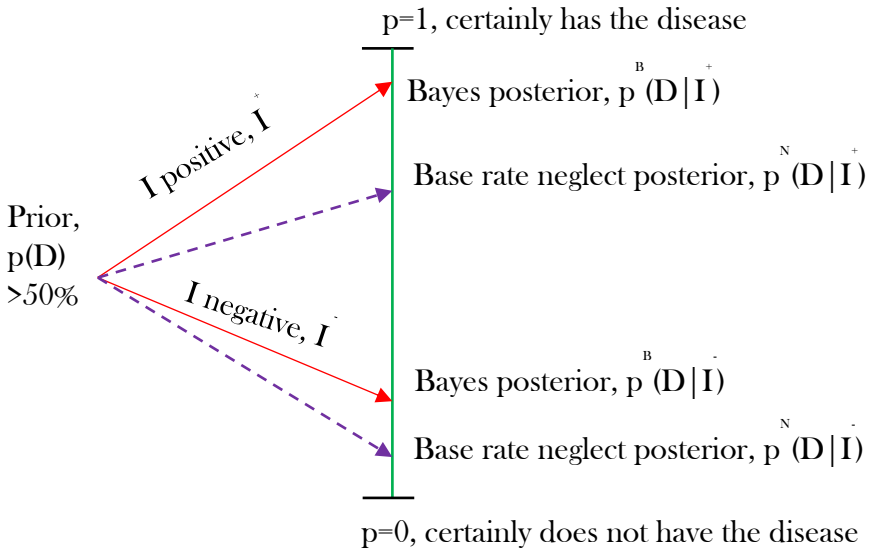


Figure 12 Base rate neglect bias



Underinference bias describes situations where people treat new information as if it is less informative (Dave and Wolfe 2003; Ambuehl and Li 2018; Phillips and Edwards 1966). Therefore probability update revisions are smaller than those implied by Bayes' theorem; insufficiently upward at some $p^C(D|I^+)$ when probability increasing signals are received and insufficiently downward at some $p^C(D|I^-)$ when probability decreasing signals are received. For example, in a suspected case where veterinarians initially believe that the animal has the disease, veterinarians with underinference bias may insist on their initial judgment even though new test results suggest disease-free.

Base rate neglect bias defines phenomena where people put less weight on priors than they should as prescribed by Bayes' theorem (Grether 1992; Griffin and Tversky 1992; Bar-Hillel 1980; Holt and Smith 2009). When veterinarians initially believe that the animal is likely to have the disease (i.e., with prior above 50%), base rate neglect bias results in posterior underestimates compared with Bayesian posteriors; in contrast, when they initially believe that the animal is not likely to have the disease (i.e., with prior less than 50%), base rate neglect bias results in posterior overestimates. For example, consider a situation where one cow has a history of mastitis and severe udder inflammation, and another cow has neither disease history nor inflammation. According to evidence before tests signals, the former cow is very likely to have recurrent mastitis while we do not have reason to believe that the latter cow has mastitis. Given that both tested positive, the likelihood of the former cow having mastitis should exceed the latter. Veterinarians who completely neglect priors estimate equal posteriors for both cows. In that case, veterinarians underestimate the likelihood that the first cow has the disease and overestimate the likelihood that the second cow does.

To identify probabilistic belief updating biases in veterinarians' diagnostic decisions, we will apply a conceptual framework introduced by Grether (1980). The posterior odds in favor of the animal having disease against the animal not having the disease can be modeled as

$$\frac{\pi(D \mid I)}{\pi(ND \mid I)} = e^{\alpha}\left[\frac{p(I \mid D)}{p(I \mid ND)}\right]^{c}\left[\frac{p(D)}{p(ND)}\right]^{d} e^{\varepsilon}, \tag{2.8}$$

where $p(I \mid D) / p(I \mid ND)$ is the likelihood ratio of observing I under alternative true states, $p(D) / p(ND)$ is prior odds in favor of the cow having the disease, and ε is a random variable with mean zero and finite variance. When $\alpha = 0$, $c = 1$, $d = 1$, $\varepsilon = 0$, then formula (2.8) converges to the standard Bayes' theorem formula. The biases caused by inappropriate use of priors or test results during probabilistic belief updating have been well-documented in the literature (Benjamin 2019). Parameters c and d measure, respectively, the magnitudes of these biases. When d is less than one, then people put less weight on priors than Bayes' theorem prescribed (depicted in Figure 12, defined as base rate neglect bias); on the contrary, when d exceeds one then people put more weight on priors, an inference that is very rarely made in empirical findings (Grether 1992). When c is less than one, then people treat test results as if they are less informative (depicted in Figure 11, defined as underinference bias); conversely, when c exceeds one then people over infer from test information (Griffin and Tversky 1992; Grether 1992; Ambuehl and Li 2018; Charness and Dave 2017; Peterson and Miller 1965). Note that inappropriate use of priors and test results can both occur in the same observation. Table 3 lists all possible combinations of parameters c and d.

Table 3 Summary of biases

	$c<1$ (dominant bias)	$c=1$	$c>1$
$d<1$ (dominant bias)	Base-rate neglect; underinference	Base-rate neglect	Base-rate neglect; overinference
$d=1$	underinference	Standard Bayesian updating	Overinference
$d>1$	Base-rate over-use; underinference	Base-rate over-use	Base-rate over-use; overinference

We can derive estimable equation (2.9) from equation (2.8).

$$\ln\left[\frac{\pi(D\mid I)}{\pi(ND\mid I)}\right]=\alpha+c\ln\left[\frac{p(I\mid D)}{p(I\mid ND)}\right]+d\ln\left[\frac{p(D)}{p(ND)}\right]+\varepsilon. \tag{2.9}$$

Therefore, we intend to test hypothesis below in veterinary diagnosis setting.

Hypothesis I (Bayesian updating): $c=1$ & $d=1$.

Hypothesis I assumes that veterinarians manage information following Bayes' theorem. As mentioned above, underinference bias ($c<1$) and base rate neglect bias ($d<1$) are dominate in the literature (Benjamin 2019). Therefore, we may reject the null hypothesis with $c<1$ and $d<1$ in diagnosis decision making experiments as well. If there were evidence for underinference bias, our experiment data allow us to make novel empirical inquiries about where underinference bias comes from. In experiments with a single signal (e.g., perform a single test to reveal new information in our setting), conservatism and extreme belief aversion are two leading theories to explain underinference bias. Conservatism refers to the actual information managing process where people underweight the likelihood ratio. In psychological literature, conservatism is assumed to be caused by difficulties in aggregating different sources of information (Slovic and Lichtenstein 1971). Another explanation for conservatism is that humans don't fully trust the new information they receive (Corner, Harris and Hahn 2010). That is, a less reliable information source would trigger more conservative belief revision and posterior beliefs deviating from standard Bayesian update results. Extreme belief aversion refers to an aversion to holding or

expressing probabilistic beliefs that are close to certainty (Benjamin, Rabin and Raymond 2016, sec.Appendix C). People with extreme belief aversion would report belief $\pi < p$ (respectively, $\pi > p$) when a true probability p is sufficiently close to one (respectively, 0); i.e., they tend to distort toward less extreme posteriors.

In addition to underinference ($c < 1$) or overinference ($c > 1$) summarized above, parameter c may vary with context. Prior-biased inference is a phenomenon whereby people use new information differently based on whether the new information weakens or reinforces priors. Some researchers have found stronger inference in response to information that reinforces priors compared to information that weakens priors (defined as "confirmatory bias") (Pitz, Downing and Reinhold 1967; Scott Geller and Pitz 1968; Pitz 1969; Charness and Dave 2017). Ducharme and Peterson (1968) disagree, finding instead that updating is stronger in response to information that weakens priors. Researchers do not find prior-biased inferences in some experiments (Möbius et al. 2022; Eil and Rao 2011). In order to test for prior-biased inferences, we interact the *log likelihood ratio* with $ConfT$, a dummy variable indicating whether the test result confirms priors or not. Consider the specificaiton and hypothesis below.

$$\ln\left[\frac{\pi(D\,|\,I)}{\pi(ND\,|\,I)}\right] = \alpha + c\ln\left[\frac{p(I\,|\,D)}{p(I\,|\,ND)}\right] + d\ln\left[\frac{p(D)}{p(ND)}\right] + \Delta c_1 \ln\left[\frac{p(I\,|\,D)}{p(I\,|\,ND)}\right] * ConfT + \varepsilon. \quad (2.10)$$

Hypothesis II (Prior-neutral inference): $\Delta c_1 = 0$;

Hypothesis II assumes that veterinarians respond to new information that is consistent with priors in the same way as to new information that contrasts to priors. When veterinarians have confirmatory bias, we expect the coefficient of the interaction to be significantly positive; conversely, when veterinarians respond more strongly to test information that weakens priors, we

expect the coefficient to be significantly negative. Suppose there are no prior-biased inferences. The estimate of Δc_1 should be insignificantly different from zero.

Preference-biased inference is a phenomenon where people update asymmetrically when receiving good news compared with bad news. The empirical findings are mixed: Some argue that people place more weight on good news than bad news (Möbius et al. 2021; Eil and Rao 2011), while some experimental evidence supports the opposite conclusion (Ertac 2011). Other studies finding no evidence for preference-biased inference (Barron 2021; Gotthard-Real 2017; Buser, Gerhards and van der Weele 2018; Coutts 2019). To examine whether veterinarians perform preference-biased inferences, we generate a dummy variable $Goodnews$ to indicate whether the animal tested negative and interact the dummy with the *log likelihood ratio*. Consider the specification and hypothesis are as follows.

$$\ln\left[\frac{\pi(D|I)}{\pi(ND|I)}\right] = \alpha + c\ln\left[\frac{p(I|D)}{p(I|ND)}\right] + d\ln\left[\frac{p(D)}{p(ND)}\right] + \Delta c_2 \ln\left[\frac{p(I|D)}{p(I|ND)}\right] * Goodnews + \varepsilon. \quad (2.11)$$

Hypothesis III (Preference-neutral inference): $\Delta c_2 = 0$.

Hypothesis III assumes that veterinarians do not have prior-biased inferences. When veterinarians update their beliefs more after receiving good news, then we expect the coefficient of the interaction to be significantly positive. Conversely when veterinarians update more after receiving bad news, then the coefficient should be significantly negative. When the coefficient is estimated to be insignificantly different from zero, we do not find evidence for preference-biased inference.

2.2.2. TREATMENT DECISIONS

When making treatment decisions, veterinarians need to assess benefits and costs of treatment alternatives based on their diagnoses. Veterinarians are assumed to choose the treatment alternative that maximizes utilities. The treatment behavior is modeled as a discrete choice model

whereby the utility of veterinarian n for an treatment alternative j in a suspected disease case i is specified as

$$U_{ijn} = \gamma_{ijn} X_{ijn} + \varepsilon_{ijn}, \tag{2.12}$$

where X_{ijn} are observed variables pertaining to treatment alternatives, context and decision maker, γ_{ijn} are coefficients of these variables representing preferences towards these variables and the ε_{ijn} are i.i.d. and follow an extreme value distribution.

Veterinarian n choosing treatment alternative j in a suspected disease case i depends on whether treatment alternative j brings utility greater than any other treatment alternatives. Therefore the choice can be defined as

$$y_{ijn} = 1[U_{ijn} > U_{ikn} \ \forall k \neq j], \tag{2.13}$$

where $1[\bullet]$ is a indication function. Whenever $U_{ijn} > U_{ikn} \ \forall k \neq j$, y_{ijn} euqals one,suggesting treatment alternative j is chosen. Ohterwise y_{ijn} euqals zero,suggesting treatment alternative j is not chosen. In multinomial logit model, the probability of choosing treatment alternative j can be written as

$$P_{ijn} = \frac{\exp(V_{ijn})}{\sum_{k=1}^{J} \exp(V_{ikn})}, \tag{2.14}$$

where there are J treatment alternatives in the choice set. We apply the mixed logit model to analyze discrete choice data on treatment decisions since mixed logit model allows for heterogeneous preference among veterinarians and accommodates the panel nature of the data. That is, coefficients γ can vary across individuals. We assume γ are random variables with density function $f(\gamma | \xi)$, where ξ are parameters characterizing the density function. Therefore the probability of choosing treatment alternative j can be revised on the basis of (2.14).

$$P_{ijn} = \int \frac{\exp(V_{ijn}(\gamma))}{\sum_{k=1}^{J} \exp(V_{ikn}(\gamma))} f(\gamma \mid \xi) d\gamma. \tag{2.15}$$

The log-likelihood function is

$$L = \sum_{n=1}^{N} \sum_{j=1}^{J} y_{ijn} \ln(P_{ijn}). \tag{2.16}$$

The vector X_{ijn} can include treatment alternative attributes x_{ij}, disease management context variables z_i, veterinarian characteristics ω_n and even any functions of these factors $\Phi(x_{ij}, z_i, \omega_n)$. Specifically, treatment alternative attributes consist of treatment costs, cure rate and benefits from treatment whenever the treatment cures diseases. Treatment costs comprise treatment expenditure and potential to increase antibiotic resistance. Veterinarians are responsible for serving healthcare needs of animals and working to protect public health. In disease cases that require antibiotic treatment, antibiotic treatment poses a private cost to livestock producers as well as potentially accelerates antibiotic resistance development and so causes a risk to public health. Therefore the potential to increase antibiotic resistance is a social cost component that may affect veterinarian's utility. It is naturally to consider main effect of treatment costs and so include treatment cost variables in the utility function.

We introduce outcome uncertainty associated with treatment, i.e., treatment may be a cure for the disease or it may not. The cure rate measures the extent of uncertainty. How individuals process the information about uncertainty in discrete choice problems is inconclusive. Extant studies explore various approaches to incorporate outcome uncertainty into utility function form (Williams and Rolfe 2017; Rolfe and Windle 2015). The utility may be determined by expected benefits/losses, i.e., including interactions between outcome uncertainty and benefits/losses associated with the realized outcome. In order to capture the direct utility of outcome uncertainty,

utility function can also introduce stand-alone uncertainty variables. In addition to weighing outcomes linearly by outcome uncertainty (i.e., expected benefits/losses), researchers examine utility functions including outcome non-linearly weighted by probabilities (e.g., include quadratics of expected benefits/losses) (Rolfe and Windle 2015; Williams and Rolfe 2017). Therefore we will examine different utility forms and let data decide the utility function form that most relevant.

Whenever the treatment cures the disease, then benefits include economic loss avoided and animal welfare improvement. Taking a mastitis case on dairy farms as an example, effective antibiotic treatment may prevent the disease from progressing, the infected cow being culled, and the infection spreading to other cows. Therefore economic loss avoided includes reduced cost due to disease control for a given cow and to the prevention of infection spread. Effective antibiotic treatment also relieves suffering and so improves animal welfare. As these benefits occur whenever treatment cures the disease, the assumptions on how veterinarians process the information about outcome uncertainty also determine the way these benefits affect utility. We consider the utility function with interactions of the benefits and cure rate and assume that expected benefits affect treatment decisions. Alternatively, we will also explore utility forms with standalone benefits variables and with nonlinear function of expected benefits (e.g., quadratic).

We also take disease management context into account in treatment decisions. The effect of context in discrete choices has been documented in other fields of research (Molin and Timmermans 2010; Charoniti et al. 2017; Wakefield and Inman 2003; Ariely and Levav 2000), however we are unaware of a literature pertaining to medical decisions. Likelihood that the animal has disease (we called "*disease likelihood*" thereafter) is a key factor in antibiotic recommendation decisions: when a veterinarian believes that the animal is unlikely to have a curable infection, she may decide to apply no antibiotic treatment, whereas when she believes that the animal is likely to have a curable infection, then she may decide to use antibiotics. In that case, *disease likelihood*

biased estimate will divert antibiotic treatment recommendations from optimal usage. In order to estimate the effect of *disease likelihood*, we need to interact *disease likelihood* with alternative attributes. Significant coefficients for these interactions would indicate that the utility attached to the attributes varies across different levels of *disease likelihood.*

In modeling of treatment decisions, we focus on understanding how the context variable *disease likelihood* can affect veterinarians' utilities and treatment choices. Connecting the conceptual framework, we intend to analyze the impact of biases in diagnosis decisions on subsequent antibiotic recommendations.

2.3. METHOD AND SURVEY DESIGN

During November 2020-April 2021, a web survey about animal disease management decisions was sent to veterinarians in practice in the United States through veterinary associations as well as a first-party data provider named Dynata. While our main interest lies in veterinarians' disease management on livestock farms, we recruited veterinarians who specialize in i) large animal health or who specialize in ii) companion animal health. The comparisons between large and small animal disease management may help us to understand common factors influencing diagnosis and treatment decisions and, more importantly, the distinctions that matter between how farmed animals and companion animals are treated. In order to accommodate differences in large and small animal clinical practice, we prepared distinct survey instruments for these two groups of veterinarians. We introduce the large animal disease survey instrument as an example below[7].

The survey proceeds in four sections. Section A presents ten simulated cases, giving priors and test information, and asks for probability belief estimates. Section B presents six simulated cases, giving information about treatment alternatives and diagnoses, and asks for preferred treatment

[7] We provide a survey sample in Appendix D.

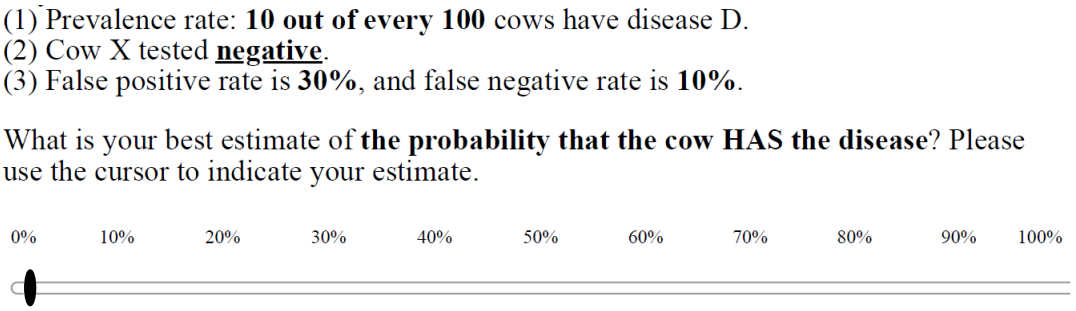
options. Section C collects ancillary information on veterinarians' views about test reliability, as well as on antibiotic resistance issues and animal welfare perspectives. Section D inquires about demographics, education, and work experience. Before being formally launched, the survey underwent two rounds of pre-tests by several graduate students in the Doctor of Veterinary Medicine program at Michigan State University.

2.3.1. DESIGN OF SECTION A

We set up diagnosis cases without specifying the disease but only describing some disease characteristics as follows: "There is a disease (named "disease D") that is circulating on dairy farms in a locality. At the early stages of disease D, there are no clinical signs, while severe signs appear as disease D progresses. In order to manage disease D, it's important to detect disease D at early stages". In the context of a hypothetical disease, veterinarians must make diagnoses relying on information given in each case instead of pre-existing experience. Thus we can observe information processing behavior with less disturbance.

At the early stages of disease D without clinical signs, prevalence rates among populations establish priors for veterinarians. A randomly selected cow was tested positive or negative. While tests can provide wrong information, they can add new evidence for diagnoses. False positive rates and False negative rates describe the accuracy of test information. A false negative (positive) rate is the probability of receiving a negative (positive) result when the cow does (does not) have disease D. Veterinarians are asked to assess the probability that the cow has disease D given prevalence rate, test result, and test information accuracy. Figure 13 shows an example question in section A.

