Five Applications of Data Analysis in Interdisciplinary Research

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„Animals, like man, feel pleasure and pain, happiness and misery.“

– Darwin, 1871

to my fury feel-good managers

Schildi, Jöra, Kiana, Maddie, Fee, Globuli, Omar, Panda, Toni, Holly and Eddy.

First Reviewer: Prof. Dr. Peter Winker

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List of Abbreviations

ANOVA	analysis of variance
COVID-19	coronavirus disease of 2019
GER	Germany
DIMDI-AMV	Deutsches Institut für medizinische Dokumentation und Information – Arzneimittelverordnung
d	days
d/yr	days per year
eCG	equine chorionic gonadotropin
EMA	European Medicines Agency
Eq.	equation
EU	European Union
GDP	gross domestic product
GHSI	global health security index
GNI	gross national income
GnRH	gonadotropin-releasing hormone
ha	hectare
HAQI	health access and quality index
HI-Tier	Herkunftssicherungs- und Informationssystem für Tiere
JHU	Johns Hopkins University
kg	kilograms
LASSO	least absolute shrinkage and selection operator
LU	livestock unit
MIA	medically important antimicrobials for human medicine
mo	month
NOEC	no observed effect concentration
NPI	non-pharmaceutical intervention
NSAID	non-steroidal anti-inflammatory drug
OLS	ordinary least squares
OOPs	out-of-pocket payments
PCU	population correction unit
PEC	predicted environmental concentration
PECgroundwater	predicted environmental concentration in groundwater
PECsoil	predicted environmental concentration in soil
PECsurfacewater	predicted environmental concentration in surfacewater
PNEC	predicted no effect concentration
PYLL	potential years of life lost

RESET	regression equation specification error test
SIR	susceptible-infected-removed
t	tons
TAB	treatment frequency for antibiotics
TAP	treatment frequency for antiparasitics
TAPH	treatment frequency for antiphlogistics
TH	treatment frequency for hormones
TO	overall treatment frequency
US	United States of America
VAR	vector autoregressive
WHO	World Health Organization
yr	year

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Chapter 1

Preface

The beginning of any doctoral study commences with the critical phase of topic exploration. While some people effortlessly identify their research focus due to early-developed interests or clearly defined areas of specialization, others encounter greater difficulty in this endeavor. Even as academia predominantly shifts away from the monograph format and gravitates toward the cumulative dissertation comprising multiple projects, the issue of topic selection remains pertinent and, for some, amplified. This evolution, however, also offers the opportunity to contribute across various thematic domains. One may begin exploring within sub-disciplines that were previously aligned with academic strengths or reflected personal interests during previous studies. Fortunately, I found excitement in several topics, culminating in this colorful bouquet of topics in my dissertation titled *"Five Applications of Data Analysis in Interdisciplinary Research"*.

The following chapters present five papers compiled for my dissertation. The title page of each chapter provides insight into the co-authors and the publication status alongside the title. Despite their content diverging considerably, a few common threads can be identified. All five papers (Chapters 2–6) are in part empirical works that encompass not only theoretical considerations but rely on data analyses as well. Broadly, four papers (Chapters 3–6) can be categorized under the theme of health economics. Two of these papers primarily delve into the field of human medicine (Chapters 3 and 4), while the other two are rooted in the realm of veterinary medicine (Chapters 5 and 6), whereby Chapter 6 includes a detour into environmental sciences as well.

All five of my papers are centered around contemporary societal topics widely recognized through media coverage. Consequently, they serve as catalysts for stimulating and engaging in-depth societal discourse. In the following, I will briefly introduce each paper in order to motivate the reader for the individual papers in the main body of this dissertation.

In determining the subjects that make headlines, the criterion often revolves around what's "true, new, relevant" (Leidecker-Sandmann et al., 2023). Hence, Chapter 2 of this doctoral thesis, in collaboration with Natalja Menold from the Technical University Dresden and Peter Winker as holder of the Chair for Statistics and Econometrics, is titled *"The Impact of Statistical Literacy and Economic Incentives on the (Mis-) Use of Survey Based Statistics in Media Reporting - A Framework"* and delves specifically into the inquiry of which survey results gain prominence in the media. Within this chapter, we scrutinize the definition of a survey, its commissioners, the demographics of respondents, and the ensuing implications. Our focus extends to analyzing the conduct of various stakeholders, ranging from survey creators to media entities and readers, while also evaluating the incentive structures interwoven within this framework. For the empirical part, we analyze a sample of DER SPIEGEL articles for survey reporting standards.

The subsequent chapters of my dissertation are similarly influenced by media discourse. At the outset of my doctoral studies in January 2020, the emergence of the coronavirus disease of 2019 (COVID-19) pandemic began to unfold. Initially dismissed by many (in retrospect, erroneously), this novel disease rapidly escalated into a global crisis. Chapter 3, entitled *"The Die is Cast - Factors Influencing Mortality during the COVID-19 Pandemic"*, delves into an analysis conducted in collaboration with my colleague Jennifer Muschol from the Chair of Health Economics. We examine the disparate spread of infection and mortality rates across various countries worldwide. During this period, numerous forecasts and expert opinions attempted to elucidate the varying degrees of impact on different nations, with multifaceted explanations for these differences. Our methodology involved utilizing cross-sectional datasets, employing OLS estimations at the country level, and leveraging existing health indices to ascertain the levels of impact worldwide.

Over time, the focus shifted away from whether a country would be affected by the virus, as it became evident that virtually all nations were impacted. Nonetheless, diverse political and societal strategies emerged to address the situation. An array of non-pharmaceutical intervention (NPI)s were increasingly implemented by policymakers to mitigate the course of the pandemic. Often cited as extremes in this context are Sweden, known for its notably liberal COVID-19 policies, and China, recognized for its stringent containment measures in affected areas. Ultimately, there was limited preexisting evidence regarding the effectiveness of these measures in containing the virus's spread. A study conducted in the United States of America (US) examined specific interventions across states during the pandemic's first year, deriving conclusions about their efficacy (Chernozhukov et al., 2021). In Chapter 4, titled *"Causal Impact of Policy Measures and Behavior on the COVID-19 Pandemic in Germany"*, I endeavored to explore this for Germany. Utilizing a panel dataset organized by federal states and daily observations, I investigated whether the implemented measures themselves led to increased social distancing and consequently contributed to curbing the pandemic's spread. Moreover, I explored whether individuals, driven by factors such as fear of the disease or other reasons, autonomously engaged in more social distancing practices, thus influencing the containment efforts independently of official mandates.

Following two years of a pandemic-induced state of shock, my dissertation also encompasses the post-pandemic period, reflected in Chapters 5 and 6. During this phase, attention returned to different topics that had been overshadowed during the COVID-19 era. Particularly, sustainable issues regained prominence with the resurgence of interest in movements like Fridays for Future, reigniting discussions on energy, nutrition, and environmental pollution. Chapter 5, titled *"Survey of drug use and its association with herd-level and farm-level characteristics on German dairy farms"*, represents a collaborative effort involving Mies Abdallah and Melanie Hamann from the Department of Veterinary Medicine, Felix Tettenborn from the Fraunhofer Institute, and Arne Hein from the Federal Environment Agency. Stemming from an overarching objective to comprehend and quantify pharmaceutical emissions within veterinary medicine, our focus was directed toward agricultural livestock. As an economist, it was concerning to observe the lack of available data on the use and consumption of veterinary pharmaceuticals in livestock farming. Conducting a survey across fifty dairy farms provided insights into the types of veterinary pharmaceuticals used, their frequency of use within a year, and the quantities administered. Leveraging survey data, descriptive statistics, and basic OLS regressions on farm characteristics such as the number of animals kept or the type of husbandry, we aimed to derive potential determinants influencing pharmaceutical usage within these agricultural settings.