Figure 13 Example question in section A



We generate 40 diagnosis cases which differ in terms of three factors: prevalence rate, test result, false positive rate. The prevalence rate is chosen from {10%, 30%, 50%, 70%, 90%}, and test result can be positive or negative. The false positive rate is chosen from {5%,10%, 20%, 30%}. We assume the false negative rate to be 10% and constant across diagnosis cases using orthorgonal design. Were the false negative rate allow to variant then orthorgonal design would produce many more diagnosis cases and so would require a larger sample size to achieve desirable statistical power. To reduce the cognitive load placed on veterinarians, we blocked these diagnosis cases into four blocks and randomly present one block of diagnosis cases (10 diagnosis cases) to each veterinarian. Within each block, these diagnosis cases are in 5 pairs. Questions within a pair present the same information except for test result. That is, in each pair of diagnosis cases, one test result is positive and another test result is negative, while other information given is the same. On each screen, veterinarians answer a pair of diagnosis cases. To address concerns about any order effect (Rottman 2017), we randomize the order of 5 pairs of diagnosis cases as well as the order of questions within each pair.

At the end of section A, a confirmation question appears whenever respondents' choices are illogical (Hammitt and Herrera-Araujo 2018). In any pair of diagnosis cases, if respondents' estimates given negative test results exceed their estimates given positive test results, then a confirmation question was displayed asking whether respondents would like to modify their initial

estimates. If they chose "Yes, I would like to revise my initial estimates", then the pair(s) of questions with their initial estimates were be presented to modify; otherwise, the survey proceeded to the next section.

2.3.2. DESIGN OF SECTION B

We present treatment choice questions in the context of suspected mastitis cases on dairy farms. In a suspected mastitis case, we introduce *disease likelihood* as a context variable which is measured by the probability that the cow has mastitis (e.g., 60%). Respondents have two treatment options which differ across five attributes: treatment cost, potential to increase antibiotic resistance, the cure rate of mastitis after treatment, and benefits associated with a cure. The benefits consists of animal welfare improvement and economic loss avoided. We provide a "No treatment" option so that they can also choose not to treat the cow. We make two assumptions. First, the withdrawal times for the treatment options are the same. Second, if the cow does not have mastitis, the signs observed will disappear themselves and treatment provides no benefit. Figure 14 shows an example question in section B.

Figure 14 Example question in Section B

You believe the cow has mastitis with probability 60%. If the cow has mastitis, treatment options can provide some benefits; otherwise, treatment options provide no benefit.

Which treatment do you prefer? Please check one.
(T1= Treatment 1, T2= Treatment 2, NT= No treatment)

	T1	T2	NT
Treatment cost	$140	$200	$0
Potential to increase antibiotic resistance	None	Low	None
Cure rate of mastitis *Note: You believe the cow has mastitis with probability 60%*	80%	100%	0
If the cow is cured, animal welfare improvement	High	Low	None
If the cow is cured, loss avoided	$450	$650	$0

Disease likelihood and treatment choice set varies across treatment choice questions. To embed a context variable into the discrete choice experiment design, we use a two-step approach similar to that in Molin and Timmermans (2010). First, we generate a regular discrete choice

experiment using the five attributes associated with treatment alternatives specified above. D-optimal experiment design generates 24 choice sets where treatment cost, the mastitis cure rate, animal welfare improvement, loss avoided, and potential to increase antibiotic resistance varied across choice sets. In the second step, instead of generating a set of context descriptions and nesting the choice set derived from the first experiment under each context description (Molin and Timmermans 2010), we randomly select *disease likelihood* level from {10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%} for each choice set and for each respondent. The adjustment sustains that context descriptions are independent of attribute profiles. We consulted veterinarians about reasonable levels for attributes and Table 4 lists attributes and context variable *disease likelihood* and the levels varied in the experiment.

Table 4 Attributes and context variables and levels used in the discrete choice experiment

Variables	Levels
Attributes	
Treatment cost	$20, $80, $140, $200
Potential to increase antibiotic resistance	None, Low, High
Cure rate	20%, 50%, 80%, 100%
Animal welfare improvement	Low, High
Economic loss avoided	$250, $450, $650, $850
Context variables	
Disease likelihood	From 10% to 100% in increments of 10%

The treatment cost is chosen from {$20, $80, $140, $200}, and the potential to increase antibiotic resistance can be none, low or high. The cure rate of mastitis is chosen from {20%, 50%, 80%, 100%}, and animal welfare improvement can be low or high. The economic loss avoided is chosen from {$250, $450, $650, $850}.

In order to reduce the cognitive load placed on respondents, we block 24 discrete choice questions into 4 blocks. Therefore each respondent is randomly presented with six treatment decision-making cases. Also, the order of the six cases is random within a block.

2.3.3. INCENTIVES FOR RESPONDENTS

We made a $30 completion payment to each qualified respondent. In addition, veterinarians can be rewarded with an additional $30 based on their answers in one diagnosis case that is drawn randomly from all diagnosis cases in Section A (called "the selected case"). In order to incentivize veterinarians to form probabilistic estimates with care and report their estimate truthfully, we applied an incentive-compatible belief elicitation approach named binarized scoring rules (Hossain and Okui 2013). Compared with elicitation approaches that assume risk neutrality, such as quadratic scoring rule and outcome matching approaches (Trautmann and van de Kuilen 2015), binarized scoring rule allows deviations from risk neutrality. We explicitly state that reporting true belief maximizes the probability of winning the additional $30. However we do not include quantitative information about binarized scoring rule, such as how their answers determine the probability of winning, in the survey instruction. This is because Danz et al. (Danz, Vesterlund and Wilson 2020) found that instructions without quantitive information outperform instructions with the information (Danz et al. 2020). We provide a link to the detailed payment rule for curious respondents[8].

2.4. DATA AND SUMMARY STATISTICS

We received 241 complete qualified responses, of which 119 are to the large animal disease management version, and 122 are to the small animal disease management version. To put these numbers in perspective, there are 75,349 veterinarians in private clinical practice in the United

[8] We provide payment rule detailed explanation in Appendix D.

States. Among these practicing U.S. veterinarians, about 75% specialize in companion animal diseases exclusively or predominantly and only 5.6% specialize in food animal disease exclusively or predominantly (American Veterinary Medical Association 2021). However, we recruit comparable sample sizes from large and small animal veterinarian populations since we are interested in comparing disease management decisions across practice areas. Table 5 summarizes some sample descriptive statistics.

Table 5 Mean (standard deviations) values of demographic and attitudinal characteristics of small and large animal veterinarian sample

	Large animal vets (total obs=119)	Small animal vets (total obs=122)	Total
Age	42.50 (13.94)	52.12 (10.19)	47.37 (13.09)
Working Experience	14.67 (11.17)	23.21 (7.35)	19.00 (10.34)
Female	0.47 (0.50)	0.59 (0.49)	0.53 (0.50)
Importance of animal welfare [0-100 scale: higher number means higher importance]	84.34 (15.20)	83.45 (16.21)	83.89 (15.69)
Acceptance of antibiotic usage [0-100 scale: higher number means higher acceptance]	65.72 (19.09)	81.57 (17.72)	73.75 (20.01)

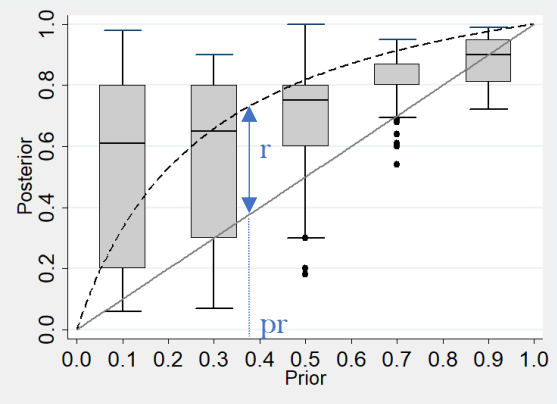
Mean age is 43 and 52 for large and small animal veterinarians respectively. Consistently, average age is 44.3 among veterinarian population (USA Data 2019). Average work experience among the large animal veterinarian sample is 8 years lower than that among small animal veterinarians sample. Consistent with the fact that male are majorities in large animal veterinarians while more than half of small animal veterinarians are female (American Veterinary Medical Association 2021), the percentages of female veterinarians are 46% and 59% in our corresponding

sub-sample.[9] We observe minor differences in the importance placed on animal welfare across veterinarian groups. Small animal veterinarians report higher acceptance of antibiotic usage in practice compared with large animal veterinarians.

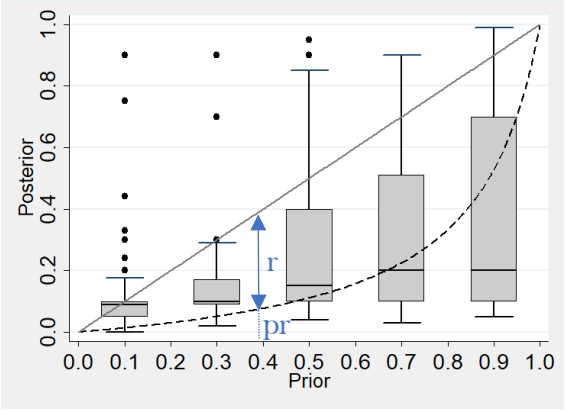
Given false positive rate is 20% and false negative rate is 10%, Figure 15 depicts differences between Bayesian posteriors and veterinarians' posteriors across prevalence rates. Fixed priors at 50%, Figure 16 illustrates a comparison between Bayesian posteriors and veterinarians' posteriors across test information accuracy (i.e., false positive rate in our setting).

Figure 15 Comparison between Bayesian posteriors and veterinarians' posterior across priors

a. With positive test result



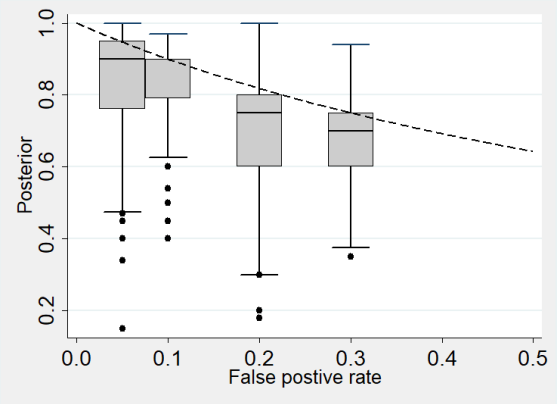
b. With negative test result



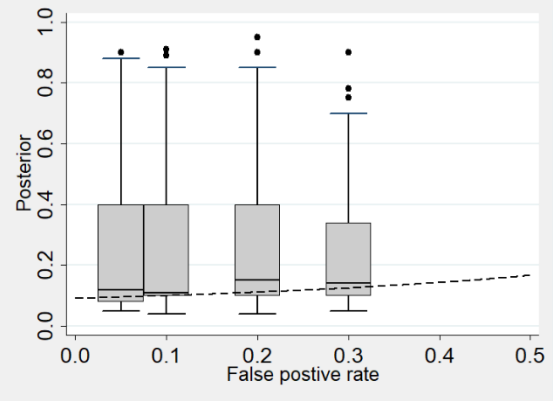
[9] Large animal practice may place high demands on physical strength. Our recruitment numbers are consistent with the prevalence of younger males in large animal practice (Wang, Hennessy and Park 2016).

Figure 16 Comparison between Bayesian posteriors and veterinarians' posteriors across test information accuracy

a. With positive test result



b. With negative test result



Dashed lines in Figure 15 illustrate that Bayesian posteriors increase non-linearly as prevalence rates increase. Solid lines depict the 45º bisector that would result were test information ignored. The probabilistic revision in response to new test information can be annotated as "r" given prevalence rate "pr". The revision decreases as the prior moves from a moderate level towards two extremes, i.e., zero and one. This is because a moderate prior contains less information when compared with an extreme prior. The same test result brings a larger information shock to the respondents with moderate prior and therefore induces a larger revision. That explains the concave Bayesian posteriors line in Figure 15.a and the convex Bayesian posteriors line in Figure 15.b.

The box and whisker plots show statistics of probability estimates by veterinarians. The discrepancies between veterinarians' posteriors and Bayesian posteriors vary. In Figure 15, when priors are close to zero then median veterinarians' posteriors exceed Bayesian posteriors, while when priors are close to one then median veterinarians' posteriors are less than Bayesian posteriors. This is consistent with base rate neglect bias as depicted in Figure 12. In both Figure 16.a and Figure 16.b, after receiving test results, veterinarians' revisions are less than prescribed by

Bayes' theorem. This finding suggests that veterinarians may underuse information from test results, as depicted in Figure 11.

2.5. EMPIRICAL RESULTS

2.5.1. EMPIRICAL RESULTS REGARDING DIAGNOSIS DECISIONS

In this section, we will first test three hypotheses proposed in section 2.1, then investigate the heterogeneity in belief updating across veterinarian characteristics and finally do robustness check.

2.5.1.1. Underinference and base rate neglect

Recall the estimable equation (2.9) which summarizes the biases of probabilistic updating biases (Grether 1980). The dependent variable *log posterior odds*, $\ln[\pi(D|I)/\pi(ND|I)]$, can be calculated using $\ln[p_v/(1-p_v)]$, where p_v values are respondents' estimates in each diagnosis case. The first independent variable *log likelihood ratio of observing I,* $\ln[p(I|D)/p(I|ND)]$, is a function of test accuracy (i.e., false positive rate fp and false negative rate fn). Whenever the test result is positive, the *log likelihood ratio of observing I* equals $\ln[(1-fn)/fp]$; conversely, the log likelihood ratio equals $\ln[fn/(1-fp)]$ whenever the test result is negative. The second independent variable *log prior odds,* $\ln[p(D)/p(ND)]$ can be calculated using $\ln(p_{pre}/1-p_{pre})$, where p_{pre} is the prevalence rate in each diagnosis case. Column (1) in Table 6 shows the regression result of the baseline model.

Table 6 Underinference and base rate neglect in diagnosis decisions

	(1) Baseline model	(2) Allow heterogeneity across posteriors and test accuracy
Log prior odds	0.447***	0.137
	[0.410,0.484]	[-0.177,0.450]
Log likelihood ratio	0.718***	0.499***
	[0.694,0.741]	[0.189,0.809]
Extreme posteriors # Log prior odds		0.373**
		[0.058,0.688]
Extreme posteriors # Log likelihood ratio		0.213
		[-0.095,0.521]
fp=0.05 # Log likelihood ratio		-0.031
		[-0.103,0.040]
fp=0.1 # Log likelihood ratio		-0.024
		[-0.099,0.051]
fp=0.2 # Log likelihood ratio		-0.033
		[-0.113,0.048]
Constant	0.340	0.364
	[-0.388,1.067]	[-0.336,1.064]
Individual Fixed Effects	Yes	Yes
Observations	2396	2396

Notes: (1) 95% confidence intervals in square brackets
(2) * p<0.05, ** p<0.01, *** p<0.001

The coefficient estimate of *log likelihood ratio* $\hat{c}$ and coefficient estimate of *log prior odds* $\hat{d}$ are 0.718 and 0.447 respectively, which do not deviate too much from estimates in extant experiment evidence. In a meta-analysis of incentivized experiments, mean $\hat{c}$ is found to be 0.86 and the standard error is 0.078; mean $\hat{d}$ is 0.434 and the standard error is 0.086 (Benjamin 2019). T-test rejects the null hypothesis H_0 that $c = d = 1$ at 1% level. The regression result shows that veterinarians' belief updating treats the test information as if it is less informative and put less weight on priors than Bayes' theorem suggests should be the case. In other words, we find

evidence for underinference bias and base rate neglect bias in veterinarians' diagnostic belief updating.

To provide some insights on which theory (conservatism or extreme belief aversion) is a more reasonable explanation for underinference bias in our setting, we investigate heterogeneity across posteriors. Dummy variable $ExtrmP$ indicates whether Bayesian posteriors in a diagnosis case are extreme. DuCharme (1970) found that when the log Bayesian posterior odds is between -1 and 1 people's posterior odds is virtually consistent with Bayesian posterior odds, while when Bayesian posterior odds is more extreme than 1 or -1 people's posterior odds are less extreme than Bayesian posteriors. Therefore we define $ExtrmP$ to be one whenever Bayesian posterior odds is between -1 and 1, and to be zero otherwise. We interact $ExtrmP$ with *log prior odds* as well as *log likelihood ratio* to allow heterogeneous updating processes in cases with and without extreme posteriors.

In addition, some argue that underinference is more severe when test information is more accurate (Benjamin 2019). Conservatism does not provide a clear reason for this tendency, while extreme belief aversion can explain the more severe underinference given more accurate test information. We investigate underinference across different test information accuracy. Dummy variables fp_1, fp_2, fp_3 indicate whether false positive rate is 5%, 10%, 20% respectively. For example, fp_1 equals one when false positive rate is 5%, equals zero otherwise. We interact of *log likelihood ratio* with fp_1, fp_2, and fp_3 to estimate the differences in underinference compared with baseline false positive rate 30%.

We jointly test heterogeneity across posteriors and across test accuracy. Were extreme belief aversion to play a role in the information processing, then we expect the coefficient of interactions

term to be significantly negative values. Conversely insignificant interaction coefficients support that conservatism is a more convincing explanation.

Column (2) in Table 6 provides the regression result. The interaction between *ExtrmP* and *log likelihood ratio* does not have a significant effect, suggesting that underinference parameter *c* does not vary across extreme posterior cases and non-extreme posterior cases. Surprisingly, the coefficient of interaction between *ExtrmP* and *log prior odds* is significantly positive, suggesting that veterinarians have more severe base rate neglect in cases without extreme Bayesian posteriors. The coefficient on interactions between test accuracy dummy variables and *log likelihood ratio* is not significant, suggesting that we do not have evidence supporting increased underinference severity due to increased test information accuracy. Therefore, we do not have evidence favoring extreme belief aversion theory. Hence,

Summary 1 Veterinarians underuse their initial beliefs and underinfer from the new test information in diagnoses. We have no evidence support that underinference bias varies across Bayesian posteriors and test accuracy. Therefore among the two main theories explaining why underinference exists, conservatism compared to extreme belief aversion theory is more likely to be a possible explanation in our setting.

2.5.1.2. Prior-biased inference and preference-biased inference

Following Charness and Dave (2017), we define *ConfT* in specification (2.10) as one when prevalence rate exceeds 0.5 and the test result is positive, or when prevalence rate is smaller than 0.5 and the test result is negative; otherwise, *ConfT* equals zero. In specification (2.11), *Goodnews* equals one whenever the animal tested negative, otherwise *Goodnews* equals zero. Column (1)-(2) in Table 7 presents empirical results regarding prior-biased inference and preference-biased inference.