Chapter 5 shed light on the specific veterinary pharmaceuticals used, yet the repercussions on human health, nature, and the environment remained ambiguous. Consequently, Chapter 6, titled *"Pharmaceutical Consumption in Human and Veterinary Medicine in Germany: Potential Environmental Challenges"*, embarked on a subsequent project involving Mies Abdallah, Melanie Hamann, Felix Tettenborn and Arne Hein. Employing a One Health approach, this chapter aimed to amalgamate insights gleaned from the utilization of human and veterinary pharmaceuticals. The effort involved cross-referencing these insights with water and soil samples to offer a comprehensive overview of environmental impacts arising from pharmaceuticals use. By extrapolating data from our own survey, data from the pharmaceutical industry, and metadata regarding environmental harm, we aimed to contribute to a more holistic understanding of the issue. However, the risk posed by individual substances in the environment can only be assessed to a limited extent, while its complexity requires further research efforts.

Chapter 7 serves as my concluding remarks, offering a succinct summary of the research findings and their implications.

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Chapter 2

The Impact of Statistical Literacy and Economic Incentives on the (Mis-)Use of Survey Based Statistics in Media Reporting – A Framework

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not yet submitted
Bethäuser, J., Menold, N., & Winker, P. (2024). The Impact of Statistical Literacy and Economic Incentives on the (Mis-) Use of Survey Based Statistics in Media Reporting – A Framework. will be submitted to *Public Opinion Quarterly*.

Abstract

Survey results are frequently reported in the media, often without providing enough background information to allow a judgment on the methodological quality of the results and its implications. This might be due to a lack of statistical literacy at different stages of the process of generating and reporting about the data as well as to economic incentives. We provide a framework for describing these effects, their interactions, and the expected implications. This framework might serve as foundation for a subsequent empirical analysis of the factors driving media reporting based on survey statistics.

2.1 Introduction

Headlines in the media landscape serve as powerful tools to captivate readers, pique their curiosity, and encourage them to delve deeper into the subject matter. Regardless of whether one navigates the world of traditional print media, such as newspapers and magazines, or ventures into the realm of online publications, headlines play a significant role in shaping readers' perceptions and interests. Frequently, survey results emerge as compelling hooks or titles, further enhancing the allure of the news articles or reports they accompany. Surprising or negative news seem to have more impact than those confirming previous findings or those with a rather positive connotation. For example, Robertson et al. (2023) show based on more than 20,000 controlled trails that for an online headline of average length, the click-through rate increases by about 2.3% for each additional negative word providing empirical evidence for the folk wisdom that "only bad news are good news".

When it comes to socioeconomic issues of current interest, citing survey results seems to provide some sort of scientific evidence, even if they are, at least in part, triggered by the media themselves. In a limited sample of articles from DER SPIEGEL, which will be examined in greater detail in section 2.4, it was observed that roughly 10% of the articles containing the keyword "survey" were based on studies commissioned by DER SPIEGEL itself.

As an illustrative example demonstrating the utilization of study findings as evidence for factual assertions we consider a recent communication by Plan International. On its website, Plan International captured the reader's attention with the slogan that one-third of surveyed men have resorted to physical violence towards women in an attempt to instill respect and perceive occasional physical altercation with their partners as acceptable (Hofmann et al., 2023). Official statistics present a different perspective and receive less media attention. For example, the Federal Ministry for Family Affairs, Senior Citizens, Women and Youth (2019) states in its Gender Equality Report that a quarter of all adult women have experienced physical and/or sexualized violence by an intimate partner at least once. According to the official police statistics, the situation report on domestic violence indicates that one-sixth of all registered victims fall under the category of violence within partnerships (Federal

Criminal Police Office, 2023). Two questions arise in this context: The first concerns the potential explanations for the discrepancies observed among the figures — specifically, the variation between one-third, one-fourth, and one-sixth — while the second question focuses on how these studies were received and portrayed in the media. Regrading the first issue, in the fine print, Plan International indicates that the published statement is based on an online survey conducted by a market research institute, comprising 1,000 men and women on the topic of masculinity. The study claims to be representative in terms of gender, educational status, location, and age within the 18 to 35-year-old cohort. In essence, the survey notably centered on a particular age group, likely more susceptible to the issue, thereby potentially amplifying the impact of the remarkably negative findings and to make the strikingly negative outcome more headline-worthy. Yet, it is important to note that this approach might have introduced a strong self-selection bias among participants, particularly within an online survey format. This bias occurs when individuals within the targeted age group are more inclined to participate due to their higher relevance or interest in the issue, possibly skewing the results and limiting their generalizability to the broader population. Regarding the second question, there does not seem to exist example empirical evidence on which survey based results make it into the news apart from such individual case descriptions. Furthermore, for published results, additional information about the statistical framework of the analysis, e.g., the questionnaire or sampling information, is not always provided. Again, not much is known about when additional information is provided and whether this might be taken as positive evidence for a higher quality of the performed analysis. Finally, nothing is known about a potential link between perceived (by the media) or actual (according to scientific standards) quality of survey findings and the probability of reports about these findings in the media.

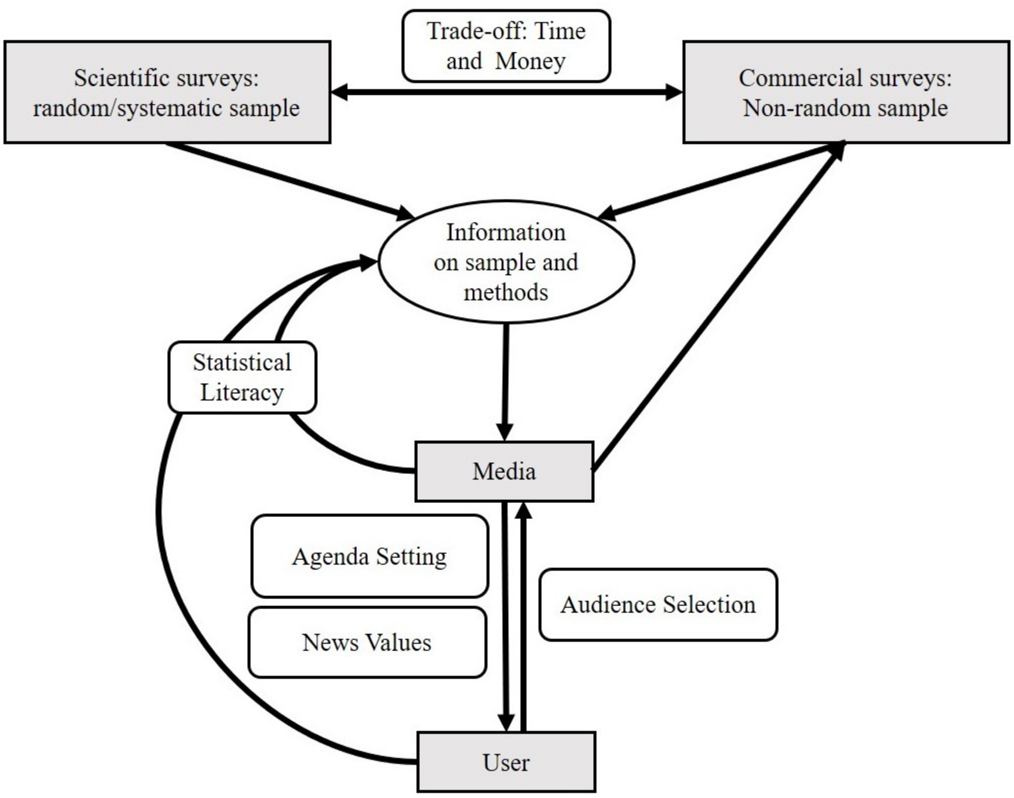
To close these knowledge gaps, we address the following two goals. First, we describe the economic incentive structure for the whole pipeline from running a survey (be it in a scientific setting or targeted for media use from the onset) to the eventual media coverage. Thereby, we describe who is doing what and why? Second, we also want to take into account the level of statistical literacy available for different actors in the process and for the final recipients of the news, which might have an influence both on the quality of the studies and the reporting of results. Addressing these issues in a common framework might serve as foundation for a subsequent empirical analysis.