Table 7 Prior-biased inference and preference-biased inference

	(1) Prior-biased inference	(2) Preference-biased inference	(3) Prior-biased inference across practice areas	(4) Preference-biased inference across practice areas
Log prior odds	0.407***	0.447***	0.254***	0.326***
	[0.347,0.466]	[0.410,0.485]	[0.169,0.339]	[0.273,0.378]
Log likelihood ratio	0.689***	0.727***	0.755***	0.770***
	[0.650,0.727]	[0.624,0.830]	[0.698,0.811]	[0.623,0.916]
Confirming test result * Log likelihood ratio	0.074*		0.132**	
	[-0.003,0.151]		[0.021,0.243]	
Good news * Log likelihood ratio		-0.018		0.075
		[-0.216,0.180]		[-0.208,0.359]
Small animal vets * Log prior odds			0.302***	0.242***
			[0.187,0.418]	[0.170,0.314]
Small animal vets * Log likelihood ratio			-0.132***	-0.096
			[-0.208,-0.057]	[-0.296,0.104]
Small animal vets with confirming test results * Log likelihood ratio			-0.113	
			[-0.264,0.038]	
Small animal vets with Good news * Log likelihood ratio				-0.162
				[-0.548,0.223]
Constant	0.329	0.323	0.297	0.220
	[-0.394,1.052]	[-0.429,1.075]	[-0.356,0.950]	[-0.483,0.922]
Individual Fixed Effects	Yes	Yes	Yes	Yes
Observations	2396	2396	2396	2396

Notes: (1) 95% confidence intervals in square brackets
(2) * p<0.05, ** p<0.01, *** p<0.001

Column (1) presents the result of specification (2.10). The interaction between confirming test results and *log likelihood ratio* has a significantly positive effect, suggesting that veterinarians have prior-biased inference. Veterinarians treat information that confirms their priors as if it is more informative compared with the test information that disconfirms priors. Column (2) presents the result of specification (2.11). The effect of interaction between good news and *log likelihood ratio* is not significant, suggesting that veterinarians do not have preference-biased inference. Veterinarians do not update asymmetrically in response to positive and negative test results. This is consistent with the argument that preference-biased inference may occur in ego-relevant belief updating while they may be absent in belief updating about external states (Barron 2021). Therefore,

Summary 2 We have evidence supporting prior-biased inferences. Veterinarians update their beliefs more strongly in response to new test information that is consistent with their initial beliefs than that contradicts their initial beliefs. We do not find evidence for preference-biased inferences in diagnoses.

2.5.1.3. Heterogeneity across veterinarian groups

We investigate heterogeneous updating across veterinarian groups. We create a dummy variable *SAV* to indicate whether veterinarians are specialized in small animal disease management. We add *SAV* and interactions between *SAV* and the two key variables (i.e., *log prior odds* and *log likelihood ratio*) on the basis of specification (2.9). We also allow heterogeneity across practice areas in terms of confirmatory bias. Column (3) in Table 7 shows the regression result. The coefficient of three-way interaction in column (3) is not significant. While for the whole sample we find evidence for confirmatory bias, the confirmatory bias is not significantly different between small and large animal veterinarians. In column (4), we investigate whether small and large animal veterinarians are heterogeneous in terms of preference bias. The findings show that we do

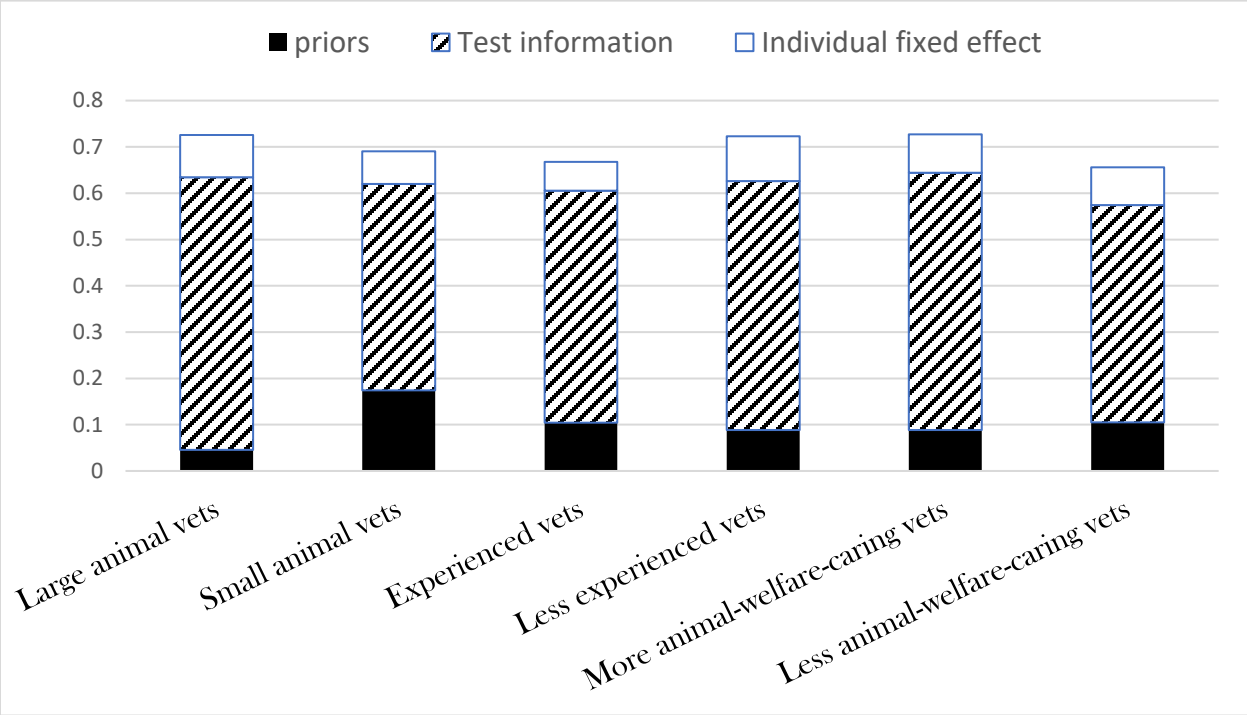
not have evidence for preference-biased inference for overall veterinarians and neither do we observe differences between small and large animal veterinarians in preference-biased inference.

Both large animal veterinarians and small animal veterinarians display underinference bias and base rate neglect bias. However, they are different in the extent of being biased. The main effects of *log prior odds* and *log likelihood ratio* are significantly less than unity. These two coefficients measure weights on priors and test information placed by large animal veterinarians. The coefficient on interaction between SAV and *log likelihood ratio* is significantly negative, suggesting that small animal veterinarians update less strongly in response to test information compared with large animal veterinarians. However, the interaction between SAV and *log prior odds* has a significant positive effect. This evidence illustrates that small animal veterinarians show less severe base rate neglect bias than do large animal veterinarians. The findings are robust when we allow heterogeneity across posteriors and test accuracy. See Table 11 in appendix B. Furthermore, while some two-way interactions that capture overall heterogeneity across posteriors and test accuracy are significant, three-way interactions in See Table 11 are insignificant. Therefore the regression results show that for the overall veterinarian sample we find evidence for heterogeneity across posteriors and test accuracy; however, the heterogeneity is not significantly different between small and large animal veterinarians.

In order to investigate heterogeneity in belief updating across veterinarian characteristics, we add to specification in Table 7 column (3) characteristic dummies $D(x_i)$ and their interactions with key explanatory variables (i.e., *log prior odds* and *log likelihood ratio*). See detailed explanations and regression results in appendix A1 and Table 13. Experienced veterinarians perform worse in managing priors and test information when compared with their less experienced colleagues. Small animal veterinarians make better use of priors but do update less in response to test information than do large animal veterinarians. Veterinarians who care more about animal

welfare have less underinference bias. We depicted the explanatory power of priors, test information and veterinarians' characteristics in Figure 17.

Figure 17 Decomposition of veterinarians' probabilistic estimates across veterinarian characteristics



We can see how variations in priors or test information can explain the variations in veterinarians' estimates. Across veterinarian populations, test information's total effects is greatest and account for more than 60% of all the explained information in veterinarians' estimates. Test information shows largest importance to small animal veterianrians's diagnosis while the importance of test information decreases in large animal veterinarian sample. Prior is ranked second or third in terms of determining veterinarians' diagnosis probability. Compared with test information, veterinarians, especially those specializing in large animal health, treat prior less important in diagnosis. To sum up,

Summary 3 Small animal veterinarians underinfer from test information more severely relative to large animal veterinarians, while small animal veterinarians show less severe base rate neglect

bias than do large animal veterinarians. More experienced veterinarians perform worse in managing priors and test information compared with their less experienced colleagues. Moreover, veterinarians who attach higher importance to animal welfare in their practice show less underinference bias.

Recall that we use a confirmation question to inform illogical estimates in diagnosis decisions and allow revisions of initial answers. Forty-six out of 241 respondents make illogical estimates and then 26 out of 46 respondents make revisions. We do robustness check robustness using revised data in appendix A2 and the findings remain largely unchanged.

2.5.2. EMPIRICAL RESULTS REGARDING TREATMENT DECISIONS

We applied mixed logit model to analyze veterinarian's treatment choices. We dummy code context variable *disease likelihood.* When veterinarians believe that the probability of the animal having disease is no more than 30%, *P(disease)_Low* equals one, otherwise *P(disease)_Low* equals zero. When veterinarians believe that the probability that the animal has the disease is greater than 30% but no more than 60% then *P(disease)_Medium* equals one, otherwise *P(disease)_Medium* equals zero. The baseline *disease likelihood* level is "greater than 60%". Note that we estimate the effect of disease likelihood by adding its interactions with alternative attributes.

Among attributes of treatment options, we treat *treatment cost*, *economic loss avoided,* and *cure rate* as continuous variables and denote them as *Cost, LossAvd,* and *CRate* respectively. Other attributes are treated as category variables. There are two approaches to handle category variables in discrete choice experiment literature: effects coding or dummy coding. Dummy coding creates *N-1* dummies for an attribute with *N* qualitative levels. Each dummy equals one whenever the qualitative level is present and equals zero otherwise. All dummies equal zeros for the reference qualitative level. Effect coding differs in coding reference qualitative level. For reference qualitative level, the *N-1* varibales equals -1 rather than 0. According to the discussion in Mariel et

al. (2021), effects coding is not superior to dummy coding but it makes results more complex to explain in our setting. Therefore we adopted dummy coding for the remaining attributes. For attribute *potential to increase antibiotic resistance*, we generate two dummies *AR_low* and *AR_high* and set them equal to one whenever the attribute level is "Low" and "High" respectively. Naturally the baseline level is "None". Regarding animal welfare improvement, *AW_high* indicates that the treatment achieves a high level of animal welfare improvement. Low level of animal welfare improvement is the corresponding baseline. Table 8 listed all attributes, the corresponding variables and expected effection direction. We expected attributes pertaining to cost: *Cost*, *AR_low,* and *AR_high* have negative impact on utilities, and attributes pertaining to benefits: *AW_high, LossAvd* and *CRate* increase utilities.

Table 8 Attributes, corresponding variables and expected effect directions.

Attribute	Variable	Expected effect direction
Treatment cost	*Cost*	-
Potential to increase antibiotic resistance	*AR_low*	-
	AR_high	-
Cure rate	*CRate*	+
Animal welfare improvement	*AW_high*	+
Economic loss avoided	*LossAvd*	+

First, we determine how veterinarians process treatment uncertainty in their treatment choices. That is, we need to decide whether: (1) attribute *cure rate* influence treatment choices; (2) expected benefits (i.e., interactions between *cure rate* and benefits) have significant explanatory power; (3) attribute *cure rate* should be treated nonlinearly; and (4) attribute *cure rate* has direct

disutility for veterinarians. Therefore we explore various possible utility function forms. Table 18 shows our multinomial logit (MNL) estimates.

Column (1) estimation excludes attribute *cure rate* and serves as a baseline model for the remaining column estimations. The underlying assumption is that attribute *cure rate* does not influence treatment decisions. Column (2) estimation assumes veterinarians use expected benefits to make treatment decisions and so includes interactions between *cure rate* and benefits (*LossAvd* and *AW_high*). In column (3) in addition to interaction, we add standalone *LossAvd* and *AW_high,* allowing benefits provide direct utilities that does not depend on uncertainty. In columns (4) and (5), we add quadratic of interactions between *cure rate* and benefits on the basis of column (2) and (3) to relax linear effect assumption on uncertainty. In Column (6)-(8), we add separate *cure rate* to allow uncertainty provide direct disutility on the basis of columns (1)-(3). According to AIC statistics, probabilistic attribute *cure rate* indeed have explanatory power for veterinarian's treatment choices. In addition, regression (8) results in smallest AIC, suggesting that the corresponding specification fit the data best. The coefficient of interaction between *cure rate* and *AW_high* is significantly positive, so is the coefficient of *cure rate*. This suggests that expected benefits increase veterinarians' utility. In addition, certainty of treatment (*cure rate*) can provide utility directly.

On the basis of specification (8), we apply mixed logit model to allow heterogeneous preferences across veterinarians. Table 9 shows the results of Monte Carlo Likelihood estimations with Halton draws.

Table 9 Mixed logit estimation: treatment utility as a function of treatment characteristics

	(1)	(2)	(3)	(4)
Cost	-0.005***	-0.004***	-0.004***	-0.004***
*Cost *P(disease)_Low*	-0.004***	-0.005***	-0.009***	-0.008***
*Cost *P(disease)_Medium*	-0.002	-0.002	-0.004***	-0.004***
AR_low	0.222	0.198	0.237	0.224
*AR_low *P(disease)_Low*	-0.357	-0.316	-0.388	-0.375
*AR_low * P(disease)_Medium*	-0.220	-0.208	-0.303	-0.291
AR_high	-1.347***	-1.432***	-1.291***	-1.332***
*AR_high * P(disease)_Low*	-0.137	-0.077	-0.452	-0.412
*AR_high * P(disease)_Medium*	-0.014	0.027	-0.122	-0.093
CRate	4.598***	4.440***	4.644***	4.624***
*CRate * P(disease)_Low*	-4.434***	-4.366***	-4.735***	-4.743***
*CRate * P(disease)_Medium*	-1.749***	-1.602***	-1.429**	-1.437***
AW_high	0.201	0.307	0.092	0.209
*AW_high * P(disease)_Low*	-0.030	-0.136	0.101	-0.025
*AW_high * P(disease)_Medium*	0.206	0.101	0.480	0.353
LossAvd	0.001	0.001***	0.002*	0.001***
*LossAvd * P(disease)_Low*	-0.003***	-0.003**	-0.004***	-0.004***
*LossAvd * P(disease)_Medium*	-0.000	-0.000	-0.000	-0.000
*CRate * AW_high*	1.163**	1.023*	1.251**	1.116**
*CRate * AW_high * P(disease)_Low*	-0.500	-0.303	-0.440	-0.287
*CRate * AW_high * P(disease)_Medium*	-1.009	-0.873	-1.344	-1.188
*CRate * LossAvd*	0.000	0.001***	-0.000	0.000
*CRate * LossAvd * P(disease)_Low*	0.002	0.001	0.004**	0.003**
*CRate * LossAvd * P(disease)_Medium*	-0.001	-0.001	-0.000	-0.001
Treat actively	0.112	0.201	0.525	0.552
variance(Cost)	0.001***	0.001***	0.355***	0.004***
variance(LossAvd)		0.000***		0.000
*variance(CRate * LossAvd)*		0.000**		0.000
variance(Treat actively)			2.255***	2.207***
Observations	4,338	4,338	4,338	4,338
Log lik.	-983.1	-980.4	-957.5	-958.4

As explanatory variables *treatment cost (Cost)*, *economic loss avoided (LossAvd)* and interactions between *cure rate* and *economic loss avoided* (*LossAvd* Crate*) have specific signs in MNL estimates, log-normal distributed is an appropriate choice (Mariel et al. 2021). Since the log-normal distribution coefficient is always positive but treatment cost have obvious negative effect on utilities, we multiply treatment cost by (-1) in column(1)-(4) estimation. In column (2), we

additionally assume log-normal distribution for coefficients of *LossAvd* and *LossAvd* CRate.* In the regressions, we include a dummy *treat actively* which equals one when veterinarians choose non-status quo alternatives, and equals zero when veterinarians choose no treatment options. In column (3), the coefficient of this dummy is assumed to be uniform distributed on the basis of column (1) specification. Column (4) assumes random parameters specified in both column (2) and (3) and is the most unrestrictive model estimated in Table 9. When we assume random parameters for other explanatory variables, the standard deviations are insignicant or the regression cannot converge due to data limitations. According to log likelihood statistics, column (3) model show better model fit than others.

To facilitate further interpretation, we write the specification in column (3) as following.

$$\begin{aligned} U = {} & \gamma_0 + \tilde{\gamma}_1 Cost + \tilde{\gamma}_2 AR\_low + \tilde{\gamma}_3 AR\_high + \tilde{\gamma}_4 CRate + \tilde{\gamma}_5 AW\_high + \tilde{\gamma}_6 LossAvd \\ & + \tilde{\gamma}_7 CRate * AW\_high + \tilde{\gamma}_8 CRate * LossAvd + \gamma_9 Treat\ actively + \varepsilon_{ijn}, \end{aligned} \tag{2.17}$$

where

$$\tilde{\gamma}_t = \gamma_t + \gamma_{t,low} P(disease)\_Low + \gamma_{t,medium} P(disease)\_medium \quad t = 1,2,...,8. \tag{2.18}$$

Note that the coefficient mean varies with the magnitude of disease likelihood. When the probability that the animal has the disease is low, the coefficient mean is $\gamma_i + \gamma_{i,low}$. When When the probability that the animal has the disease is medium, the coefficient mean is $\gamma_i + \gamma_{i,medium}$. When the probability of the animal has the disease is high, the coefficient mean is γ_i. The willingness to pay (WTP) for one unit improvement in attributes (excluding *treatment cost*) can be obtained by

$$WTP = -\frac{\tilde{\gamma}_t}{\tilde{\gamma}_1} \quad t = 2,...,8. \tag{2.19}$$

In Column (3), the treatment cost coefficient is significantly negative and its standard deviation is significant. This finding supports the view that the heterogeneity exists in veterinarian's

preferences about treatment cost. Unobserved factors may contribute to the heterogeneity, such as veterinarians' risk attitudes and clients average income. With more risk aversion and higher clients average income, veterinarians may attach less disutility to treatment cost. Furthermore, preference regarding treatment cost interacts with disease likelihood. As might be expected, the disutility of treatment cost is largest when disease likelihood is in the *P(disease)_Low* category, declines when disease likelihood is in the *P(disease)_Medium* category, and is smallest when veterinarians believes that the animal is very likely to have disease.

The cure rate coefficient is significantly positive. The effect of *cure rate* depends on context variable disease likelihood. When veterinarians make treatment decisions in the low disease likelihood context, *cure rate* provide smallest direct utility. When disease likelihood increases then the direct utility from cure rate increases. The *LossAvd* coefficient is significantly positive, while the interactions between *LossAvd* and *P(disease)_Low* is significantly negative. This suggests that when animals are very unlikely to have the disease then the utility from potential benefit associated with treatment is lower.

The other coefficient signs are reasonable. For instance, the *AR_high* coefficient is significantly negative. Compared with treatment alternatives that have no potential to increase antibiotic resistance, veterinarians are less likely to choose treatment alternatives that have high potential to increase antibiotic resistance. The coefficient of benefit variables, *AW_high* is positive. This is consistent with expectation that veterinarians are more likely to prescribe antibiotics when treatment comes with more benefits. Preferences pertaining to antibiotic resistance cost and animal welfare improvement are not sensitive to disease likelihood since the corresponding interactions coefficients are insignificant. Notably, the dummy *treat actively* coefficient is insignificant but its standard deviation is significant. Large heterogeneity among veterinarians exists in the preference of treating actively in suspected disease cases.

Once proved that disease likelihood affect treatment choices, we calculate the WTP for one unit improvement in attributes (excluding *treatment cost*) following formula (2.19). Table 10 shows the results. As mentioned above preferences associated with antibiotic resistance cost, animal welfare improvement and expected economic loss avoided do not interact with disease likelihood, we mainly focus on WTP for improvement in *cure rate* and *economic avoided*. The WTP for a *cure rate* increase depends on disease likelihood. The higher the probability that the animal has the disease, the higher value assigned to cure rate increase. Similarly, the WTP for a *economic loss avoided* increase increases as disease likelihood increases.

Table 10 Mean WTP estimates (in US dollars) in different disease likelihood situations

	Low disease likelihood (p<30%)	Medium disease likelihood (30%<p<60%)	High disease likelihood (p>60%)
AR_low	-11.62	-8.25	59.25
AR_high	-134.08	-176.63	-322.75
CRate	-7.00	401.88	1161.00
AW_high	14.85	71.50	23.00
LossAvd	-0.15	0.25	0.50
*CRate * AW_high*	62.38	-11.63	312.75
*CRate * LossAvd*	0.31	0.00	0.00

Summary 4 Veterinarians are less likely to use treatment alternatives that comes with higher treatment cost. Treatment cost disutility increases as disease likelihood increases. Treatment certainty provide separate utility directly. In addition, the directly utility decreases as the disease likelihood increases. Similarly, economic loss avoided associated with treatment has positive effects on utility and the effect reduces as disease likelihood increases. Veterinarian's preferences towards antibiotic resistance cost and animal welfare improvement do not depend on disease likelihood.

2.6. CONCLUSION

Doctors are usually not certain when making a diagnosis of a disease but make probabilistic assessments of the disease based on evidence available. How doctors make such probabilistic

assessment and how uncertain assessment affects treatment decisions are very important factors in efficient disease management which includes the efficient use of antibiotics. However, there is very limited study and understanding regarding diagnosis decision making when there is incomplete information. We study the issue with veterinarians' decision making. We model a diagnosis as a belief updating process whereby veterinarians form their initial probabilistic beliefs (priors) about animal health conditions based on initial inspections and revise their beliefs in response to test results (new information). The efficiency of information management by veterinarians directly affects the efficiency of antibiotic treatment prescription in subsequent steps.

In a survey to veterinarians in practice across the United States we asked for probabilistic assessments in stylized disease diagnosis settings. Instead of following Bayes' theorem, veterinarians deviate from efficient belief updating. Veterinarians make less use of priors and follow-up test information than prescribed by Bayes' theorem. These deviations have been documented in laboratory experiments, named base rate neglect bias and underinference bias respectively. In addition, veterinarians update their beliefs more strongly in response to test information that confirms their priors than test information that contradicts their priors.

Furthermore, we investigate the effect of diagnosis on veterinarian's treatment choices using discrete choice data collected in the survey. The findings support the view that diagnosis biases affect treatment choices. We define disease likelihood in treatment decisions as the posteriors in diagnosis decisions. Disease likelihood affects veterinarians preferences towards treatment attributes, such as treatment cost, cure rate and benefits. The findings that biases exist in diagnosis decisions and that diagnosis affects treatment choices jointly imply that antibiotic prescriptions based on biased diagnoses is likely to be inefficient.

Combining the findings that biases exist in diagnosis decisions and that diagnosis affect treatment choices, the veterinary oversight requirement as an approach to relying on veterinarians

for promoting judicious antibiotic use may fail to manage on-farm antibiotic consumption efficiently. Training programs for veterinarians to improve their information management capability may complement veterinary oversight requirement. To address heterogeneous updating biases across practice areas, training programs should vary. Since large animal veterinarians perform better in test information use but worse in the use of priors than small animal veterinarians, training should emphasize the importance of priors for large animal veterinarians but underline test information use for small animal veterinarians. Furthermore, our findings suggest recurrent training may promote efficiency of diagnosis and so antibiotic stewardship. This is because, and contrary to the evidence that experience improves information management (Camerer 1987), experienced veterinarians are found to deviate more from Bayes' rule in the use of priors and test information than do their less experienced colleagues.

APPENDICES

APPENDIX A

Additional text content

A1. BELIEF UPDATING BIASES ACROSS VETERINARIAN CHARACTERISTICS

Table 12 lists characteristic dummies including genders, work experience, and attitudes towards animal welfare and antibiotic usage. *Female* equals one whenever veterinarians choose "female" in the gender question, and equals 0 otherwise. *ExpVets* indicates veterinarian's experience. *ExpVets* equals one whenever a large (small) animal veterinarian's work year is greater than median work years among large (small) animal veterinarian sample, otherwise *ExpVets* is 0. *Welf* indicates veterinarian's view point about animal welfare. When a large (small) animal veterinarian attaches a higher importance to animal welfare than median level of importance among large (small) animal veterinarian sample, *Welf* is 1; otherwise *Welf* is 0. *Ant* represent the acceptance of antibiotic usage in their practice. When a large (small) animal veterinarian reports a higher acceptance of antibiotic usage than median level of acceptance among large (small) animal veterinarian sample, *Ant* is 1, otherwise *Ant* is 0.

Table 13 presents the regression results. Column (1) in Table 13 estimates specification considering heterogeneity across all characteristics using the whole sample, while columns (2) and (3) allow full heterogeneity as column (1) but using large and small animal veterinarian samples respectively. The interaction between *ExpVet* and *log likelihood ratio* is significantly negative across columns (1)-(3), suggesting that veterinarians with more practice experience have more severe underinference bias. In column (2) the interaction between *ExpVet* and *log likelihood ratio* has a significantly negative effect, suggesting that experienced large animal veterinarians place less weight on priors than do their less experienced counterparts. In column (3) the coefficient on the interaction of *Welf* and *log likelihood ratio* is significantly positive, suggesting that small animal veterinarians who attached high importance to animal welfare respond to test information more strongly than do those who report less importance. Columns (4)-(6) shows that findings in column (1)-(3) persist without characteristics that do not have significant coefficients in the full specification.

A2. ROBUSTNESS CHECKS FOR BELIEF UPDATING BIASES

In diagnosis cases where all information given is the same except test results, some veterinarians report higher probability estimates given negative test results than probability estimates given positive test results. We inform any veterinarians that make illogical estimates and ask whether they would like to revise their initial answers. Forty-six responses triggered confirmation questions and twenty-six respondents subsequently revised their initial estimates. Therefore, we updated with revised estimates for the fifteen respondents and kept the initial estimates for the five respondents who insisted on their initial estimates. Table 14-Table 17 show the regression results using revised data. The findings remain largely unchanged compared to when using initial data.

APPENDIX B

Tables for robustness check

Table 11 Belief updating heterogeneity across veterinary practice areas

	(1) Heterogeneity across posteriors	(2) Heterogeneity across test accuracy
Log prior odds	0.082	0.327***
	[-0.342,0.505]	[0.274,0.379]
Log likelihood ratio	0.650***	0.832***
	[0.244,1.057]	[0.745,0.919]
Small animal vets # Log prior odds	0.075	0.240***
	[-0.513,0.664]	[0.169,0.312]
Small animal vets # Log likelihood ratio	-0.387	-0.159***
	[-0.958,0.184]	[-0.278,-0.040]
Extreme posteriors # Log prior odds	0.330	
	[-0.096,0.755]	
Extreme posteriors # Log likelihood ratio	0.113	
	[-0.296,0.522]	
Small animal vets with extreme posteriors # Log prior odds	0.118	
	[-0.473,0.710]	
Small animal vets with extreme posteriors # Log likelihood ratio	0.237	
	[-0.337,0.812]	
fp=0.05 # Log likelihood ratio		-0.030
		[-0.133,0.073]
fp=0.1 # Log likelihood ratio		-0.065
		[-0.174,0.043]
fp=0.2 # Log likelihood ratio		0.028
		[-0.088,0.145]
Small animal vets with fp=0.05 # Log likelihood ratio		-0.045
		[-0.186,0.096]
Small animal vets with fp=0.1 # Log likelihood ratio		0.065
		[-0.082,0.213]

Table 11 (cont'd)

Small animal vets with fp=0.2 # Log likelihood ratio		-0.101
		[-0.260,0.058]
Constant	0.330	0.306
	[-0.299,0.959]	[-0.343,0.954]
Individual Fixed Effects	Yes	Yes
Observations	2396	2396

Notes: (1) 95% confidence intervals in square brackets
(2) * p<0.05, ** p<0.01, *** p<0.001

Table 12 Characteristic dummy variables of veterinarians

Variables	explanations
Female	Female: 1; otherwise: 0.
ExpVets	Experienced than median cohort: 1; otherwise: 0.
Welf	Attaching a higher importance to animal welfare than median level: 1; otherwise: 0.
Ant	Attaching a higher acceptance of antibiotic usage than median level: 1; otherwise: 0.

Table 13 Heterogeneity in belief updating across individual characteristics

	(1) Whole sample	(2) Large animal vets	(3) Small animal vets	(4) Whole sample	(5) Large animal vets	(6) Small animal vets
Log prior odds	0.305***	0.314***	0.550***	0.295***	0.295***	0.534***
	[0.200,0.411]	[0.168,0.460]	[0.412,0.688]	[0.217,0.372]	[0.195,0.394]	[0.439,0.628]
Log likelihood ratio	0.821***	0.827***	0.644***	0.797***	0.802***	0.625***
	[0.753,0.890]	[0.734,0.920]	[0.552,0.736]	[0.739,0.855]	[0.725,0.879]	[0.552,0.697]
Confirming test result * Log likelihood ratio	0.063*	0.125**	-0.000	0.066*	0.132**	0.001
	[-0.012,0.139]	[0.013,0.237]	[-0.101,0.100]	[-0.009,0.140]	[0.021,0.243]	[-0.098,0.100]
Small animal vets * Log prior odds	0.242***			0.241***		
	[0.169,0.314]			[0.170,0.313]		
Small animal vets * Log likelihood ratio	-0.177***			-0.173***		
	[-0.223,-0.130]			[-0.219,-0.128]		
Experienced vets * Log prior odds	-0.014	-0.086	0.057	-0.009	-0.081	0.063
	[-0.087,0.060]	[-0.195,0.024]	[-0.041,0.156]	[-0.080,0.063]	[-0.185,0.023]	[-0.034,0.160]
Experienced vets * Log likelihood ratio	-0.107***	-0.075**	-0.146***	-0.097***	-0.072**	-0.129***
	[-0.154,-0.059]	[-0.146,-0.004]	[-0.209,-0.083]	[-0.143,-0.051]	[-0.139,-0.005]	[-0.191,-0.067]
Female * Log prior odds	-0.013	0.006	-0.042			
	[-0.087,0.061]	[-0.103,0.116]	[-0.141,0.056]			
Female * Log likelihood ratio	-0.045*	-0.046	-0.042			
	[-0.093,0.002]	[-0.116,0.025]	[-0.107,0.022]			
Ant * Log prior odds	0.028	0.022	0.034			
	[-0.047,0.102]	[-0.087,0.130]	[-0.064,0.133]			
Ant * Log likelihood ratio	0.020	-0.003	0.040			
	[-0.027,0.067]	[-0.071,0.066]	[-0.024,0.104]			

Table 13 (cont'd)

Welf * Log prior odds	-0.028	-0.051	-0.010			
	[-0.102,0.046]	[-0.161,0.059]	[-0.107,0.087]			
Welf * Log likelihood ratio	0.057**	-0.004	0.118***	0.059**	-0.018	0.137***
	[0.009,0.105]	[-0.074,0.066]	[0.054,0.182]	[0.013,0.106]	[-0.086,0.050]	[0.074,0.200]
Constant	0.306	-0.659**	0.334	0.307	-0.647**	0.334
	[-0.325,0.938]	[-1.191,-0.127]	[-0.326,0.995]	[-0.319,0.934]	[-1.194,-0.099]	[-0.323,0.991]
Individual Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	2346	1168	1178	2396	1188	1208

Table 14 Underinference and base rate neglect in diagnosis decisions using revised data

	(1) Baseline model	(2) Allow heterogeneity across posteriors and test accuracy
Log prior odds	0.440***	0.121
	[0.404,0.476]	[-0.185,0.428]
Log likelihood ratio	0.735***	0.538***
	[0.712,0.758]	[0.235,0.841]
Extreme posteriors # Log prior odds		0.389**
		[0.081,0.698]
Extreme posteriors # Log likelihood ratio		0.208
		[-0.094,0.510]
fp=0.05 # Log likelihood ratio		-0.060*
		[-0.128,0.009]
fp=0.1 # Log likelihood ratio		-0.060
		[-0.132,0.012]
fp=0.2 # Log likelihood ratio		-0.034
		[-0.110,0.042]
Constant	0.345	0.376
	[-0.387,1.076]	[-0.325,1.076]
Individual Fixed Effects	Yes	Yes
Observations	2395	2395

Notes: (1) 95% confidence intervals in square brackets
(2) * p<0.05, ** p<0.01, *** p<0.001

Table 15 Prior-biased inference and preference-biased inference using revised data

	(1) Prior-biased inference	(2) Preference-biased inference	(3) Prior-biased inference across practice areas	(4) Preference-biased inference across practice areas
Log prior odds	0.391***	0.439***	0.233***	0.311***
	[0.333,0.449]	[0.403,0.476]	[0.150,0.315]	[0.260,0.361]
Log likelihood ratio	0.700***	0.716***	0.769***	0.768***
	[0.662,0.737]	[0.615,0.816]	[0.714,0.825]	[0.626,0.910]
Confirming test result * Log likelihood ratio	0.090**		0.144***	
	[0.015,0.164]		[0.036,0.252]	
Good news * Log likelihood ratio		0.039		0.117
		[-0.154,0.232]		[-0.157,0.390]
Small animal vets * Log prior odds			0.312***	0.256***
			[0.200,0.424]	[0.186,0.325]
Small animal vets * Log likelihood ratio			-0.139***	-0.116
			[-0.213,-0.065]	[-0.311,0.079]
Small animal vets * Confirming test result * Log likelihood ratio			-0.105	
			[-0.252,0.041]	
Small animal vets * Good news * Log likelihood ratio				-0.129
				[-0.504,0.245]
Constant	0.332	0.380	0.298	0.292
	[-0.395,1.059]	[-0.376,1.136]	[-0.349,0.944]	[-0.405,0.988]
Individual Fixed Effects	Yes	Yes	Yes	Yes
Observations	2395	2395	2395	2395

Table 16 Belief updating heterogeneity across veterinary practice areas using revised data

	(1) Heterogeneity across posteriors	(2) Heterogeneity across test accuracy
Log prior odds	0.044	0.312***
	[-0.356,0.444]	[0.262,0.363]
Log likelihood ratio	0.660***	0.885***
	[0.276,1.043]	[0.803,0.967]
Small animal vets # Log prior odds	0.079	0.254***
	[-0.488,0.647]	[0.185,0.323]
Small animal vets # Log likelihood ratio	-0.404	-0.186***
	[-0.955,0.147]	[-0.298,-0.073]
Extreme posteriors # Log prior odds	0.365*	
	[-0.037,0.767]	
Extreme posteriors # Log likelihood ratio	0.116	
	[-0.269,0.501]	
Small animal vets with extreme posteriors # Log prior odds	0.124	
	[-0.446,0.694]	
Small animal vets with extreme posteriors # Log likelihood ratio	0.253	
	[-0.301,0.807]	
fp=0.05 # Log likelihood ratio		-0.068
		[-0.166,0.030]
fp=0.1 # Log likelihood ratio		-0.114**
		[-0.218,-0.010]
fp=0.2 # Log likelihood ratio		0.002
		[-0.108,0.111]
Small animal vets with fp=0.05 # Log likelihood ratio		-0.028
		[-0.163,0.107]
Small animal vets with fp=0.1 # Log likelihood ratio		0.088
		[-0.054,0.231]

Table 16 (cont'd)

Small animal vets with fp=0.2 # Log likelihood ratio			-0.049
			[-0.198,0.100]
Constant		0.336	0.316
		[-0.287,0.958]	[-0.326,0.957]
Individual Fixed Effects		Yes	Yes
Observations		2395	2395

Table 17 Heterogeneity in belief updating across individual characteristics using revised data

	(1) Whole sample	(2) Large animal vets	(3) Small animal vets	(4) Whole sample	(5) Large animal vets	(6) Small animal vets
Log prior odds	0.283***	0.306***	0.530***	0.277***	0.283***	0.524***
	[0.180,0.385]	[0.166,0.445]	[0.395,0.665]	[0.201,0.352]	[0.186,0.381]	[0.434,0.614]
Log likelihood ratio	0.850***	0.858***	0.664***	0.830***	0.831***	0.657***
	[0.783,0.916]	[0.768,0.947]	[0.573,0.754]	[0.775,0.885]	[0.757,0.904]	[0.588,0.727]
Confirming test result	0.080**	0.138**	0.019	0.082**	0.145***	0.021
* Log likelihood ratio	[0.007,0.153]	[0.029,0.246]	[-0.078,0.117]	[0.010,0.155]	[0.037,0.253]	[-0.075,0.116]
Small animal vets *	0.253***			0.256***		
Log prior odds	[0.182,0.323]			[0.187,0.325]		
Small animal vets *	-0.181***			-0.177***		
Log likelihood ratio	[-0.226,-0.136]			[-0.221,-0.133]		
Experienced vets *	-0.020	-0.097*	0.056	-0.020	-0.102**	0.061
Log prior odds	[-0.092,0.052]	[-0.203,0.010]	[-0.041,0.152]	[-0.090,0.049]	[-0.203,-0.001]	[-0.033,0.154]
Experienced vets *	-0.123***	-0.086**	-0.167***	-0.115***	-0.083**	-0.154***
Log likelihood ratio	[-0.169,-0.076]	[-0.155,-0.018]	[-0.229,-0.105]	[-0.159,-0.071]	[-0.147,-0.019]	[-0.215,-0.094]
Female * Log prior odds	0.009	0.043	-0.037			
	[-0.063,0.081]	[-0.063,0.150]	[-0.133,0.060]			
Female * Log likelihood ratio	-0.036	-0.044	-0.024			
	[-0.083,0.011]	[-0.113,0.025]	[-0.088,0.039]			

Table 17 (cont'd)

Ant * Log prior odds	0.015	-0.004	0.034			
	[-0.057,0.088]	[-0.109,0.102]	[-0.062,0.130]			
Ant * Log likelihood ratio	0.019	-0.008	0.044			
	[-0.027,0.065]	[-0.075,0.058]	[-0.019,0.106]			
Welf * Log prior odds	-0.031	-0.071	0.004			
	[-0.102,0.041]	[-0.177,0.035]	[-0.091,0.098]			
Welf * Log likelihood ratio	0.036	-0.020	0.092***	0.040*	-0.034	0.115***
	[-0.011,0.082]	[-0.088,0.047]	[0.030,0.154]	[-0.005,0.085]	[-0.099,0.031]	[0.054,0.176]
Constant	0.307	-0.656**	0.335	0.307	-0.640**	0.335
	[-0.317,0.931]	[-1.193,-0.119]	[-0.317,0.987]	[-0.312,0.927]	[-1.202,-0.077]	[-0.320,0.991]
Individual Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	2,345	1,168	1,177	2,395	1,188	1,207

Notes: (1) 95% confidence intervals in square brackets
(2) * p<0.05, ** p<0.01, *** p<0.001

Table 18 Multinomial logit estimation: treatment utility as a function of treatment characteristics

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
AW_high	0.523***		-0.782**		0.806	0.819***		-0.009
LossAvd	0.001***		-0.002***		-0.003***	0.001***		0.001
AW_high *CRate		1.491***	2.551***	-2.539***	-3.114		1.283***	1.267**
LossAvd *CRate		0.004***	0.005***	0.005***	0.011***		0.001**	0.000
$(AW\_high*CRate)^2$				4.917***	4.238**			
$(LossAvd *CRate)^2$				-0.000*	-0.000***			
CRate						4.562***	3.616***	3.941***
Observations	4,338	4,338	4,338	4,338	4,338	4,338	4,338	4,338
AIC	2,485.9	2,236.8	2,175.6	2,198.3	2,155.4	2,081.1	2,084.1	2,080.5

Notes: (1) Column (1)-(8) regression control other attributes, interactions between disease likelihood with all attribute related variables included in the model, and a no treatment option dummy
(2) 95% confidence intervals in square brackets* p<0.05** p<0.01*** p<0.001

APPENDIX C

A survey sample of large animal disease management

Survey of Veterinarians Decision Making in Animal Disease Management

You are being invited to complete this online survey. The purpose of the research is to examine veterinarians' diagnostic and treatment decision-making.