The paper is structured as follows. In Section 2.2 we describe the economic incentives of different actors along the path from running a survey to its media coverage. Section 2.3 is doing the same with regard to the statistical literacy of actors, i.e. their capabilities of assessing both the quality of methods and the possible conclusions from a survey. In Section 2.4, we dive into empirical literature and examine articles from DER SPIEGEL that discuss survey results. Section 2.5 concludes and indicates how future empirical research might quantify the impact of different actors in our framework.

2.2 Economic Incentives

In order to investigate the pathways through which survey results make their way into headlines, we will analyze the various actors involved, as illustrated in Figure 2.1.

Figure 2.1: Theoretical framework on the question "Which survey results are published when, how, where and why?"



Surveys

Let us begin with the surveys themselves. A survey is a collection of questions designed to gather specific data from a particular group of individuals. Unlike opinion polls, which may require anonymous responses to one or a few questions, surveys are more comprehensive in nature. They are conducted through various methods such as interviews, telephone calls, mail, and internet-based platforms, with the objective of extrapolating the responses to the broader population. Surveys come in different types; the most extensive form is the census, also known as population count. Methodologically, a census involves a complete enumeration of the characteristics of the entire population. However, surveys often rely on samples, which are subsets of the population, as they are more practical and consume less time and resources. Nonetheless, the ultimate goal of sample-based surveys remains to make inferences about the entire population. To achieve this, it is crucial for the survey to be representative, meaning that the sample should mirror the characteristics of the population. This necessitates drawing a random sample from the population and understanding the process of sample selection, while also acknowledging and considering potential biases. At this point, we distinguish between scientific and commercial surveys. Scientific surveys generate results based on a random or at least systematic sample, while non-scientific surveys often employ a non-random sample (Kowalik, 2019). Examples of data sets based on random sampling include the European Labor Force Survey (Eurostat, n.d.), the Socio-Economic Panel (DIW Berlin, n.d.) in Germany, and the National Health Interview Survey (National Center for Health Statistics, n.d.) in the US. Many other smaller, quick and inexpensive surveys that lack randomness are often conducted by market research firms or other commercial entities (Kowalik, 2019) such as IQVIA[1], Gartner Inc.[2], and GfK[3] to name a few major players in the field.

Apart from participant selection, several other aspects must be considered to ensure the quality of survey data, which depends on several actors, their incentives and possible information asymmetries between them (Winker, 2016). It is imperative to acknowledge and address these aspects due to their profound implications for

[1] https://www.iqvia.com/
[2] https://www.gartner.com/en
[3] https://www.gfk.com/home

the objectivity, validity and reliability of survey research. Survey results can only be accurately and meaningfully evaluated within the framework of their underlying conditions and assumptions. For instance, failing to incorporate information on a non-random sample may lead to erroneous conclusions about the entire population. Furthermore, it is possible for implications to be mistakenly assessed as causal, even when such causality is not supported by the research methods and the result merely indicates a correlation.

Media

As we move further down in Figure 2.1, the second agent to emerge after the researchers conducting and analyzing surveys is the media. The term media refers to mass media, which are communication tools that convey content to an undetermined number of people through technical reproduction and distribution using text, images, or sound. Mass media encompass print media (e.g., pamphlets, posters, books, newspapers), audiovisual media like film, radio, and television, widely distributed storage media, and websites on the internet (Burkart, 2021). Common to all mass media is the aim to reach as many people as possible. Our focus centers on media that employ text, specifically print media and the internet. In contrast to print media, which seeks to maximize the number of copies sold, websites on the internet strive to maximize the number of clicks on their articles (Robertson et al., 2023).

The ultimate role of media and professional journalism is to inform citizens about the current issues in different areas of the political, economic and societal life. Therefore, the media plays a pivotal role in the dissemination of survey results to the public. Media reports, particularly news, claim to report proven information and facts, or provide their audience with different and diverse information to enable people to develop own informed decisions and opinions. In doing so, media reports claim to be objective, neutral, and critical according to Paul and Nisbett (2022).

In theory, Lippmann (1922) initially introduced the concept of news value, in order to provide an explanation for why journalists choose to cover certain events while overlooking many others. He posited that events become newsworthy due to specific attributes, later termed news factors, that make them stand out. Over time, the theory of news selection has made significant advancements. Östgaard

(1965) delved into the discussion of three categories of news factors – simplification, identification, and sensationalism – that contribute to an event's newsworthiness. Meanwhile, Galtung and Ruge (1965) went a step further by defining 12 news factors. Schulz (1976) took a different approach by defining news values as the hypotheses journalists form about the relevance of events. He developed interval scales to gauge the intensity of news factors and utilized the placement and length of news stories as indicators of their news value.

More recently, the two-component theory by Kepplinger and Ehmig (2006) offers an explanation and prediction of the newsworthiness of stories, which is the likelihood of these stories being chosen for publication. Central to their theory are news factors and news values. News factors represent the characteristics of news stories and can vary in their intensity. Their collective impact on the selection of news stories is referred to as news value. Unlike news factors, news values are not inherent qualities of news stories but rather reflect the judgments made by journalists regarding the relevance of these factors. However, it is important to note that Kepplinger and Ehmig (2006) acknowledge that news factors and their news values are not the sole determinants of decisions made in newsrooms. Other factors, such as the editorial stance of a newspaper, general preferences for specific topics, individual preferences of journalists, and external pressures from politics and business, are relevant among others.

In reality, the selection criteria in (quality) journalism and in research are fairly similar, as they seek to identify topics that are true, new, relevant and likely to resonate with their audience (Leidecker-Sandmann et al., 2023). The more an event satisfies these conditions, the more likely it is selected as news (Maniou & Papa, 2023). In the context of particularly time-sensitive subjects, it is noteworthy that high quality survey results are often absent due to the protracted nature of comprehensive, representative studies. Such studies demand a considerable investment of time and resources, leading to a time delay in the release of pertinent data. Moreover, the process of data analysis further exacerbates this temporal discrepancy. Consequently, media organizations employ pragmatic strategies, such as enlisting commercial service providers to execute surveys on their behalf, or in some instances, conducting surveys autonomously, as means to address this challenge.