In addition to your $30 completion payment, you will have a chance to earn an additional $30 based on your answers.

This survey proceeds in four sections and takes approximately 25 minutes to complete. In sections A and B, we will ask you to make diagnostic and treatment decisions on given disease cases and available treatment options. In sections C and D, we will collect ancillary information including some basic demographics, views about test reliability, antibiotics resistance, and animal welfare.

Participation in this survey is completely voluntary and you can withdraw at any time. Your response and any information you shared with us will be kept strictly confidential. We will not disclose any personally identifiable information to the public when we present survey data and analysis results.

You must be 18 or older to participate. If you have any questions, please contact Dr. David Hennessy at hennes64@msu.edu or Dr. Angel Abuelo at abuelo@msu.edu. You indicate that you voluntarily agree to participate in this research study by submitting the survey.

Section A. Diagnostic decisions under different case scenarios

Background: There is a disease (named "disease D") that is circulating on cattle farms in a locality. At the early stages of disease D, there are no clinical signs, while severe signs appear as disease D progresses. To manage disease D, it's important to detect it at the early stages.

Make diagnostic decisions: As a veterinarian, you know the prevalence rate of the disease. An inexpensive test can also be used. The test result can be positive, suggesting the cow is likely to have disease D. Or it can be negative, suggesting the cow is likely not to have disease D. We say 'likely' because there can be false negative or false positive test results.

You will face ten scenarios which differ in four factors: prevalence rate, test result, false positive rate, and false negative rate. The specific meanings of the factors are given on the following page. In each scenario that we present you with, you are asked to estimate the probability that a randomly drawn cow (named cow X) has disease D based on the information given. Note that cow X being considered in one scenario may or may not be the same cow under consideration in another scenario. Therefore, please consider each scenario separately. There are no good or bad answers. We are only interested in your true beliefs.

We describe each scenario in terms of four factors.

1. Prevalence rate measures the proportion of cows among a population that have disease D.

2. Test result can be positive or negative. A positive test result provides information suggesting that the cow is likely to have disease D while a negative test result provides information suggesting that the cow is likely not to have the disease.

3. False positive rate is the percentage of all cows tested who do not have disease D but have tested positive.

4. False negative rate is the percentage of all cows tested who do have disease D but have tested negative. In all scenarios, the false negative rate is fixed at 10%.

Payment rules: Besides a completion fee of $30, we will pay you earnings based on one of your estimates that is drawn randomly from all of the estimates that you make in Section A. All of your estimates have an equal chance of being drawn, that is, anyone of your estimates could be the one that determines your earnings. We use a payment rule that guarantees that reporting your true beliefs leads to the highest chance of receiving $30. If you want to learn about the details of the payment rule, you can click here (https://msu.co1.qualtrics.com/jfe/form/SV_1BLU2fQC4fr8ltb). However, you don't need to know payment rule details in order to answer questions in Section A. You just need to remember that providing truthful answers maximizes your chance of winning.

[Please try to take each scenario as a real world situation, and make sure your answers make common sense. For example, a positive test result would suggest a higher likelihood of disease occurring than would a negative test result.]

Section A Scenario 1

Key information:

(1) Prevalence rate: 70 out of every 100 cows have disease D.

(2) Cow X tested positive.

(3) False positive rate is 30%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()	

Section A Scenario 2

Key information:

(1) Prevalence rate: 70 out of every 100 cows have disease D.

(2) Cow X tested negative.

(3) False positive rate is 30%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()

Section A Scenario 3

Key information:

(1) Prevalence rate: 90 out of every 100 cows have disease D.

(2) Cow X tested positive.

(3) False positive rate is 20%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()

Section A Scenario 4

Key information:

(1) Prevalence rate: 90 out of every 100 cows have disease D.

(2) Cow X tested negative.

(3) False positive rate is 20%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()	

Section A Scenario 5

Key information:

(1) Prevalence rate: 70 out of every 100 cows have disease D.

(2) Cow X tested positive.

(3) False positive rate is 5%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()	

Section A Scenario 6

Key information:

(1) Prevalence rate: 70 out of every 100 cows have disease D.

(2) Cow X tested negative.

(3) False positive rate is 5%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()	

Section A Scenario 7

Key information:

(1) Prevalence rate: 10 out of every 100 cows have disease D.

(2) Cow X tested positive.

(3) False positive rate is 30%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()	

Section A Scenario 8

Key information:

(1) Prevalence rate: 10 out of every 100 cows have disease D.

(2) Cow X tested negative.

(3) False positive rate is 30%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()

Section A Scenario 9

Key information:

(1) Prevalence rate: 30 out of every 100 cows have disease D.

(2) Cow X tested positive.

(3) False positive rate is 20%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.

0 10 20 30 40 50 60 70 80 90 100

The probability that the cow has disease D (%) ()

Section A Scenario 10

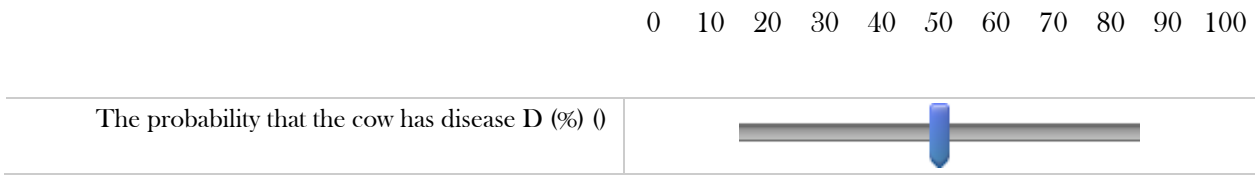
Key information:

(1) Prevalence rate: 30 out of every 100 cows have disease D.

(2) Cow X tested negative.

(3) False positive rate is 20%, and false negative rate is 10%.

What is your best estimate of the probability that the cow HAS the disease? Please use the cursor to indicate your estimate.



A.1 In some scenarios you have answered, the only difference is that the cow tested positive in one scenario while the cow tested negative in the other scenario for disease D. Your estimate of the probability that the cow has disease D is higher given negative test result than your estimate given positive test result. Do you wish to adjust your estimates before continuing? Choose "Yes" and click on the "Continue" button, you will be presented with the scenarios; choose "No" and click on the "Continue" button, you will be presented with the remaining part of the survey.

- ○ Yes. I will revisit and reconsider my estimate.
- ○ No. I am content with my initial estimate.

A.2 Would you like to modify your probabilistic estimates in the above questions? If so, you can click the "Previous" button to modify your answers. Once you confirm your answers by clicking the box below and click the "Continue" button, you will not be able to go back to modify your answers.

○ I confirm my answers in the above questions

Section B. Treatment decisions under different case scenarios

Rounds: Section B proceeds in six rounds.

Background: A dairy producer called you about a suspected mastitis case. As requested, you visited the farm and conducted a thorough inspection. You inspected the suspected sick cow, checked its disease history, tested milk samples from the cow, and learned their management procedures.

Treatment decision-making: Based on information available to you, you believe that the cow has mastitis with some probability (e.g., 30%). If the cow has mastitis, you have two treatment options which differ in five factors: treatment cost, cure rate of mastitis, animal welfare, loss avoided, and potential to increase antibiotic resistance. The specific meanings of the factors are given on the following page. Explicitly, the withdrawal times for the two treatment options are the same. You can also choose not to treat the cow. If the cow doesn't have mastitis, the signs observed will disappear themselves and treatment provides no benefit. The focus of this survey is on treatment decisions. There are no right or wrong answers. We are just interested in your point of view.

We describe each treatment alternative in terms of five main factors.

Treatment costs: {$20, $80, $140, or $200}, including antibiotic cost, labor cost, and discarded milk due to antibiotic residue.

Potential to increase antibiotic resistance: {none, low, or high}, impacts on the future effectiveness of antibiotics in human or animal uses due to the development of antibiotic resistance.

Cure rate of mastitis: {20%, 50%, 80% or 100%}, the probability that the animal is cured which depends on antibiotics used, pathogen susceptibilities to antibiotics, disease history, etc.

Animal welfare improvement: {low or high}, benefits to the animal if treatment is effective through health condition improvement.

Loss avoided: {$250, $450, $650, or $850}, additional treatment costs that would have occurred due to the disease but are avoided if treatments cure the animal.

Section B Scenario 1

You believe the cow has mastitis with probability $e{ e://Field/rand1_1 * 10 }%. If the cow has mastitis, treatment options can provide some benefits; otherwise, treatment options provide no benefit.

Which treatment do you prefer? Please check one. (T1= Treatment 1, T2= Treatment 2, NT= No treatment)

	T1	T2	NT
Treatment cost	$20	$80	$0
Potential to increase antibiotic resistance	None	Low	None
Cure rate of mastitis	20%	50%	0
*Note: you believe the cow has mastitis with probability $e{ e://Field/rand1_1 * 10 }%*			
If the cow is cured, animal welfare improvement	Low	High	None
If the cow is cured, loss avoided	$250	$450	$0

Explanations for reader: rand1_1 is randomly selected from natural number in the range of 1 to 10. That is, when rand1_1 is 2, respondents are presented with "You believe the cow has mastitis with probability 20%" The same logics apply to random numbers (e.g., rand1_2) in the remaining questions in this section.

- ○ My decision would be to use Treatment 1 (T1)
- ○ My decision would be to use Treatment 2 (T2)
- ○ My decision would be No treatment (NT)

Section B Scenario 2

You believe the cow has mastitis with probability $e{ e://Field/rand1_2 * 10 }%. If the cow has mastitis, treatment options can provide some benefits; otherwise, treatment options provide no benefit.

Which treatment do you prefer? Please check one. (T1= Treatment 1, T2= Treatment 2, NT= No treatment)

	T1	T2	NT
Treatment cost	$20	$80	$0
Potential to increase antibiotic resistance	Low	High	None
Cure rate of mastitis	80%	100%	0
*Note: you believe the cow has mastitis with probability $e{ e://Field/rand1_1 * 10 }%*			
If the cow is cured, animal welfare improvement	Low	High	None
If the cow is cured, loss avoided	$450	$650	$0

- ○ My decision would be to use Treatment 1 (T1)
- ○ My decision would be to use Treatment 2 (T2)
- ○ My decision would be No treatment (NT)

Section B Scenario 3

You believe the cow has mastitis with probability $e{ e://Field/rand1_3 * 10 }%. If the cow has mastitis, treatment options can provide some benefits; otherwise, treatment options provide no benefit.

Which treatment do you prefer? Please check one. (T1= Treatment 1, T2= Treatment 2, NT= No treatment)

	T1	T2	NT
Treatment cost	$200	$20	$0
Potential to increase antibiotic resistance	Low	High	None
Cure rate of mastitis	100%	20%	0
*Note: you believe the cow has mastitis with probability $e{ e://Field/rand1_1 * 10 }%*			
If the cow is cured, animal welfare improvement	Low	High	None
If the cow is cured, loss avoided	$850	$250	$0

- ○ My decision would be to use Treatment 1 (T1)
- ○ My decision would be to use Treatment 2 (T2)
- ○ My decision would be No treatment (NT)

Section B Scenario 4

You believe the cow has mastitis with probability $e{ e://Field/rand1_4 * 10 }%. If the cow has mastitis, treatment options can provide some benefits; otherwise, treatment options provide no benefit.

Which treatment do you prefer? Please check one. (T1= Treatment 1, T2= Treatment 2, NT= No treatment)

	T1	T2	NT
Treatment cost	$140	$200	$0
Potential to increase antibiotic resistance	High	None	None
Cure rate of mastitis			0
*Note: you believe the cow has mastitis with probability $e{ e://Field/rand1_1 * 10 }%*			
If the cow is cured, animal welfare improvement	50%	80%	None
If the cow is cured, loss avoided	$450	$650	$0

- ○ My decision would be to use Treatment 1 (T1)
- ○ My decision would be to use Treatment 2 (T2)
- ○ My decision would be No treatment (NT)

Section B Scenario 5

You believe the cow has mastitis with probability $e{ e://Field/rand1_5 * 10 }%. If the cow has mastitis, treatment options can provide some benefits; otherwise, treatment options provide no benefit.

Which treatment do you prefer? Please check one. (T1= Treatment 1, T2= Treatment 2, NT= No treatment)

	T1	T2	NT
Treatment cost	$140	$200	$0
Potential to increase antibiotic resistance	High	None	None
Cure rate of mastitis	50%	80%	0
*Note: you believe the cow has mastitis with probability $e{ e://Field/rand1_1 * 10 }%*			
If the cow is cured, animal welfare improvement	Low	High	None
If the cow is cured, loss avoided	$650	$850	$0

- ○ My decision would be to use Treatment 1 (T1)
- ○ My decision would be to use Treatment 2 (T2)
- ○ My decision would be No treatment (NT)

Section B Scenario 6

You believe the cow has mastitis with probability ${e{ e://Field/rand1_6 * 10 }%. If the cow has mastitis, treatment options can provide some benefits; otherwise, treatment options provide no benefit.

Which treatment do you prefer? Please check one. (T1= Treatment 1, T2= Treatment 2, NT= No treatment)

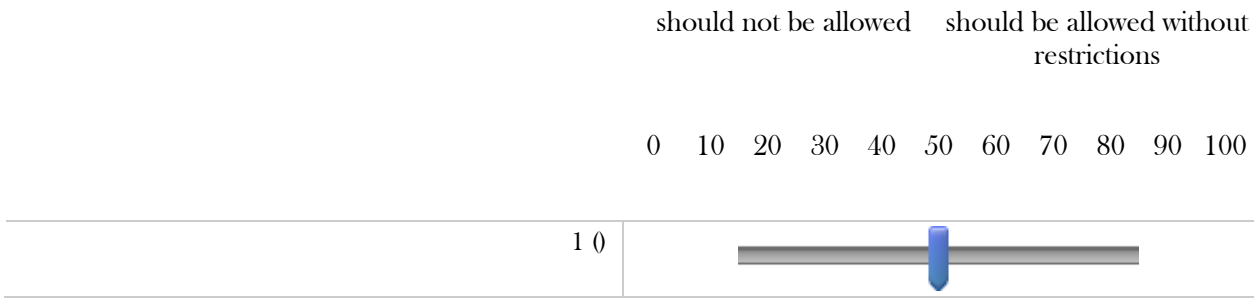
	T1	T2	NT
Treatment cost	$80	$140	$0
Potential to increase antibiotic resistance	High	None	None
Cure rate of mastitis	80%	100%	0
*Note: you believe the cow has mastitis with probability ${e{ e://Field/rand1_1 * 10 }%*			
If the cow is cured, animal welfare improvement	High	Low	None
If the cow is cured, loss avoided	$850	$250	$0

- ○ My decision would be to use Treatment 1 (T1)
- ○ My decision would be to use Treatment 2 (T2)
- ○ My decision would be No treatment (NT)

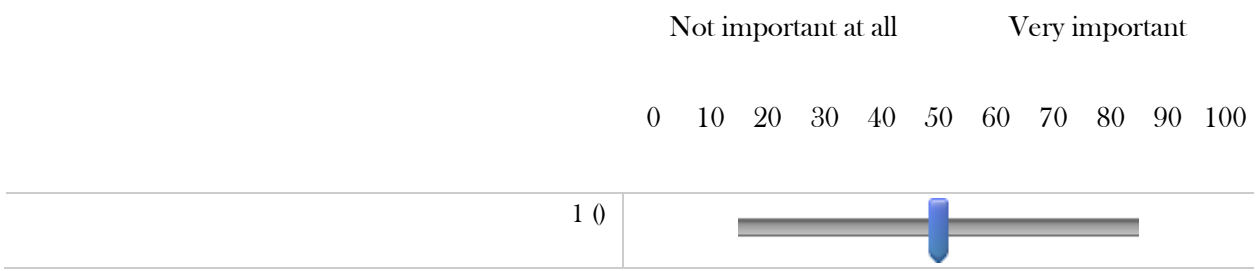
Section C. Viewpoints

C.1 Regarding the debate on how to manage antibiotics in production agriculture, what is your position concerning whether antibiotics should be used in production agriculture? A larger number means higher acceptance of antibiotics in production agriculture. (0 = antibiotics use

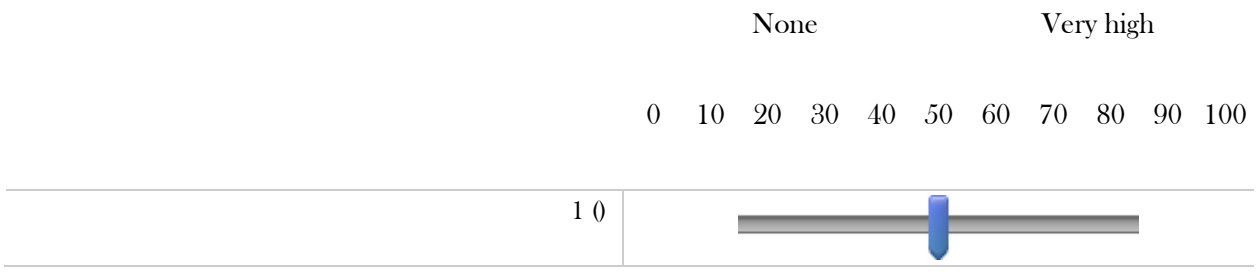
should not be allowed in production agriculture, 100 = antibiotics use should be allowed in production agriculture without restrictions.)



C.2 How important should animal welfare consequences be in decisions concerning antibiotics use in production agriculture? A larger number means greater importance. (0 = Not important at all, 100 = Very important)



C.3 What confidence do you have in the accuracy of diagnostic tests in general? A larger number indicates greater confidence (1 = None, and 100 = Very high).



C.4 Please identify the most important factors for your antibiotic prescriptions in regard to treating suspected mastitis. Please allocate 100 points to the importance you attach to the following factors, i.e., points allocated should sum to 100.

Farmers' profit : _____

Animal welfare : _____

Probability that mastitis spreads in the herd : _____

Veterinary client relationship : _____

Uncertainty about treatment outcome in the case at hand : _____

Concerns about the development of antibiotics resistance : _____

Other (Please specify) : _____

Total : _____

Section D. Demographic information and professional experience

D.1 In what year were you born?

Year (4)

▼ 1940 (1) ... 1999 (60)

D.2 What is your gender?

- ○ Male
- ○ Female
- ○ Other (Please specify) _____
- ○ Prefer not to say

D.3 What is your postal code?