User

The last agent considered in Figure 2.1 is the user of the media. In the past, the prevailing notion was that the user existed somewhat outside the sphere of influence when it came to determining the topics covered in daily newspapers. The editorial decisions seemed insulated from direct user input or feedback, positioning the audience as passive recipients rather than active participants in shaping the news agenda. The traditional belief held that journalists and editors dictated the content without immediate regard for the specific preferences or interests of the audience. However, the landscape has evolved, with the rise of user-centric approaches in news production acknowledging and incorporating the user's voice and preferences in shaping the stories that make it to print or digital platforms. Wendelin et al. (2017) explore current differences between journalistic news selection and selections of the audience using user rankings. The results show similarities in news values, but differences in preferred topics. While this user-centric approach empowers users with more control over their news consumption, it also challenges news organizations to balance audience demands with journalistic integrity and societal impact.

Until now, we have delineated the individual actors and examined how survey outcomes transition into news within the media and eventually reach the reader. Viewing Figure 2.1 from bottom to top prompts the question of whether both the reader and the journalist are indeed capable of accurately contextualizing and interpreting the information presented in surveys, assessing its nuances and implications.

2.3 The Impact of Statistical Literacy

Before addressing the role of statistical literacy in the context of media reporting and public understanding of survey based results on socioeconomic topics, we first have to introduce the concept of statistical literacy itself, which might be seen as a subset or derivative of the broader idea of scientific literacy. These two concepts will be introduced separately in Subsections 2.3.1 and 2.3.2. Subsequently, Section 2.3.3 will apply these concepts to the framework introduced in Subsection 2.2.

2.3.1 Scientific Literacy

The OECD (2015) defines scientific literacy as ”the ability to engage with science-related issues, and with the ideas of science, as a reflective citizen.”. Scientific literacy integrates aspects of literacy in writing, numeracy, and digital skills, focusing on the comprehension of science, including its methods, measurement techniques, units, observations, and theoretical frameworks. It involves foundational knowledge in key scientific domains like natural sciences and computer science as well. Overall, the concept of scientific literacy refers to the public understanding of science, which is a result of citizens' knowledge, beliefs and opinions about science (Miller, 2004). Scientific literacy reflects the level of scientific education and competences to gather and analyze information. It is a prerequisite for informed citizens' decisions, e.g. to vote for a political party or to accept governmental measures (Miller, 2004).

Referring to Figure 2.1, scientific literacy is pivotal at two junctures: amongst the media and journalists, as well as the end-users. Stephen et al. (2017) state that “Since most people do not read raw data-sets, journalism has a key role to play in the discovery, translation, and interpretation of statistics”. This highlights its significance in both disseminating and comprehending scientific information. The media report on current societal and economic issues and provide so called “hard news” or have the aim to trustworthy display the current situation, why they often refer to scientific information (see e.g., Paul and Nisbett (2022) for an overview). Therefore, journalists' competence in the selection, preparation and dissemination of scientific results might be a crucial feature as is their methodological background knowledge to evaluate the quality of statistics and studies they are referring to. Unfortunately, Zhang and Wang (2022) report, based on a survey conducted among 281 journalists from various countries, that these journalists possess only average information skills and statistical literacy. The findings of the survey indicate that a majority of the respondents (52%) acknowledge the significance of statistical literacy, while 38% believe that information literacy and skills are unnecessary for their job. However, the informed public should be provided with information that allows an assessment of the quality of the scientific and statistical data.

Apart from the journalists also the scientific literacy of the public is of interest for the present analysis. In past research, it was found to exhibit some deficiencies, but little more recent evidence seems to be available on this aspect. For example, in an early analysis for the U.S., Withey (1959) found that only 10% of respondents agreed to the statement that doing science also means to implement systematic and controlled variation. Durant et al. (1989) conducted a study in UK, where only 34% of participants responded correctly that earth orbits the sun once during the year. 28% knew that antibiotics kill bacteria but not viruses. Krause (2019) show that Americans' confidence in scientists has been high for roughly 40 years. Sturgis and Allum (2004) found a correlation between scientific literacy and political knowledge as well as with trust in science and institutional trust. Little trust in science was found to be associated with neglecting and rejection of established scientific knowledge and acceptance of conspiracy theories (Plutzer, 2013).

2.3.2 Statistical Literacy

Statistical literacy is a subdomain of scientific literacy (Miller, 2004). It refers specifically to the statistical knowledge and reasoning which is relevant to deal with statistical information and solve corresponding problems in all day situations. Gal (2002) describes statistical literacy — in a similar vein as scientific literacy — as one of the basic competences that is relevant to deal with information flow and to participate in the social life. Similarly to the concept of scientific literacy, statistical literary is conceptualized containing so called "knowledge" and "dispositional" elements, both relevant for informed problem solving, decisions, and statistically literate actions (Gal, 2002). Let's have a detailed look at those to categories: Knowledge elements encompass literacy skills, which include the ability to read and understand numeric data and their visual representations, as well as contextual knowledge in the form of basic scientific knowledge in the natural sciences. Additionally, mathematical and statistical knowledge is crucial, covering topics such as sampling, the research process and design, and statistical inference. This knowledge category also emphasizes the importance of critically questioning the given statistical information. In contrast, dispositional elements are less clearly delineated. These involve beliefs and attitudes, including the willingness to invest mental effort and the holding of beliefs and opinions with respect to the given methodologies. Overall, a critical stance is a significant component of these dispositional elements.

For understanding surveys, statistical literacy is relevant as it contains the knowledge and understanding of terms such as “data” and “variables”, knowledge about the research process including sampling, research design, instrumentation as well as knowledge about statistical inference (Scheaffer et al., 1998). Even if there are no statistical background information for the survey given, statistical literacy is helpful to contextualize results or to scruntinize how these results were generated.

2.3.3 The Interaction of Incentives and Statistical Literacy

Scientific and statistical literacy are relevant concepts for everyone in order to deal with informations flows in our daily lives. Unfortunately, the level of statistical literacy in the overall population is low (Durant et al., 1989; Withey, 1959) but generally improving as a linear trend since 1989 in Europe, Japan, China and the US (Bauer & Falade, 2014). The average user cannot understand survey results directly and relies on the information processing through journalists.

Upon receiving the research findings, journalists and media outlets critically assess the significance and newsworthiness of the survey results. Mass media organs prepare and present or even adequately translate and interpret professional research information. The reasons why and the extent to which this occurs vary according to the type of media, ranging from the information mandate of public broadcasters, who are obligated to inform about all matters of importance, to more self-serving motives and selective reporting aimed at generating high click rates and circulation. It is important to note that, during the process of transforming survey results into headlines, some degree of simplification or sensationalism can hardly be avoided. This can lead to the potential distortion or oversimplification of complex survey findings. Nevertheless, reputation is also a relevant asset of media. Therefore, reputable media outlets strive to maintain accuracy and transparency in their reporting, citing the original sources and providing sufficient context for readers to grasp the nuances of the survey results.

2.4 Insights into Empirics

The considerations thus far have been theoretical, prompting us to turn our attention to empirical findings. Section 2.4.1 deals with the body of empirical literature concerning media reporting of polls. Given the absence of empirical literature on the reporting of surveys, we conducted our own small empirical study using articles from DER SPIEGEL, the results of which are presented in Section 2.4.2.

2.4.1 Reporting polls

Existing literature has predominantly focused on the media's portrayal of polls, particularly in the context of pre-election periods. For instance, Chang (1999) delved into the representation of public opinion polls within the two leading newspapers in Singapore, revealing that such surveys are marred by both theoretical and methodological issues, with their presentation in news media significantly lacking. In the Canadian context, Andersen (2000) identified a concerning lack of essential technical details in the television and newspaper coverage of pre-election polls during the 1997 Canadian election, noting the infrequent mention of even basic information such as sample size. Similarly, Ferguson and De Clercy (2005) observed in Canada that the most commonly reported elements were the organizations sponsoring and conducting the survey, alongside the dates of survey conduct. This trend of minimal disclosure, obstructing the public's ability to assess a poll's reliability and validity, was corroborated by Welch (2002) in the United States, where the sponsor and sample size were the most frequently cited details by both national and local newspapers. Brettschneider (2008)s examination of federal election coverage from 1980 to 2002 across four major German newspapers highlighted that reports frequently mentioned polling organizations, commissioning bodies, and fieldwork periods. Holtz-Bacha (2012), in a subsequent analysis involving the same newspapers, plus additional tabloid and weekly magazines, found the polling institute's name to be the most common detail provided, though absent in 30% of the articles. In Brazil, the trend of publishing an increasing number of articles on poll results, including some methodological information albeit briefly, was noted by Biroli et al. (2012). This scarcity of detailed information was similarly reported in South African media (Mattes, 2012) and in Taiwanese newspapers and television (Willnat et al., 2012). Mateos and Penadès (2013) scrutinized coverage of electoral polls, distinguishing between those sponsored by media entities (but conducted by private organizations) and those originating from public institutions, finding that while key methodological details were often included, they were never comprehensive. Recent studies continue to highlight concerns; for instance, in Spain, where newspapers are legally mandated to disclose the methodologies behind election polls, a study of articles leading up to the 2012 Catalan parliamentary elections found that only two-thirds included such information, which was at times incomplete or inaccurate (Portilla, 2016). Louwerse and an Dijk (2022) noted a similar paucity in the quality of Dutch poll coverage, with few reports offering details on the polled universe, sampling methods, non-response rates, sample sizes, weights, or fieldwork dates. However, the data collection method and margin of error were more frequently mentioned, particularly regarding the 2017 elections.

2.4.2 Reporting surveys in DER SPIEGEL

Building upon the existing body of literature on polls, we contribute an explorative empirical study specifically focused on reporting of surveys. To evaluate the information provided by newspapers on statistical findings we analyzed articles published by DER SPIEGEL online in the second half of 2023.

DER SPIEGEL is a German weekly news magazine established in 1947 and accessible online since 1994. With a weekly circulation of about 700,000 copies each quarter in 2023 (German Audit Bureau of Circulation, 2024), it is one of the most widespread publications of this type in Europe. Renowned for its investigative journalism, DER SPIEGEL has been pivotal in revealing major political misconduct and scandals. According to The Economist (2002), it stands as one of continental Europe's most influential magazines. Known for its incisive analysis and accessible approach, DER SPIEGEL often incorporates elements of popular science, making it particularly appealing to a broad readership.

DER SPIEGEL is available in both print and digital formats; for this study, we utilized the digital format, accessing the online articles through the Nexis Uni database. We filtered all articles between July 2023 and the end of the year for the occurrence of the word "survey"[4], excluding overview articles that summarize the most significant news of the day ("Lage am Morgen/Abend"). These overview articles occasionally provide information on surveys; however, this information is often sourced from other articles, resulting in duplication if not excluded. This pre-processing step resulted in 266 unique articles containing the word "survey" as observation units.

DER SPIEGEL categorizes its articles by themes. The content of the survey articles predominantly addresses economics (37.60%) and politics (18.80%). Additionally, 13.91% of the articles provide information on foreign news, while only a small fraction, specifically 6 out of 266 articles (2.3%), fall under the category of science assigned by DER SPIEGEL itself. However, our primary interest lies not in the content itself but in the surveys and the reporting of them. To further investigate this, we manually searched for source references, information on the sample and its size, as well as keywords from the statistical domain such as methodology, (non-) representative, statistical error and bias.

223 out of the 266 articles (83.83%) contained information about the source of the survey. Even though in most articles a source is mentioned, most times it is only the institution/author without any information on a related research paper or (quality) report on the survey. The source most frequently cited in the research corpus is the pollster firm Civey, which appears in 28 instances, accounting for 10.52% of all articles analyzed. This institute primarily conducts political research, focusing significantly on the opinion poll on sundays, measuring the prevailing political sentiments within the German population by posing the question, "Who would you vote for if the general election were held this sunday?". Additionally, the ifo institute is another commonly referenced source, cited in 22 articles, representing 8.27% of the total. The majority of these articles discuss the ifo Business Climate Index, a monthly economic indicator that assesses the economic growth prospects in Germany.

In the survey sample, 95 articles (35.71%), gave further information about the number of participants, ranging from 9 to 100,000 with a median value of 1,775. Regarding the statistical methodologies employed, the provided data are notably sparse. 57 articles (21.43%) gave insights into statistical background, e.g. about

[4]All keywords were used in German due to DER SPIEGEL's primary publication language, and then translated into English for result documentation.

representativity, error rates or further methodological issues. Although 29 articles, constituting 10.90% of the total, declare that the underlying research is representative of a specific part of the population, none delineates the statistical techniques utilized in analyzing the survey data. Furthermore, in 19 articles (7.14%), additional methodological details are accessible via a hyperlink to the website of the source, exclusively the pollster firm Civey in these instances. In another seven articles (2.63%) statistical considerations such as potential biases, averages, or errors are addressed, indicating a level of critical engagement with the statistical validity of the reported data.

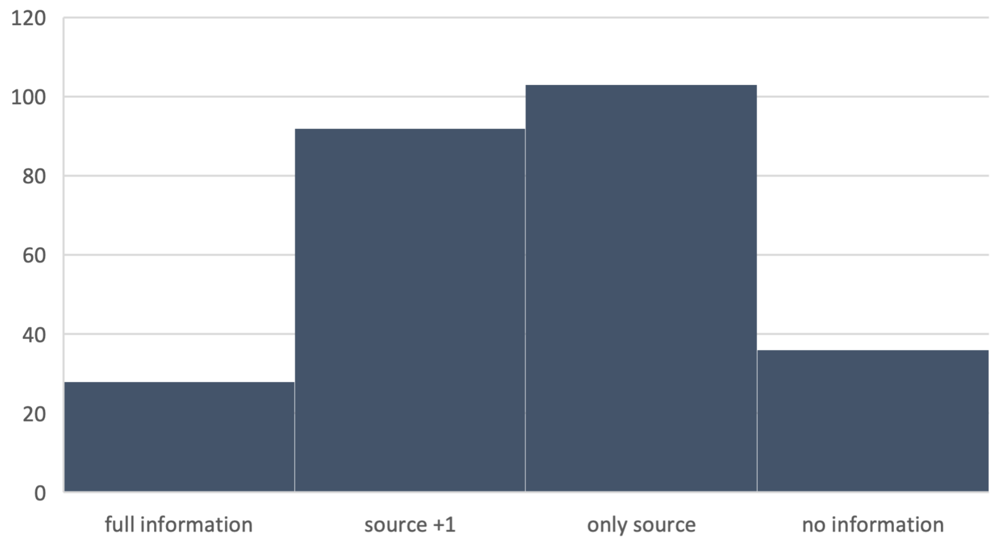
In an examination of a random sample of seven articles, efforts were made to identify the primary survey sources referenced within each article. The research papers were readily located in four instances. For another article, while the specific research paper was not retrieved, the underlying survey and its findings were successfully identified. However, in the case of the remaining two articles, definitive identification of the sources proved elusive, though supplementary information was obtained directly from the authors. This highlights the varying degrees of source transparency and accessibility in journalistic reporting.