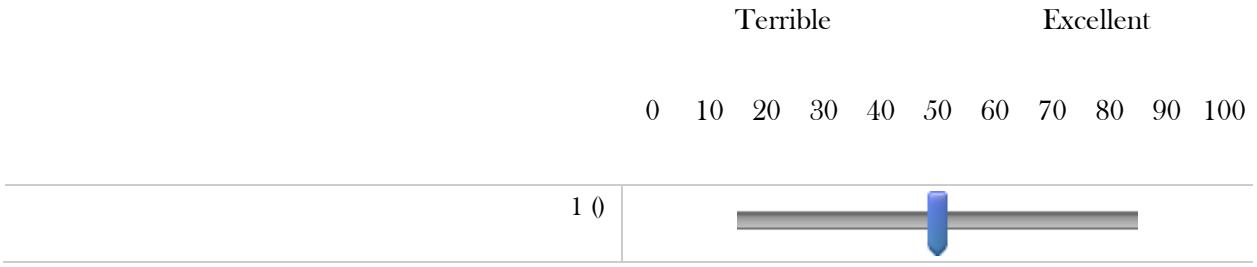
_____

D.4 What is your bachelor's degree?

- ○ Animal science
- ○ Other (e.g. biology, please specify)

_____

D.5 How well would you self-rate your statistics knowledge? A larger number means better knowledge (0 = I'm terrible at statistics, 100 = I'm excellent at statistics). Please use the cursor to indicate your answer.



D.6 Did you use Bayes theorem to calculate answers when you made probabilistic estimations in section A?

- ○ Yes
- ○ No

This is for our information only. Using or not using the theorem does not imply your answers are "good" or "not good," we are only interested in your earnest assessment.

D.7 In what year did you get your Doctor of Veterinary Medicine (DVM) degree?

Year

▼ 1940 (1) ... 2020 (81)

D.8 How many years have you worked as a veterinarian making diagnosis and treatment decisions?

I have worked for

▼ Less than 1 year (1) ... Over 30 years (32)

D.9 Do you serve clients who work in production agriculture?

- ○ Yes
- ○ No

D.10 How often have you visited cattle farms in a professional capacity in the last three years?

- ○ Daily
- ○ 1-3 times per week
- ○ 1-3 times per month
- ○ Seldom
- ○ Never

Please record any comments you have concerning veterinarians' diagnostic and treatment decision-making related to antibiotics use.

_____

_____

Thank you for completing the survey!

Please leave your email address below for payment. Make sure your email address is correct, otherwise we won't be able to contact you and make payment.

We won't disclose any private information to the public. If you have any questions, please contact us at hennes64@msu.edu.

_____

Payment rule explanations:

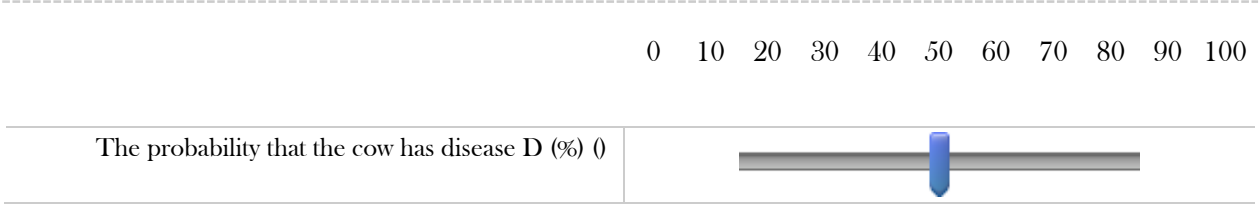
This is an extra explanation that you do not need to know to answer the questions in this survey. Click here (https://msu.co1.qualtrics.com/jfe/form/SV_0SBIcoJBHiqhrmt) to go back to the survey.

In the following illustration, denote your probability assessment in the drawn scenario as p %.

1. The computer will randomly and independently draw two integers in the range of [1, 100].
2. The computer simulates a cow random draw to reveal whether the cow has the disease.

If the cow is revealed to have the disease: You will earn $30 if your report p is greater than or equal to either of the two numbers drawn by the computer in the first step; otherwise you will earn $0. If the cow is revealed to not have the disease: You will earn $30 if your report p is less than either of the two numbers drawn by the computer in the first step; otherwise you will earn $0.

You can use the cursor to indicate any probability belief in the following screen. The computer will inform you of the corresponding probabilities of earning $3010.



Based on your answer above, your probabilities of receiving $30 are described in the following:

If the cow is revealed to have the disease, then you will receive $30 with probability (%) _____

If the cow is revealed to not have the disease, then you will receive $30 with probability (%) __

[10] In the online survey, participants can move the cursor and then the corresponding probability of $30 will be presented in the underlined areas.

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CHAPTER 3: ESSAY THREE: BT CORN, INSECTICIDE USE, AND RESISTANCE TIME TREND IN THE UNITED STATES

3.1. INTRODUCTION

To minimize damage and increase agricultural yield, growers apply efforts to control organisms that are detrimental to agriculture, such as (1) spray pesticides to control pests, (2) administer antibiotics to fight against bacteria, and (3) use antimalarial drugs to kill malarial parasites (Laxminarayan and Herrmann 2015). Whatever control measures are used, nature inevitably will fight back. The targeted organisms gradually become less susceptible and develop resistance to these control tactics, which used to be highly effective. Nowadays, resistance is a widespread problem and causes staggering consequences. For example, in addition to economic losses (Fullybright 2019), antibiotic resistance causes over 2.8 million antibiotic resistant infections and more than 35,000 deaths annually in the United States (U.S. Center for Disease Control and Prevention [US CDC] 2019). It has been argued that antibiotic use in agriculture (e.g., crop production, livestock and animal husbandry) is a driving force for antibiotic resistance development (Witte 1998). Pesticide resistance is another salient issue which incurs billions of additional economic losses annually (Palumbi 2001; Frisvold, Bagavathiannan and Norsworthy 2017; Davis and Frisvold 2017) and may impose risks on public health as well (Ranson and Lissenden 2016). Weed species are found to be resistant to every herbicide class available and many insect species are resistant to at least one insecticide (Gould, Brown and Kuzma 2018a; Munro 1997). As insect resistant genetically modified crops (GMC) which produce Bt (Bacillus thuringiensis) toxins and control pests have been widely adopted, Bt resistance emerges and increases, causing productivity damage in the fields (Tabashnik, Brévault and Carrière 2013; Calles-Torrez et al. 2019; Tabashnik, Carrière and Gassmann 2019). Since the first Bt crops were introduced, at least 19 cases of field-evolved resistance have emerged (Tabashnik et al. 2019). Such

resistance is a negative externality associated with control tactics use since every use by individual farmers may contribute to resistance development and degrade effectiveness for all farmers' future use. Therefore, in response to resistance development, actions need to be taken to conserve the control tactics effectiveness for long term use.

Even though there are high uncertainties in resistance management, it is agreed that reducing use can delay resistance development (Gould, Brown and Kuzma 2018b). However, the optimal extent of the reduction is not straightforward. This is because, in addition to the resistance issue, some control tactics used may cause other external effects. Therefore, optimal resistance management should address both the resistance issues and the other external effects. Chemical pesticide use is an illustrative example of such situations. When considering resistance (i.e., a negative externality) in isolation, growers may use more chemical pesticides than socially optimal levels. The adverse health and environmental effects are other negative external effects associated with chemical pesticide use and may exacerbate the overuse tendency. In contrast to chemical pesticides, Bt toxins, another type of pesticides, brings other external effects that are beneficial. The first external benefit is that Bt crops suppress pest populations within a region (Hutchison et al. 2010; Dively et al. 2018a; Lu et al. 2022; Wan et al. 2012) so that both insecticide use and pest damage decline among non-Bt adopters. Secondly, Bt crops are more environment friendly compared to insecticide which may cause adverse health and environmental effects (Bilal, Iqbal and Barceló 2019; Rajmohan, Chandrasekaran and Varjani 2020; Samsidar, Siddiquee and Shaarani 2018; Rani et al. 2021; Kaur et al. 2019). In order to develop a regulation that balances Bt resistance development and external benefits, the first step is to justify and evaluate externalities associated with Bt crops. Specifically, in this study we investigate whether and how Bt crops reduce insecticide use. Furthermore, we evaluate these effects on insecticide use in terms of health and environmental impacts.

Western corn rootworm (WCR), *Diabrotica virgifera virgifera* LeConte, is one of most significant pests in corn in the United States (Gassmann 2021). WCR larva feeds on corn root and can cause significant yield losses (Dun, Mitchell and Agosti 2010; Tinsley, Estes and Gray 2013). Annual cost pertaining to WCR, including yield loss and control cost, is estimated to be more than one billion in the United States (Wechsler and Smith 2018). Before Bt corn was introduced, corn rootworm was responsible for the largest single use of insecticides in the United States (Naranjo 2009). When Bt corn with the rootworm resistance trait becomes available, growers can plant Bt corn as an alternative strategy to manage WCR and potentially substitute away soil insecticide use.

The first Bt corn that controlling WCR was first commercialized in the United States in 2003 and produced Bt toxin *Cry3Bb1* (Gassmann et al. 2011). Afterwards, three other Bt toxins, *mCry3A*, *eCry3.1Ab* and *Cry34/35Ab1*, were introduced to manage WCR. To delay resistance development, Bt pyramids that can produce multiple Bt toxins against WCR were subsequently brought to the market, such as *Cry3Bb1* with *Cry34/35Ab1*, *mCry3A* with *Cry34/35Ab1*. There exists evidence suggesting that some WCR populations are resistant to all available Bt toxins (Gassmann et al. 2020). During 2009 and 2010, WCR was found to be resistant to the *Cry3Bb1* toxin in Iowa (Gassmann et al. 2011) and then evidence of resistance arose in Nebraska, Minnesota and Illinois (Gassmann et al. 2020). Furthermore, WCR populations resistant to *Cry3Bb1* have been documented to be resistant to *mCry3A* and *eCry3.1Ab* due to cross resistance mechanism (Zukoff et al. 2016; Wangila et al. 2015; Gassmann et al. 2014; Jakka, Shrestha and Gassmann 2016). In addition, field resistance to *Cry34/35Ab1* was first reported in 2013 in Iowa and Minnesota (Ludwick et al. 2017; Gassmann et al. 2016). Therefore, resistance management among WCR populations is urgent and significant.

In this study, we employ farm-level panel data to investigate the impact of Bt corn with *Cry3Bb1* on insecticide use patterns over time. The findings add farm-level evidence on WCR

resistance together with its production and environmental implications. To estimate the net effect of Bt crops adoption, we need to address endogeneity caused by selection bias. Farmers decide themselves whether to adopt Bt crops or not. There are studies suggesting that adopters and non-adopters may differ significantly (Liu 2013; Ngcinela et al. 2019; Mal et al. 2015). Analysis without controlling for the differences between adopters and non-adopters may produce biased effect estimates. Despite studies that do not take account of endogeneity problems (Sisterson et al. 2007; Cattaneo et al. 2006; Brookes and Barfoot 2006; Kranthi and Stone 2020), several approaches have been used to address self-selection bias. The first approach requires conducting randomized controlled trials (RCT). For instance, Huang et al.(2005) conducted RCT of rice in China and found that Bt rice increased rice yield and reduced pesticide use. Ahmed et al. (2021) implemented an RCT of Bt eggplant in Bangladesh and found that Bt adoption reduces pesticide cost significantly. When RCT is not an available option, various approaches have been applied depending on observed data structure. When cross sectional data are available, propensity score match (PSM) or instrumented approach have been commonly used dealing with cross sectional data (Yorobe and Smale 2012; Khonje et al. 2015; Shiferaw et al. 2014; Kouser and Qaim 2013). While PSM only controls observed differences among adopters and non-adopters, an instrumented approach can address unobserved differences. However, weak instrument variables are a main concern when applying an instrumented approach (Huang et al. 2002; Shankar and Thirtle 2005). When panel data are available, researchers can use a fixed effect or a difference-in-difference approach. In earlier studies, a fixed effect approach is commonly used to control within-farm effect (Kathage and Qaim 2012; Crost et al. 2007; Veettil, Krishna and Qaim 2017). A recent study implemented a difference-in-difference approach to estimate the impact of Bt cotton on pesticide use in India (Peshin et al. 2021). They argued that Bt cotton reduced insecticide use for

the same pests but increased the need for insecticide targeting on other pests as well as fungicides and herbicides.

Utilizing a unique farm-level panel dataset, which contains more than 5,000 corn U.S. growers' information about seed type choices and insecticides uses during 1998-2016, we are able to apply a generalized difference-in-difference (DID) approach to address endogeneity and ascertain any causal effects. Although studies on Bt cotton in India by Peshin et al (2021) apply a DID approach, as far as we know, no extant literature applies DID approach to investigate the impact of Bt corn in the United States. In the DID analysis, farmers who ever adopt *Cry3Bb1* toxin form a treatment group and farmers who never adopt *Cry3Bb1* toxin serve as a control group. We compare insecticide use of treatment and control group, controlling time variant shocks and static differences between regions. The *Cry3Bb1* adoption results in a decrease in substituting insecticides, justifying environmental benefits induced by Bt adoption. Compared with Peshin et al (2021), we also scrutinize the dynamics of the impact after adoption and found that the magnitude of this decrease diminishes over time. This trend is consistent with emergence of WCR resistance to *Cry3Bb1*.

In addition, we examine the pest suppression effect of *Cry3Bb1* toxin that brings external benefits to non-adopters. There is a downward trend in insecticide use among non-adopters, which is consistent with the pest suppression effect of Bt crop documented in the extant literature (Hutchison et al. 2010; Dively et al. 2018a; Lu et al. 2022; Wan et al. 2012). Supposing *Cry3Bb1* adoption suppresses pest population within the region but the non-adopters are unaware of the magnitudes of Bt suppression effects, non-adopters learn about the pest pressure over years and eventually reduce insecticide use. In this study, we use a Bayesian learning model to explain non-adopters' beliefs adjustment patterns of pest pressure. By relying on historical data, farmers' prior beliefs are likely to exceed the true pest pressure. In that case, we prove that, along with Bayesian

learning, insecticide use by risk averters will start from a high level and decrease until farmers' beliefs eventually converge to the true pest pressure. This finding is consistent with the decreasing and then sustained low insecticide use trend among non-adopters from empirical analysis.

The paper is organized into six sections. Section two introduces the dataset analyzed in this study. We explain the identification strategy in section three and summarize empirical findings in section four. Section five presents a theoretical model for farmer's Bayesian learning in insecticide input choices. Section six concludes the study.

3.2. DATA

The data analyzed is from *AgroTrak*, a farm-level panel data covering 1998 to 2016. *AgroTrak* contains information on farmers' seed choices (Do farmers plant conventional corn or Bt corn? If Bt corn, what is the seed trait?) and chemical input choices (Which insecticides are applied? What is the amount of active ingredients? What are the targeted pests?). On average, about 5,154 corn farmers and 4,863 soybean farmers are randomly sampled annually. Many farmers responded across multiple years. The samples are representative at the Crop Reporting Districts (CRD) level and cover the 48 contiguous states. According to the United States Department of Agriculture National Agricultural Statistics Service, CRDs are groupings of counties in each state which have similar geography, climate and cropping practices.

We conducted empirical analyses on insecticide and seed choices by US corn farmers during 1998-2014. Soil insecticide, foliar insecticide and seed treated insecticides (neonicotinoids) are alternative insect control options for WCR used by farmers (Meinke, Souza and Siegfried 2021). Nowadays, nearly all corn seeds are coated with neonicotinoids in the United States (Stevens and Jenkins 2014; Gurian-sherman 2015), meaning that in most cases growers cannot make decisions regarding seed-treated insecticide use. Thus, our study focuses on, controlling for neonicotinoids use, how *Cry3Bb1* adoption affects WCR-targeting insecticide use (excluding seed-treated

neonicotinoids). Since neonicotinoids use is missing during 2015-2016 in the *AgroTrak* dataset, our analysis uses data from 1998 to 2014. Table 19 summarizes insecticide active ingredients applied for WCR in the dataset.

Table 19 Active ingredient that control western corn rootworm in the dataset

Active Ingredient
Bacillus Thuringiensis
Bifenthrin
Carbofuran
Chlorethoxyfos
Chlorpyrifos
Clothianidin
Cyfluthrin
Cyhalothrin-Gamma
Cyhalothrin-Lambda
Diazinon
Esfenvalerate
Fipronil
Imidacloprid
Methyl Parathion
Permethrin
Phorate
Tebupirimphos
Tefluthrin
Terbufos
Thiamethoxam

This paper mainly focuses on comparing i) farmers who switch from planting corn with no Bt toxins controlling WCR to *Cry3Bb1* corn with ii) farmers who plant corn with no Bt toxins controlling WCR all the time. These two types of farmers are henceforth called *Cry3Bb1* adopter

and non-adopters respectively. Corn with no Bt toxins controlling WCR can be conventional corn or Bt corn which is not targeted at WCR. *Cry3Bb1* corn specifically refers to Bt corn varieties which produce *Cry3Bb1* toxin specifically but no other WCR-controlling toxins, such as *mCry3A* and *eCry3.1Ab*. Table 20 lists seed type choices by *Cry3Bb1* adopter and non-adopters in the dataset. There are 27,521 farmers in total in the control and treatment group, of which 13.46% are *Cry3Bb1* adopters. Our interest is in investigating the impact of *Cry3Bb1* adoption on farmers' insecticides use which controls WCR.

Table 20 Seed type choices in *Cry3Bb1* adopter[11]

Seed type choice in adopters	Bt toxins
Gen VT3 Pro RIB	Cry3Bb1, Cry2Ab2_Cry1A.105
Genuity DroughtGard VT Triple Pro RIB	Cry3Bb1, Cry2Ab2_Cry1A.105
Genuity VT Triple Pro	Cry3Bb1, Cry2Ab2_Cry1A.105
YG PL	Cry1Ab, Cry3Bb1
YG PL - CLRFLD	Cry1Ab, Cry3Bb1
YG PL - RRC 2	Cry1Ab, Cry3Bb1
YGRW	Cry3Bb1
YGRW - CLRFLD	Cry3Bb1
YGRW - RR	Cry3Bb1
YGRW - RRC 2	Cry3Bb1
YGVT RW - RR2	Cry3Bb1
YGVT3	Cry1Ab, Cry3Bb1
Seed type choice in non-adopters	Bt toxins
Conventional	None
Agrisure Artesian 3010A	Cry1Ab
Agrisure CB - LL	Cry1Ab

[11] Note: Seed types "Agrisure GT", "CLRFLD", "CLRFLD – LL", "LL", "RR/GT", "RRC 2", "SR" describe genetically modified seeds that do not produce Bt toxins but have other characteristics, such as herbicide resistance, drought resistance, etc.

Table 20 (cont'd)

Agrisure CB - LL - CLRFLD	Cry1Ab
Agrisure GT - CB - LL	Cry1Ab
Agrisure Viptera 3110	Cry1Ab, Vip3A
Agrisure Viptera 3220 E-Z Refuge	Cry1Ab, Cry1F, Vip3A
Bt (ECB)	Cry1Ab
Bt (ECB) - CLRFLD	Cry1Ab
Bt (ECB) - LL	Cry1Ab
Bt (ECB) - LL - CLRFLD	Cry1Ab
Bt (ECB) - RR	Cry1Ab
Genuity DroughtGard VT Double Pro	Cry2Ab2_Cry1A.105
Genuity DroughtGard VT Double Pro RIB	Cry2Ab2_Cry1A.105
Genuity VT Double PRO RIB	Cry2Ab2_Cry1A.105
Genuity VT Double Pro	Cry2Ab2_Cry1A.105
HX I - LL	Cry1F
HX I - LL - CLRFLD	Cry1F
HX I - LL - RRC 2	Cry1F
Optimum AcreMax	Cry1Ab, Cry1F
Optimum AcreMax-R	Cry1Ab, Cry1F
Optimum Intrasect	Cry1Ab, Cry1F
Optimum Leptra	Cry1Ab, Cry1F, Vip3A
YGCB	Cry1Ab
YGCB - CLRFLD	Cry1Ab
YGCB - GT	Cry1Ab
YGCB - RRC 2	Cry1Ab
YieldGard CB-Herculex 1-LL-RR2	Cry1Ab, Cry1F
Agrisure GT	None
CLRFLD	None
CLRFLD - LL	None
LL	None

Table 20 (cont'd)

RR/GT	None
RRC 2	None
SR	None

Farmers may plant on multiple land plots. Some farmers only plant on one plot but some others plant on multiple plots. Their seed choices on different plots can be different. For each plot, farmers may use more than one insecticide product. In order to calculate a plot-level insecticide use, we need to first define "land plot" and add up all insecticides used on each land plot. We define a "land plot" as a land unit planted with the same seed trait, tillage type, farmer and year. According to Perry et al. (2016), each year, we can measure any farmer's insecticide use by considering the total amount of active ingredients used per acre y_i .

$$y_i = \frac{1}{L_i} \sum_{l(i)} \sum_{k} \sum_{j} Q_{l(i)}^{k} a_{l(i),j}^{k}. \tag{3.1}$$

Specifically, $Q_{l(i)}^{k}$ denotes the quantity of insecticide product k applied on plot $l(i)$ by farmer i, $a_{l(i),j}^{k}$ denotes the quantity of an active ingredient j contained by per-unit of product k that applied on plot $l(i)$, and L_i denotes the total acres planted by the farmer i.

The drawback of measurement in equation (3.1) is that it does not address the fact that varied active ingredients have heterogenous impacts on environment and health. Alternatively, we used Environmental Impact Quotient (EIQ) to determine the environmental and health impacts of each insecticide active ingredient contained within insecticide products (Kovach et al. 1992), and then calculate total impacts of insecticide use per acre as

$$y_i^E = \frac{\kappa}{L_i} \sum_{l(i)} \sum_{k} \sum_{j} Q_{l(i)}^{k} E_j a_{l(i),j}^{k}. \tag{3.2}$$

Specifically, E_j denotes the EIQ value pertain to active ingredient $a^k_{l(i),j}$, and κ is a constant to normalize y_i^E such that y_i^E and y_i have the same overall mean. This normalization facilitates the comparison of regression results using these two measures of insecticide use.

Thus, over 17 years, we have 94,956 land plots. For each land plot, crop planting information is recorded, including seed trait and crop area. Seed trait information allows us to identify an individual farmer as a *Cry3Bb1* Bt corn adopters or non-adopters. Plot-level insecticide consumption data includes active ingredients, pests controlled, application method, and treated area.

3.3. IDENTIFICATION STRATEGY

When estimating the impact of *Cry3Bb1* adoption on insecticide use, the main issue to address is the endogeneity caused by self-selection of *Cry3Bb1* adoption. Since we have access to a farm-level panel data, we use a generalized difference-in-difference approach to investigate the impact Cry3Bb1 adoption on insecticide use and how the impact changes as adopters keep using the Bt corn after adoption. *Cry3Bb1* adopters form the treatment group and *Cry3Bb1* non-adopters forms the control group. To study the impact of *Cry3Bb1* corn, we compare WCR-targeting insecticide use by farmers from the treatment group and control group. First, we ran a linear regression to specify the impact of *Cry3Bb1* corn on WCR-targeting insecticide use:

$$y_{i,t} = \alpha + \beta * Tr_i + \sum_{T=1}^{J_{1,i}} \gamma_T * Tr_i * D_{i,T} + \delta_1 * x_{i,t} + \delta_2 * \bar{x}_i + \eta_t + \rho_{FPR} + u_{i,t}, \quad (3.3)$$

where $y_{i,t}$ is WCR-targeting insecticide used by farmer i in year t. Dummy variable Tr_i indicates whether farmer i belongs to the treatment group (i.e., a *Cry3Bb1* adopter), and $D_{i,T}$ are a series of dummy variables indicate whether it's T years after the adoption. In other words, $D_{i,T} = 1$ whenever the survey year minus the year preceding the adoption equals T, and $D_{i,T} = 0$

otherwise. After the adoption, there are $J_{1,i}$ periods of records for farmer i. The interactions between Tr_i and $D_{i,T}$ are the key explanatory variables, where coefficient γ_T is the difference-in-difference effect in the years of using *Cry3Bb1* corn. We also included a vector of control variables $x_{i,t}$, including the WCR-targeting neonicotinoids application, pest pressure, and operation scale. We controlled farmer i's use of WCR-targeting neonicotinoids using variable $NNIs_{i,t}$. Specifically, $NNIs_{i,t}$ is the share of acreage that farmer i use WCR-targeting neonicotinoids. We use one-year lagged at state level of WCR-targeting insecticide use as a proxy for pest pressure $pp_{i,t}$. Specifically, we calculate $y_{state,t}$ following equation (3.1). Variable L_i denotes the total acres planted by the farmer i. We include L_i and its quadratic to allow operation scale to have non-linear effects. Table 21 summarizes statistics of dependent variable $y_{i,t}$ and control variables $x_{i,t}$.

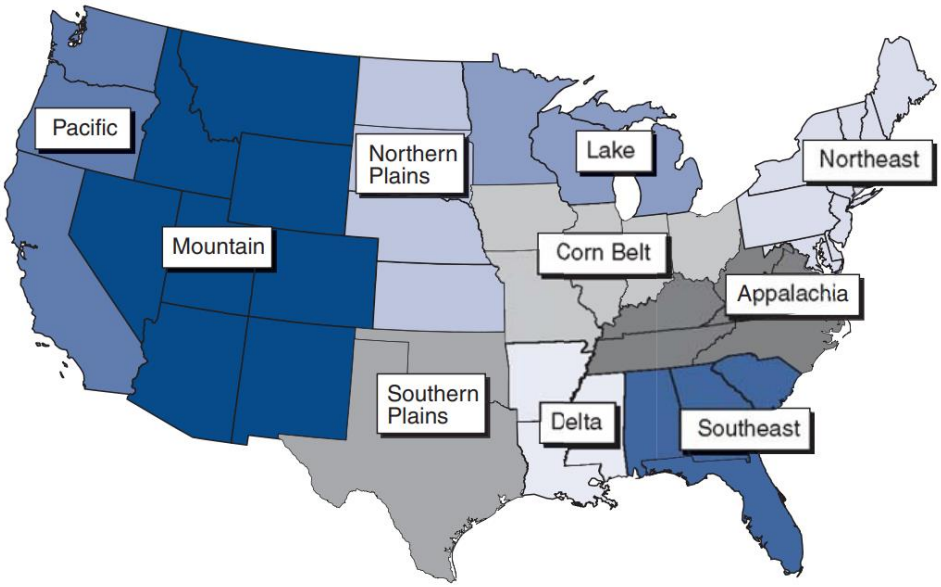
Table 21 Statistics of WCR-targeting insecticide use and other control variables

Variables	Obs	Mean	Std. Dev.	Min	Max
Total amount of WCR-targeting active ingredient per acre (lb/acre)	61433	0.045	0.203	0	13.8
EIQ measure of WCR-targeting active ingredient per acre (EIQ/acre)	61433	0.044	0.222	0	4.807
Share of NNIs application acreage	61433	0.042	0.197	0	1
Operation Scale (acres)	61433	14421.689	20548.618	18	697939
Pest pressure within state (lb/acre)	55101	0.057	0.058	0	0.578

The averages of $x_{i,t}$ across time are included to control fixed effects. In addition, Year dummy η_t and farm production regions ρ_{FPR} controls are used. The United States Department of Agriculture defines the farm production regions as states with similar production practices and

resource characteristics and group these states together. Figure 18 presents ten USDA farm production regions. These control variables are intended to remove concerns caused by omitted variables (Perry et al. 2016). Error component is $u_{i,t}$.

Figure 18 USDA Farm Production regions[12]



Noteworthy is that there are 54,085 zero WCR-targeting insecticide use observations in our sample, which account for 88% of total observations. Since we observe excessive zeros in insecticide use, we also construct a Tobit regression:

$$y_{i,t} = \max(0, \alpha + \beta * Tr_i + \sum_{T=1}^{J_{1,i}} \gamma_T * Tr_i * D_{i,T} + \delta_1 * x_{i,t} + \delta_2 * \bar{x}_i + \eta_t + \rho_{FPR} + u_{i,t}),$$
$$u_{i,t} \mid x_{i,t} \sim Normal(0, \vartheta^2). \tag{3.4}$$

The second term in max function has been explained in the linear model specified in equation (3.3). We assume that $u_{i,t}$ is independent of $x_{i,t}$ and its conditional distribution is a normal distribution with variance ϑ^2. Therefore, we can write log likelihood maximization problem as

[12] Note: The figure is from *Managing Manure to Improve Air and Water Quality* by Aillery et al. (2005)

$$\max \sum_{i=1}^{N}\sum_{t=1}^{J} 1[y_{i,t}=0]\log[1-\Phi(A_{i,t}/\vartheta)]+1[y_{i,t}>0]\{\log\phi[(y_{i,t}-A_{i,t})/\vartheta]-\log(\vartheta)\},$$
$$\text{where } A_{i,t}=\alpha+\beta*Tr_i+\sum_{T=1}^{J_{1,i}}\gamma_T*Tr_i*D_{i,T}+\delta_1*x_{i,t}+\delta_2*\bar{x}_i+\eta_t+\rho_{FPR} \quad (3.5)$$

Indication function $1[y_{i,t}=0]$ equals one when farmer i does not use WCR-targeting insecticides in year t, otherwise the indication function equals zero. Similarly, indication function $1[y_{i,t}>0]$ equals one when farmer i uses WCR-targeting insecticides in year t, otherwise the indication function equals zero. Function $\Phi(.)$ is the cumulative distribution function of standard normal distribution and $\phi(.)$ is density distribution of standard normal distribution. In the Tobit model, the probability of farmer using WCR-targeting insecticide is

$$P(y>0\mid X)=\Phi(X\beta/\vartheta), \quad (3.6)$$

where y denotes insecticide use, and X denotes all explanatory variables which are specified in equation (3.4). In addition, ϑ denotes standard deviation of error term and $\Phi(.)$ is cumulative distribution function of standard normal distribution. The conditional mean of WCR-targeting insecticide use is

$$E(y\mid X, y>0)=X\beta+\vartheta\left[\frac{\phi(X\beta/\vartheta)}{\Phi(X\beta/\vartheta)}\right], \quad (3.7)$$

where $\phi(.)$ is density distribution of a standard normal distribution.

The estimated coefficient indicates the impact of *Cry3Bb1* toxin on insecticide use in year T th after the adoption. Supposing that the *Cry3Bb1* toxin effectively controls for WCR and substitutes chemical insecticides, γ_T should be significant negative after adoption ($T>0$). The magnitude of partial effect on probability of a farmer using WCR-targeting insecticide is to compare the probabilities at $Tr_i*D_{i,T}=1$ and $Tr_i*D_{i,T}=0$, which can be written as

$$P(y>0\mid X^{-},1)-P(y>0\mid X^{-},0)=\frac{1}{NJ}\sum_{i=1,t=1}^{N,J}\{\Phi[(X^{-}\beta^{-}+\gamma_T)/\vartheta]-\Phi(X^{-}\beta^{-}/\vartheta)\}. \quad (3.8)$$

The vector X^{-} denotes all explanatory variables except interaction $Tr_i * D_{i,T}$ and the vector of parameters β^{-} denotes all parameters excluding γ_T, N is the total number of farm γ_T ers and J is the total number of years. The magnitude of partial effect on conditional mean of farmer using WCR-targeting insecticide is to compare the probabilities at $Tr_i * D_{i,T}=1$ and $Tr_i * D_{i,T}=0$, which can be written as

$$E(y\mid X^{-},1,y>0)-E(y\mid X^{-},0,y>0)=\gamma_T+\vartheta\left\{\frac{\phi[(X^{-}\beta^{-}+\gamma_T)/\vartheta]}{\Phi[(X^{-}\beta^{-}+\gamma_T)/\vartheta]}\right\}-\vartheta\left[\frac{\phi(X^{-}\beta^{-}/\vartheta)}{\Phi(X^{-}\beta^{-}/\vartheta)}\right], \quad (3.9)$$

Also, if Bt resistance emerges over the years of Bt toxins being used, we expect to observe the magnitude of γ_T decreases as T increases.

The parallel trend assumption underpins the validity of the causal effect derived from the difference-in-difference approach. The parallel trend assumption in our context requires that, in the absence of the *Cry3Bb1* corn, the treatment and control groups share a common parallel time trend in WCR-targeting insecticide use. To test parallel trend assumption, it is conventional to perform a "placebo" test specified as

$$y_{i,t}=\alpha+\beta * Tr_i+\sum_{T=1}^{J_{1,i}}\gamma_T * Tr_i * D_{i,T}+\sum_{T=J_{0,i}}^{-1}\gamma_T * Tr_i * D_{i,T}+\eta_t+u_{i,t}, \quad (3.10)$$

where dummy Tr_i indicates whether farmer i eventually adopted *Cry3Bb1*, $D_{i,T}$ are a series of period dummies and η_t is year dummies. We included interactions between dummy Tr_i and $D_{i,T}$ $(T=J_{0,i},...,-2,-1;\ J_{0,i}<0)$. According to the definition of dummies $D_{i,T}$, $D_{i,T}$ $(T<0)$ refers the year that is T years before the adoption. Therefore, we are estimating the adoption effect before adoption took place by adding the interactions between dummy Tr_i and $D_{i,T}$

($T<0$). When the coefficients of $Tr_i * D_{i,T}$ ($T<0$) are insignificantly different from zeros, we do not find violations of parallel trend.

3.4. IMPACT OF BT CORN ADOPTION ON INSECTICIDE USE

Our empirical findings are discussed in this section. We will explain the impact of *Cry3Bb1* corn on adopters' insecticide use and the spill-over effects on non-adopters' insecticide inputs. Table 22 shows the average marginal effects of *Cry3Bb1* adoption on adopters' insecticide use estimated by linear and Tobit models. Columns 1-2 show results from the linear model with two measures of insecticide use respectively. Columns 3-4 show results from the Tobit model with two measures of insecticide use. The average partial effect of *Cry3Bb1* corn adoption on insecticide use among adopters during the first six years of adoption is estimated to be significantly negative throughout all columns. That means during the first several years of adoption, *Cry3Bb1* corn adoption significantly reduced adopters' insecticide use. In earlier years of adoption, the average partial impact estimated from the Tobit model is greater than that from the linear model. In addition, the Tobit model results in a decreasing average partial effect trend, suggesting that the insecticide use reduction as a result of *Cry3Bb1* corn adoption is diminishing over years.

Table 22 Average partial effect of *Cry3Bb1* corn on adopters' insecticide use

	(1)	(2)	(3)	(4)
Variables	Linear (lb/acre)	Linear (EIQ)	Tobit (lb/acre)	Tobit (EIQ)
Tr # D_1	-0.0296***	-0.0259***	-0.0430***	-0.0424***
	(0.00467)	(0.00478)	(-10.21)	(-10.42)
Tr # D_2	-0.0284***	-0.0256***	-0.0401***	-0.0397***
	(0.00502)	(0.00495)	(-6.13)	(-6.27)
Tr # D_3	-0.0283***	-0.0234***	-0.0364***	-0.0347***
	(0.00541)	(0.00584)	(-5.03)	(-4.82)
Tr # D_4	-0.0308***	-0.0259***	-0.0407***	-0.0390***
	(0.00527)	(0.00594)	(-4.95)	(-4.75)
Tr # D_5	-0.0334***	-0.0294***	-0.0433***	-0.0421***
	(0.00536)	(0.00559)	(-4.80)	(-4.76)

Table 22 (cont'd)

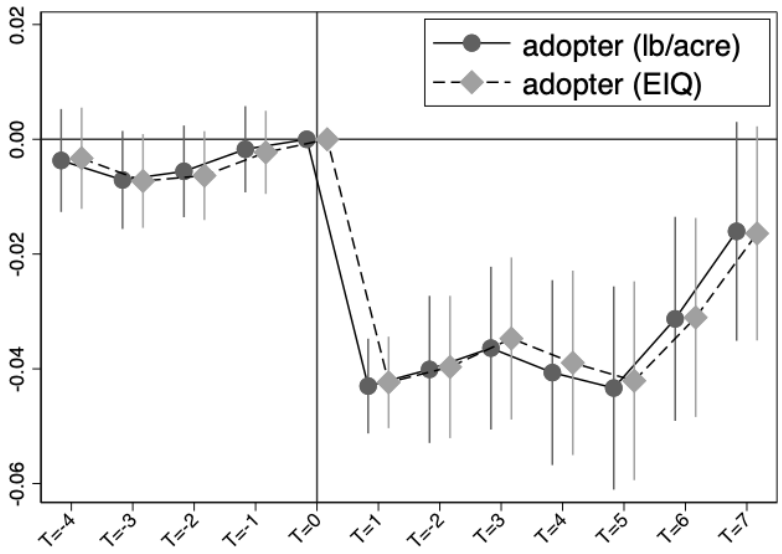
Tr # D_6	-0.0322***	-0.0308***	-0.0313***	-0.0310***
	(0.00610)	(0.00578)	(-3.45)	(-3.51)
Tr # D_7	-0.0298***	-0.0307***	-0.0160	-0.0164
	(0.00722)	(0.00660)	(-1.65)	(-1.72)
Tr # D_{-1}	0.00112	-0.000931	-0.00174	-0.00228
	(0.00729)	(0.00656)	(-0.45)	(-0.62)
Tr # D_{-2}	0.00131	-0.00101	-0.00559	-0.00633
	(0.00710)	(0.00669)	(-1.37)	(-1.60)
Tr # D_{-3}	0.00284	0.00274	-0.00708	-0.00726
	(0.00787)	(0.00718)	(-1.63)	(-1.74)
Tr # D_{-4}	0.00406	0.00708	-0.00369	-0.00331
	(0.00821)	(0.00852)	(-0.81)	(-0.73)
N	50649	50649	50649	50649

t statistics in parentheses * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Figure 19 illustrates the average partial effect of *Cry3Bb1* adoption on adopters' WCR-targeting insecticide use from the Tobit model. The dark solid line with dots indicates the amount of insecticide use per acre patterns and the light dashed line with diamonds indicates the pattern of the environmental and health impact caused by insecticide use. The short vertical lines going through the dots represent standard errors of the average partial effects estimations. Taking WCR-targeting insecticide use in the year preceding the adoption (T=0) as the reference level, we see a decrease in insecticide use caused by *Cry3Bb1* adoption. In addition, the magnitude of the reduction decreases as T increases. One explanation for the upward trend after T=0 is the advent of WCR resistance (Shrestha, Gassmann and Anderson 2019). We also observe evidence suggesting no violations of parallel trend assumption from Figure 19. That is, in the years preceding the adoption the average partial effect is insignificantly different from zero. One may notice that we included five periods preceding the adoption but more post-adoption years. This is because *Cry3Bb1* Bt corn was first adopted in 2003 and the records in the dataset are starting from 1998. We also ran the placebo test. The F-statistics with clustered robust standard errors is 0.03 so

that we cannot reject the null hypothesis that the coefficients are zeros at 5% level. Therefore, the placebo test result suggests no violation of parallel trend assumption.