With these insights, it is feasible to categorize all articles in the sample into four groups based on the level of information they provide about the surveys referenced.

- `full information`: includes the source, number of participants, and statistical keywords.
- `source +1`: entails either the number of participants or statistical keywords, alongside the source.
- `only source`: mentions solely the source of the information.
- `no information`: lacks any mention of the source or additional survey details.

Figure 2.2 shows the distribution of articles among the four groups. Out of the total corpus of 266 articles, 36 articles (13.53%) contain no information whatsoever regarding the basis of the statements they present. Conversely, 223 articles (83.83%) at least cite a source. Within this subset, 120 articles (45.11%) provide the source along with at least one additional piece of information, while only 28 articles (10.53%) offer comprehensive details, including both the number of participants and insights into the statistical methods or associated keywords used. It is crucial to note that these figures may not necessarily reflect the actual information published by the

Figure 2.2: Categorization of articles based on the extent of survey information disclosure



researchers or companies conducting the surveys but rather the details selected and reported by the journalists.

2.5 Implications

In this paper, we have developed a theoretical framework for survey reporting in the media. Thereby, we have systematically analyzed the role of different actors. Furthermore, a small scale empirical pilot study highlights the relevance the topic of media reporting in the media. The analysis implies that the use of scientific as well as survey data or informed and critical reference to them require a high level of scientific and statistical literacy, which might be above the average level in the general population. Journalists and individuals responsible for news production should be therefore qualified in science methodology and statistics, at least to a level allowing them to evaluate the methodology and credibility of data and studies they select for their references. Furthermore, they should be able to communicate not only the content of the studies, but also some information related to their quality. However, our findings from the small scale empirical pilot study indicate a selective and a sloppy use of statistical references or a provision of statistical information without context as well. Overall, the information communicated by journalists or media about surveys is quite limited.

Based on the findings of our analysis, several important implications and avenues for future research might be highlighted.

Firstly, our analysis suggests that while we can describe theoretically selection effects and relevance mechanisms in media reporting on surveys, we do not yet fully understand the magnitude and impact of these effects. Therefore, there is significant potential for further empirical research in this area. Future studies should aim to quantify these selection effects and investigate the factors that influence the decision-making process of different media outlets when choosing to report on certain surveys. This will help in understanding the extent of biases and limitations inherent in media reporting of surveys.

In this context, for allowing the analysis of larger corpora of news data, it is crucial to develop automated methods for coding and analyzing media content. Currently, as in our pilot study, the process of screening articles for specific information often relies on human coders, which is time-consuming and subject to human error. For clearly defined characteristics, such as sample size (N) or the source of the survey, keyword searches could simplify the coding process. However, for more complex statistical measures that require contextual understanding, more sophisticated automated tools need to be developed. Thereby, exploiting recent advances in natural language processing appears to be a promising avenue.

Our pilot study revealed that the information provided by journalists about surveys is often insufficient, highlighting the need for better training in scientific and statistical literacy. In particular, journalists and individuals responsible for news production should be qualified in scientific methodology and statistics, at least to a level that allows them to evaluate the methodology and credibility of the data and studies they reference. In addition, the observed issues of selective and sloppy use of statistical references, or providing statistical information without context, can partly be attributed to the pressure of reporting interesting news (sensation seeking) as well as time and budget constraints. Thus, further research would also have to address the incentive structure for people working in this domain. Only a combination of appropriate incentives and adequate levels of statistical literacy of media professionals will help to improve the quality of survey reporting in the media and thus to ensure that the public receives accurate and contextually sound information.

Moreover, further scientific research on statistical literacy of populations, among others in Germany and Europe, is required to extend the analysis presented in this paper to the perspective of recipients of media news. In addition, studies on statistical literacy of mass media maker and journalists could help to critically reflect the current practices. Finally, future studies should explore how media report on social science research results, whether their reports adhere to scientific standards, and how these reports influence public understanding and trust in (social) sciences.

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Chapter 3

The Die is Cast – Factors Influencing Mortality during the COVID-19 Pandemic

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Abstract

Since 2020, the world has encountered a profound disruption due to the emergence of the COVID-19 pandemic, precipitating multifaceted challenges encompassing health, societal, and economic dimensions. Within a cross-national comparison, there exists a substantial divergence in mortality rates among nations. This study aims to investigate the efficacy of healthcare systems, along with their potential contributory factors to mortality differentials. Our study, using OLS regressions, reveals that more hospital beds per capita correlate with reduced mortality, while a higher proportion of individuals over 80 elevates mortality rates as expected. Incorporating a health economic index, capturing the goodness of healthcare sector, partly explains disparate mortality rates. The outcomes of this study hold potential relevance for informing policy decisions during the pandemic and for preemptive strategies against future pandemics.

3.1 Introduction

The global outbreak of COVID-19 has marked one of the most significant and impactful health crises of our time (Hu et al., 2020; WHO, 2020c). Since its emergence, the virus has traversed international borders, affecting populations across the globe in a heterogeneous manner. While the virus itself does not differentiate between countries, the observed mortality rates have displayed substantial variation (JHU, 2020). Some nations have managed to mitigate the devastation caused by the virus, reporting lower mortality rates, while others have struggled to cope, witnessing a surge in fatalities. This inconsistency in COVID-19 mortality rates between countries has prompted a pressing need to comprehensively investigate the underlying factors that contribute to this divergence.

Speculation runs rife regarding why certain countries seem more adept at managing the pandemic's impact, while others grapple with high fatalities (Cummings et al., 2020; Docherty et al., 2020; Guan et al., 2020; Petrilli et al., 2020; Wang et al., 2020; Yang et al., 2020). The puzzle is further complicated by the array of potential determinants that may influence the probability of succumbing to the virus. These determinants span from individual risk factors to the quality of medical care and encompass broader demographic, economic, political, and healthcare system-related attributes inherent to each country. Previous research has underscored that, among others, variables such as the density of physicians and hospital beds (Nap et al., 2007; Roy & Khalse, 2020; Sinha et al., 2020; Sobieraj et al., 2007; Weissman et al., 2020), risk factors like advanced age (Docherty et al., 2020; Sathyabhama & Suresh, 2020) or economic status (Lippi et al., 2020; Sarmadi et al., 2020), out-of-pocket payments (OOPs) (Viboud et al., 2016), the quality of care for diseases like influenza (Nap et al., 2007), and the extent of testing facilities (Sinha et al., 2020) could all contribute to the observed mortality disparities (Jüni et al., 2020; Rudge et al., 2012). However, the existing body of research often takes a reductionist approach, concentrating on single factors in isolation. This narrow focus hinders the development of a comprehensive understanding that integrates the intricate interplay among these diverse determinants. Consequently, addressing this issue is imperative not only for the immediate crisis management but also for formulating evidence-based policies that can effectively mitigate future pandemics.

This research paper endeavors to fill this knowledge void by conducting a comprehensive investigation into the determinants of varying COVID-19 mortality rates across countries worldwide. Two principal avenues of inquiry are pursued. Firstly, we scrutinize whether a country's standing in established health indices, like the HAQI and the GHSI, correlates with its COVID-19 fatality rate. This approach aims to discern the role of pre-existing healthcare infrastructure and preparedness in pandemic outcomes. Secondly, we delve into an array of meticulously selected health, economic, and societal factors, dissecting their collective impact on the observed mortality variations. This two-fold approach intends not only to expand our comprehension of pandemic dynamics but to furnish actionable insights that guide current and future global health strategies.