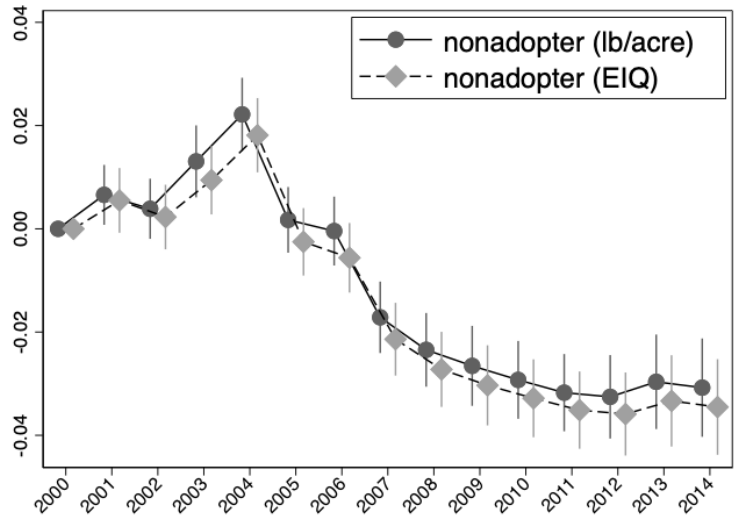
Figure 19 The impact of Cry3Bb1 on insecticide use among adoters



Note: (1) The dark solid line with dots indicates the amount of insecticide use per acre patterns; the light dashed line with diamonds indicates the pattern of the environmental and health impact caused by insecticide use. The short vertical lines going through the markers represent standard errors of average partial effects estimation.
(2) The year preceding adoption is defined as $T=0$, the first year of adoption is defined as $T=1$, the two years preceding adoption is defined as $T=-1$. The same logic applies to definition of T $(-4<T<7)$.

Cry3Bb1 adoption also has spill-over effects on non-adopters. Were Bt adoption to suppress pest population, then non-adopters would eventually reduce insecticide use. We also graph the estimated coefficient of year dummies in Figure 20, enabling a better vision about non-adopters' insecticide use patterns.

Figure 20 Year-specific insecticide use trend by non-Bt corn farmers



Note: The dark solid line represents the quantity of insecticide use per acre patterns and the light dashed line represents the pattern of the environmental and health impact caused by insecticide use. The short vertical lines illustrate standard errors of average partial effects estimation.

Similar to Figure 19, the dark solid line represents the quantity of insecticide use per acre patterns and the light dashed line represents the pattern of the environmental and health impact caused by insecticide use. The vertical short lines illustrate standard errors of average partial effects estimation. There is a downward trend in insecticide use by non-adopters. The reduction in insecticide use is generally consistent with the suppression effect mentioned above (Dively et al. 2018b). To better understand Figure 20, in the section to follow we set up a Bayesian learning model.

3.5. THEORETICAL MODEL

Farmers are uncertain about pest pressure and therefore, according to available information, form beliefs about the amount of insecticide use, θ, that maximizes yield. We show that farmers, as expected utility maximizers, will adjust their insecticide use decisions based on beliefs about θ. Bayesian learning takes place over years, and so we modeled after Perry, Hennessy, and Moschini's (2021) but relaxed the risk neutral assumption used in their setting. We show that the

risk averse farmers' beliefs converge to the true value as information accrues. Bt adoption may suppress pest populations (Tinsley et al. 2018), resulting in a lower θ when compared with historic levels. By relying on historical data, farmers' priors are likely to exceed the true value. In that case, we proved that, along with Bayesian learning, insecticide use by risk averters will start from a high level and decrease until farmers' beliefs eventually converge to the true value. This finding is consistent with the decreasing trend until it bottoms out at a low level of insecticide use as seen in Figure 20. In this section we construct a theoretical model in two parts. We first solve for an expected utility maximizing farmer's optimal insecticide input choice and then investigate how Bayesian learning about pest pressure affects optimal insecticide choice.

3.5.1. OPTIMAL INSECTICIDE DECISIONS

Farmers choose insecticide use levels to maximize their expected utilities from corn production. The analysis in this paper consists of insecticide use by many farmers, each choosing over one or more plots, and over several years. For clarification reasons, we will first introduce a theoretical model of a single farmer on a given plot with a given level of western corn rootworm pressure. We assume a yield function

$$Q = A - \frac{1}{2}(\theta - z)^2, \tag{3.11}$$

where θ is yield-maximizing insecticide input level, z is the actual insecticide input level, and A is the maximum yield under ideal conditions. When the actual insecticide input level $z = \theta$, farmers can achieve maximum yield A. Instead of using a damage abatement framework to model how insecticide use affects yield (Mutuc, Rejesus and Yorobe 2011; Lichtenberg and Zilberman 1986; Qaim and de Janvry 2005; Babcock, Lichtenberg and Zilberman 1992), we apply quadratic yield functions since: 1) quadratic yield functions can be second order approximations of any smooth yield function; 2) their corresponding optimal insecticide input function for risk averse

farmers can be solved in analytical closed form (Devilliers and Carpentier 2019). Accordingly, profit can be expressed as

$$profit = p\left[A - \frac{1}{2}(\theta - z)^2\right] - \omega z, \tag{3.12}$$

where p is output price and ω is insecticide price. To account for farmers' risk aversion, we first introduced a constant absolute risk averse (CARA) utility function in insecticide use decisions. Specifically, the utility function can be written as

$$U(profit) = -e^{-\lambda * profit}, \tag{3.13}$$

with $\lambda > 0$. As a utility maximizer with full information, the optimal insecticide input level is

$$z^* = \theta - \frac{\omega}{p}. \tag{3.14}$$

In the case of a lack of complete information, farmers are uncertain about pest pressure in the locality, therefore yield-maximizing insecticide input level, θ. Yield-maximizing insecticide input level is a random variable for farmers, denoted as $\tilde{\theta}$. We assume that $\tilde{\theta}$ has a normal distribution as

$$\tilde{\theta} \sim N(\bar{\theta}, \sigma^2). \tag{3.15}$$

Mean of the distribution is $\bar{\theta}$ and the standard deviation is σ^2. Therefore, farmer's expected utility maximization problem is

$$\max_z E\left(-e^{-\lambda * profit}\right) = \max_z \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{\infty} -e^{-\left\{\lambda\left\{p\left[A - \frac{1}{2}(\theta - z)^2\right] - \omega z\right\} + \frac{(\tilde{\theta} - \bar{\theta})^2}{2\sigma^2}\right\}} d\tilde{\theta}. \tag{3.16}$$

We provide a detailed solution to the utility maximization problem in the appendix. The optimal insecticide input level is

$$\bar{z}^* = \bar{\theta} - \frac{\omega}{p} + \omega\lambda\sigma^2. \tag{3.17}$$

We show that farmers' risk parameters (λ) and beliefs about yield-maximizing insecticide input level, $\tilde{\theta}$, will affect insecticide use decisions. In addition, input and output price (p and ω) also play a key role in those decisions. Specifically, farmer's optimal insecticide use increases with the expectation and variance of yield maximum insecticide use, i.e., $\bar{\theta}$ and σ^2. As information about yield-maximizing insecticide input level accrued, farmers will update their beliefs about $\tilde{\theta}$ and adjust their insecticide use accordingly.

3.5.2. BAYESIAN LEARNING PROCESS

Suppose the farmer learns about $\tilde{\theta}$ over time. In each period t, the farmer will receive a signal s_t about the true θ, as shown in equation (3.18),

$$s_t = \theta + \varepsilon_t. \tag{3.18}$$

For adopters, we assume the yield-maximizing insecticide input level, θ_a, increases over years due to Bt resistance development in equation (3.19),

$$\theta_a(t) = \theta_n\left(1 - re^{-t}\right); \tag{3.19}$$

where θ_n is the yield-maximizing insecticide input level for non-adopters, and r is a parameter for Bt resistance evolution. As t goes to infinity, $\theta_a \to \theta_n$. The signal is noisy; therefore, we assume ε_t to be an i.i.d. normal across periods,

$$\varepsilon_t \sim N(0, \upsilon^2). \tag{3.20}$$

Recall that in equation (3.15) we assume a normal distribution for the farmers' prior $\tilde{\theta}$. Then, the posterior $\tilde{\theta}_t$ also follows a normal distribution (Perry et al. 2021) with mean, $\bar{\theta}_t$, and variance, σ_t^2, specified in equations (3.21) and (3.22),

$$\bar{\theta}_t = \frac{\upsilon^2}{\sigma_{t-1}^2 + \upsilon^2}\bar{\theta}_{t-1} + \frac{\sigma_{t-1}^2}{\sigma_{t-1}^2 + \upsilon^2}s_t, \quad t \in \{1, 2, \ldots\}; \tag{3.21}$$

$$\frac{1}{\sigma_t^2} = \frac{1}{\sigma_{t-1}^2} + \frac{1}{\upsilon^2}. \tag{3.22}$$

Therefore, farmers' belief about the variance of yield-maximizing insecticide input level decreases as information accrued. From equation (3.22), we can write variance σ_t^2 as in equation (3.23), suggesting that the variance converges to zero when t goes to infinity,

$$\sigma_t^2 = \frac{\upsilon^2 \sigma_0^2}{\upsilon^2 + t\sigma_0^2}. \tag{3.23}$$

Then, we transformed equation (3.21) by incorporating equation (3.22) and developed equation (3.24),

$$\bar{\theta}_t = \frac{\sigma_t^2}{\sigma_0^2}\bar{\theta}_0 + \frac{\sigma_t^2}{\upsilon^2}\left(\sum_{k=1}^{t} s_k\right), \quad t \in \{1, 2, \ldots\}; \tag{3.24}$$

By inserting equation (3.18) and (3.23) into equation (3.24), we have equation (3.25) for non-adopters,

$$\bar{\theta}_t = \frac{\upsilon^2 \bar{\theta}_0}{\upsilon^2 + t\sigma_0^2} + \frac{t\sigma_t^2}{\upsilon^2}\left(\theta_n + \frac{\sum_{k=1}^{t} \varepsilon_k}{t}\right), \quad t \in \{1, 2, \ldots\}. \tag{3.25}$$

When we inserted equation (3.23) into equation (3.25), we see

$$\bar{\theta}_t = \frac{\upsilon^2 \bar{\theta}_0}{\upsilon^2 + t\sigma_0^2} + \frac{t\sigma_0^2}{\upsilon^2 + t\sigma_0^2}\left(\theta_n + \frac{\sum_{k=1}^{t} \varepsilon_k}{t}\right), \quad t \in \{1, 2, \ldots\}. \tag{3.26}$$

As t goes to infinity, non-adopters' beliefs about the expectation of yield-maximizing insecticide input $\bar{\theta}_t$ will converge to the true θ_n. Inserting equation (3.18), (3.19) and (3.23) into equation (3.24), we have equation (3.27),

$$\bar{\theta}_t = \frac{\upsilon^2 \bar{\theta}_0}{\upsilon^2 + t\sigma_0^2} + \frac{t\sigma_t^2}{\upsilon^2}\left(\theta_n - \frac{\sum_{k=1}^{t} re^{-k}}{t} + \frac{\sum_{k=1}^{t} \varepsilon_k}{t}\right), \quad t \in \{1, 2, \ldots\}. \tag{3.27}$$

According to Stolz–Cesàro theorem, $t^{-1}\sum_{k=1}^{t} re^{-k} \to 0$ as t goes infinity. Therefore, adopters'

beliefs about the expectation of yield-maximizing insecticide input will converge to the true θ value as more signals are observed over time.

Recall from equation (3.17), farmer's insecticide use increases with her perceived $\bar{\theta}_t$ and σ_t^2. The trend of $\bar{\theta}_t$ depends on the relationship between the initial guess, $\bar{\theta}_0$, and the true value, θ, while σ_t^2 decreases over periods. Supposing that $\bar{\theta}_0 > \theta$ then we are likely to observe a downward trend in farmer's insecticide input level, while, when $\bar{\theta}_0 < \theta$, the trend of farmer's insecticide input is not straightforward from the theoretical model. This is because, in that case, increasing perceived expectation pushes insecticide input upward and shrinking variance pushes insecticide input downward. We need more information to tell which dominates the trend of insecticide use.

3.6. CONCLUSION

Bt crops have been widely used for pest control as a substitute for chemical insecticide use. As pest damage to Bt crops emerges and increases, regulations regarding Bt resistance management have expanded across countries and over years, focusing on delaying Bt resistance development. On the other hand, Bt crops bring external benefits on health and environment through reducing insecticide use among adopters and non-adopters. Therefore, it is important to justify and evaluate all externalities associated with Bt crops before making regulation decisions. In this study, we investigate the long-term impact of *Cry3Bb1* corn on insecticide use among adopters and non-adopters over years. In addition, we measure insecticide use of the same two groups in terms of health and environmental impacts.

In the empirical analysis, we find that the adoption of *Cry3Bb1* corn successfully reduces farmers' insecticide input, suggesting that Bt toxins can be substituted for chemical insecticides in the suppression of western corn rootworm. The amount of insecticide reduction decreases as

Cry3Bb1 corn is planted over the years. This diminishing impact of *Cry3Bb1* corn is consistent with the emergence of western corn rootworm resistance. We also observe a downward trend in insecticide use by non-adopters, which is consistent with the spill-over effects of Bt toxin documented in extant literature. Supposing that *Cry3Bb1* adoption suppresses pest populations within the region, non-adopters initially lack full knowledge of the Bt pest suppression effects but eventually learn about the pest pressure over time and ultimately reduced insecticide use. By relying on historical data, farmers' prior beliefs are likely to exceed the true pest pressure. In that case, following the Bayesian learning process, insecticide use by risk averters will start from a high level and decrease until farmers' beliefs eventually converge with to the true pest pressure. This pattern is the same as what is found in our empirical analysis. The findings should be of interest to those concerned with the ecosystem services provided by insects, integrated pest management (IPM) regulators and practitioners, as well as others interested in the stewardship of biological resources.

APPENDIX

Inserting farmer's profit function (3.12) into utility function (3.13) and writing the expected utility as an integral of utility with respect to variable $\tilde{\theta}$, we have farmer's utility maximization problem

$$\max_{z} \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{\infty} -e^{-\lambda\left\{pA-\frac{1}{2}p\left(\tilde{\theta}-z\right)^2-\omega z\right\}} e^{-\frac{\left(\tilde{\theta}-\bar{\theta}\right)^2}{2\sigma^2}} d\tilde{\theta}. \tag{A.1}$$

We transform the objective function into an equivalent form following approach used in finance theory under normal random variables and CARA (Cochrane 2005). Rewrite the exponent in equation (A.1) to group terms that depend on $\tilde{\theta}$ and terms that don't depend on $\tilde{\theta}$.

$$\begin{aligned} &-\lambda\left\{pA-\frac{1}{2}p\left(\tilde{\theta}-z\right)^2-\omega z\right\}-\frac{\left(\tilde{\theta}-\bar{\theta}\right)^2}{2\sigma^2} \\ &=-[\lambda pA-\frac{1}{2}\lambda pz^2-\lambda\omega z+\frac{(1-\lambda p\sigma^2)\tilde{\theta}^2-(2\bar{\theta}-2\lambda pz\sigma^2)\tilde{\theta}+\bar{\theta}^2}{2\sigma^2}]. \end{aligned} \tag{A.2}$$

Then our target is to write $(1-\lambda p\sigma^2)\tilde{\theta}^2-(2\bar{\theta}-2\lambda pz\sigma^2)\tilde{\theta}+\bar{\theta}^2$ in the form of $\left(a\tilde{\theta}-b\right)^2+c$. We first define

$$\alpha=1-\lambda p\sigma^2; \tag{A.3}$$

$$\beta=2\bar{\theta}-2\lambda pz\sigma^2; \tag{A.4}$$

$$\gamma=\bar{\theta}^2. \tag{A.5}$$

Since

$$(a\tilde{\theta}-b)^2+c=a^2\tilde{\theta}^2-2ab\tilde{\theta}+b^2+c, \tag{A.6}$$

we can map

$$a^2=\alpha=1-\lambda p\sigma^2; \tag{A.7}$$

$$\beta=2\bar{\theta}-2\lambda pz\sigma^2=2ab; \tag{A.8}$$

$$\gamma=\bar{\theta}^2=b^2+c. \tag{A.9}$$

Therefore, we can obtain

$$a = (1 - \lambda p \sigma^2)^{0.5} \quad \text{assuming } 1 \geq \lambda p \sigma^2; \tag{A.10}$$

$$b = \frac{\bar{\theta} - \lambda p z \sigma^2}{(1 - \lambda p \sigma^2)^{0.5}} \quad \text{assuming } 1 \geq \lambda p \sigma^2; \tag{A.11}$$

$$c = \bar{\theta}^2 - \frac{\left(\bar{\theta} - \lambda p z \sigma^2\right)^2}{1 - \lambda p \sigma^2}. \tag{A.12}$$

Then maximization problem becomes $\max_z \lambda pA - \lambda pAz^2 - \lambda \omega z + \frac{c}{2}$ (A.13)

$$\max_z \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{\infty} -e^{-\left[\lambda pA - \frac{1}{2}\lambda p z^2 - \lambda \omega z + \frac{\left(a\tilde{\theta} - b\right)^2 + c}{2\sigma^2}\right]} d\tilde{\theta}. \tag{A.14}$$

After some transformation, we have

$$\begin{aligned} &\max_z \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{\infty} -e^{-\left[\lambda pA - \frac{1}{2}\lambda p z^2 - \lambda \omega z + \frac{\left(a\tilde{\theta} + b\right)^2 + c}{2\sigma^2}\right]} d\tilde{\theta} \\ &== \max_z -\frac{1}{a} \frac{e^{-\left[\lambda pA - \frac{1}{2}\lambda p z^2 - \lambda \omega z + \frac{c}{2\sigma^2}\right]}}{\sigma\sqrt{2\pi}} \int_{-\infty}^{\infty} -e^{-\left[\frac{\left(a\tilde{\theta} - b\right)^2}{2\sigma^2}\right]} d(a\tilde{\theta} - b). \end{aligned} \tag{A.15}$$

The integral part embedded in equation (A.15) is the area under the normal distribution density function over the entire support when the mean is zero and the standard deviation is σ. That said,

$$\frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{\infty} -e^{-\left[\frac{\left(a\tilde{\theta} - b\right)^2}{2\sigma^2}\right]} d(a\tilde{\theta} - b) = 1. \tag{A.16}$$

So when we insert equation (A.16) into equation (A.15), maximization problem becomes

$$\max_z -\frac{1}{a} e^{-\left[\lambda pA - \frac{1}{2}\lambda p z^2 - \lambda \omega z + \frac{c}{2\sigma^2}\right]}, \tag{A.17}$$

which is equivalent to

$$\max_{z}(\lambda pA-\frac{1}{2}\lambda pz^{2}-\lambda\omega z+\frac{c}{2\sigma^{2}}). \tag{A.18}$$

Now we insert equation (A.12) into maximization problem (A.18) and solve for the first order condition:

$$-2\lambda pz-\lambda\omega+\frac{1}{2\sigma^{2}}\left[-\frac{2\lambda p\sigma^{2}}{1-\lambda p\sigma^{2}}\left(\lambda p\sigma^{2}z-\bar{\theta}\right)\right]=0. \tag{A.19}$$

At the end, we can obtain optimal input level

$$z^{*}=\bar{\theta}-\frac{\omega}{p}+\omega\lambda\sigma^{2}. \tag{A.20}$$

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