In summary, this research captures both micro-level risk factors and macro-level societal attributes. In doing so, we strive to equip policymakers, health practitioners, and global communities with the knowledge needed to navigate the current crisis and future pandemics more effectively.

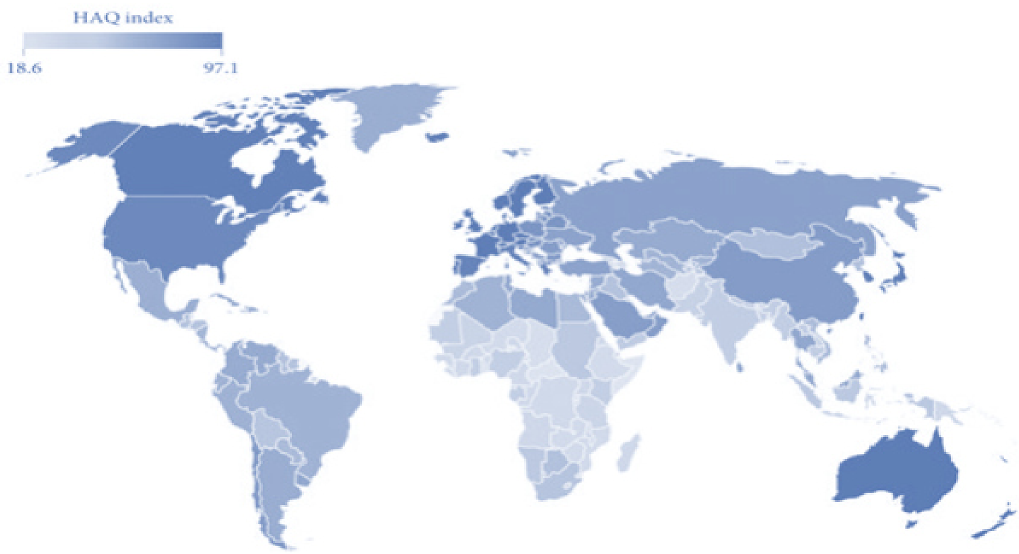
The paper is organized into several sections, each contributing to the comprehensive understanding of varying COVID-19 mortality rates across countries. Section 3.2 delineates the research approach and data sources. In Section 3.3, empirical findings regarding key determinants and fatality rates are presented. Section 3.4 critically examines results in the context of existing literature and pandemic strategies. Section 3.5 concludes, highlighting implications for current and future global health challenges.

3.2 Methods and Data

For the empirical analysis, we utilize two already existing health economic indices on a country-level basis, namely HAQI and GHSI.

The HAQI serves as a comprehensive metric for approximating access to and quality of personal healthcare at a country level for 174 countries worldwide. Derived from the updated estimates of the Global Burden of Disease Study 2016, this index incorporates 32 distinct causes of death to gauge the effectiveness of healthcare systems. Encompassing a spectrum of diseases from communicable to non-communicable

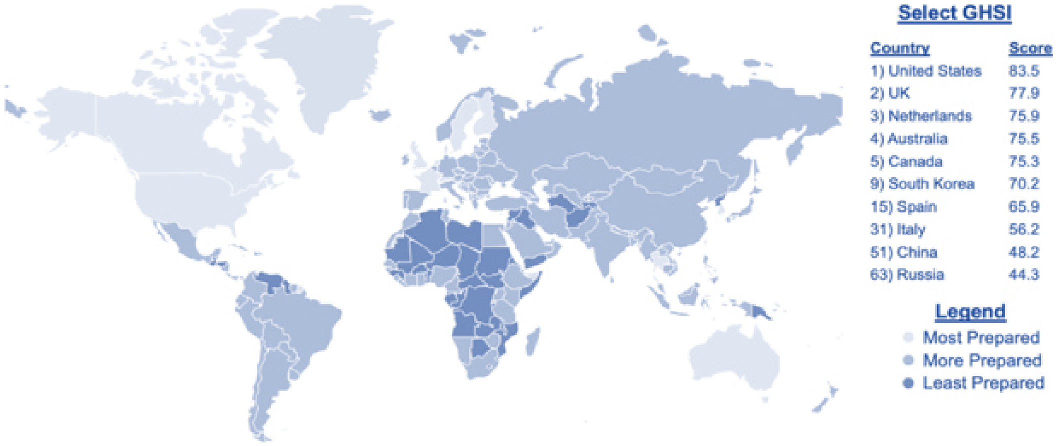
Figure 3.1: HAQI values around the globe.



diseases, HAQI translates each cause of death onto a scale, with 0 representing the lowest (worst) percentile observed between 1990 and 2016, and 100 indicating the highest (best) percentile. Through principal component analysis, the index combines these scaled values to construct a proxy for healthcare access and quality across locations. In Figure 3.1, light blue countries have low HAQI values and dark blue countries have high HAQI values. As seen in Table 3.1, HAQI values in 2016 spanned from a pinnacle of 97, referring to Iceland, to a nadir of 19 for the Central African Republic, underscoring its capacity to encorporate diverse healthcare landscapes. A significant advantage of HAQI is its ability to encapsulate the seemingly intangible aspects of healthcare quality into a quantifiable metric. While the index's strength continues to burgeon alongside advancements in cause-specific data, it fundamentally links medically preventable causes of death to the prevailing health systems in respective countries (Global Burden of Diseases Study 2016 Healthcare Access and Quality Collaborators, 2018).

Another important index in this context is the GHSI, which has gained notable attention through media coverage, particularly due to its focus on evaluating countries' preparedness to manage pandemics and epidemics. Created by the Johns Hopkins University (JHU), the GHSI stems from a comprehensive global survey involving 195 countries. This survey, in collaboration with the Center for Health Security at JHU, the Nuclear Threat Initiative, and the Economist Intelligence Unit, employs a questionnaire comprising 140 inquiries grouped into six categories. These inquiries

Figure 3.2: GHSI values worldwide.



aim to gauge a nation's capacity for averting and mitigating pandemics and epidemics. Crucially, all responses are sourced from publicly available information, and a panel of 21 international experts from 13 countries contribute to answering these questions. In Figure 3.2, it can be seen that the initial publication of the index in 2019 unveiled GHSI scores ranging from a maximum of 83.5 out of a 100 (light blue) for the United States, followed by 77.9 in the United Kingdom and 75.6 in the Netherlands, to a low (dark blue) of 16.2 for Equatorial Guinea, 16.6 for Somalia, and 17.5 for North Korea (see Table 3.1). The GHSI underscores that no nation worldwide is entirely immune to the challenges of epidemics and pandemics, revealing room for improvement across the global landscape (Bell, 2020; Nuclear Threat Initiative et al., 2020).

In addition to the two indices, we have incorporated other risk factors as explanatory variables, depicted in Table 3.1 as well. We used data from official sources such as the WHO (WHO, 2020a, 2020b; WHO Europe, 2020), the Organisation for Economic Co-operation and Development (OECD) (OECD, 2020b, 2020c, 2020d, 2020e), Eurostat (Eurostat, 2020), Our World in Data (Roser et al., 2020) and the World Bank (The World Bank, 2020). Typically, we utilized the most recent available data, drawn from 2018 or 2019, for 178 countries included in our cross-sectional dataset. We conducted the acquisition of COVID-19 data until June 24, 2020.

In the scope of medical care's individual risk factors, we opted for physician density and the quantity of hospital beds each per 1,000 inhabitants as metrics. Physician density assumes importance as it influences adequate patient care, especially during exceptional circumstances like pandemics. Moreover, the number of physicians

Table 3.1: Summary statistics.

	Dependent Variables		Explanatory Variables			
	Relative Number of Deaths	Deaths per Tests	HAQI[1]	GHSI[2]	Population 80	Hospital Beds
Min	0.080	0.0002	19	16.2	0.8%	0.100
Mean	2.280	0.0032	67	40.1	4.1%	2.155
Max	66.108	0.0477	97	83.5	8.8%	13.050
N	83	58	174	169	62	164

	Explanatory Variables				
	Physicians Density	PYLL[3] Influenza	GNI[4] per Capita	OOPs[5]	Number Tests in 30 Days
Min	0.32	0.0	390	2.99%	16.92
Mean	3.21	5.5	6,395	31.79%	765.99
Max	506.13	22.0	116,430	84.35%	5658.73
N[6]	61	41	170	164	58

Note: [1]Health access and quality index; [2]Global health security index;[3]Potential years of life lost; [4]Gross national income; [5]Out-of-pocket payments; [6]Number of observations per variable.

impacts the quantum of treatment accessible. The OECD acknowledges the inclusion of physicians not directly engaged in patient care but active within the health sector for certain countries (OECD, 2020c). Complementing personnel, infrastructure, predominantly represented by hospital beds, dictates a healthcare system's capacity to concurrently manage severe cases. Quality considerations were anchored in potential years of life lost (PYLL) per 100,000 inhabitants, attributable to influenza among patients aged over 75. Although COVID-19 is unique in nature, its comparison to influenza — both being common respiratory viral infections — provides valuable insights (Itaya et al., 2020). PYLL serves as an indicator for preventable deaths, potentially reflecting healthcare system treatment quality (OECD, 2020f).

General risk factors encompass a diverse array of exposures throughout individuals' lifespans. Economic prosperity, as approximated by per capita gross national income (GNI) in current US dollars, assumes significance in pandemic response due to its influence on a country's financial resilience (OECD, 2020a). The data was normalized to US dollars to mitigate exchange rate fluctuations (The World Bank, 2020). Demographic dynamics are considered through the percentage of the population aged 80 or above, particularly pertinent given the increased vulnerability of older individuals to severe COVID-19 outcomes due to pre-existing comorbidities (Docherty et al., 2020). Health policy and financing, including OOPs as a percentage of total health expenditures, are crucial determinants. OOPs can hinder necessary medical care due to financial constraints, thus posing risks (United Nations Department of Economic and Social Affairs, 2019). Additionally, health policy choices manifest in pandemic management, reflected in metrics like the number of tests conducted. The total number of tests within 30 days after the 50^{th} reported death per 100,000 inhabitants serves as a proxy for testing efforts and outbreak control. Unfortunately, variations in reporting units were encountered, necessitating meticulous data handling to ensure standardization across the dataset (Roser et al., 2020).

In general, our aim is to examine the variations in mortality figures. In addition to the reported absolute number of deaths per country by JHU (2020), an endeavor has been made to address data accuracy disparities across countries. The absolute figures have been normalized to 100,000 inhabitants to account for population differences (United Nations Department of Economic and Social Affairs, 2019). To ensure comparability over time, a consistent 30-day interval following the 50^{th} reported death is utilized, mitigating biases stemming from early documentation inconsistencies. The resultant variable, designated as "Relative Number of Deaths", is adopted as a proxy for COVID-19 mortality in subsequent regressions. A second approach involves incorporating the number of tests to accommodate international variations in testing methodologies. The quantity of tests conducted influences the tally of infections, deaths, and uninfected cases. To gauge mortality rates among the tested population, "Relative Number of Deaths" from the first approach is divided by the "Relative Number of Tests". The numerator and denominator correspond to the increase in deaths and tests within the same 30-day period following the 50^{th} death. The derived ratio in Equation 3.1, designated as "Deaths Per Tests", signifies mortality prevalence within the tested cohort (Roser et al., 2020).

$$\text{Deaths per Tests} = \frac{\text{Relative Number of Deaths}}{\text{Relative Number of Tests}} \tag{3.1}$$

Utilizing the presented data as a foundation, we conducted an initial OLS regression analysis to ascertain the potential impact of the indices and variables on the "Relative Number of Deaths". In a subsequent regression analysis, we sought to ascertain the impact on the variable "Deaths per Tests." For a comprehensive robustness assessment, we refined the analysis by altering the variable "Relative Number of Deaths" to encompass the count of cases occurring 60 days subsequent to the 50^{th} reported case. Furthermore, we stratified the countries into subgroups based on their respective entry points into the pandemic event and subsequently investigated the contributing factors.

3.3 Results

Table 3.2: OLS regression results explaining the relative number of deaths.

	Relative Number of Deaths		
	(1)	(2)	(3)
HAQI	-0.706^{**}		
	(0.290)		
I(HAQI^2)	0.007^{***}		
	(0.002)		
GHSI		-0.224	
		(0.473)	
I(GHSI^2)		0.004	
		(0.005)	
Hospital Beds			-1.350^{**}
			(0.590)
Population 80			289.338^{**}
			(116.278)
Physicians Density			-0.635
			(1.873)
GNI per Capita			0.0001
			(0.0001)
Constant	15.755^{*}	6.464	1.290
	(8.674)	(11.474)	(4.552)
Observations	83	83	43
R^2	0.302	0.063	0.346
Adjusted R^2	0.284	0.040	0.277

Note: Heteroscedasticity adjusted standard errors. $^{*}p<0.1$; $^{**}p<0.05$; $^{***}p<0.01$

The outcomes of the regression analysis on the relative number of deaths are presented in Table 3.2. We observe a significant correlation of the HAQI with the relative number of deaths. The direction of this impact appears to differ between countries that are well-positioned on the HAQI scale and those that are not. Consequently, a non-linear relationship between the HAQI and the relative number of deaths is posited, an assumption corroborated by the regression equation specification error test (RESET) (Ramsey, 1969). Specifically, an increment of one unit in the HAQI, indicating health system enhancement, is associated with a reduction of 0.699 deaths per 100,000 inhabitants within the 30-day interval following the 50^{th} reported death. Notably, this marginal effect is non-constant; in countries with a HAQI score surpassing the threshold of 50, the initially negative impact reverses, becoming positive. This intriguing phenomenon signifies that countries with more robust healthcare systems exhibit a higher value for the variable "Relative Number of Deaths". This is likely because these countries conduct more extensive testing, thereby identifying and reporting a higher number of COVID-19 related deaths.

Likewise, we explored the correlation between the GHSI and the relative number of deaths, though a significant relationship was not observed. The divergent explanatory power of the two indices is further demonstrated by the adjusted R^2 values. Notably, fluctuations in the HAQI can account for approximately 28% of the variance in the dependent variable, whereas the GHSI merely elucidates 4% of the variance.

Within column 3, a highly significant and inverse association emerges between the "Hospital Beds" variable and the "Relative Number of Deaths". This signifies that one more available hospital bed per 1,000 inhabitants corresponds to a reduction of 1.35 in the "Relative Number of Deaths" per 100,000 inhabitants. This finding aligns with the rationality that COVID-19, being a viral ailment necessitating medical attention and intensive care provision. The coefficient reflecting the link between the proportion of the population aged over 80 and the "Relative Number of Deaths" is statistically significant as well, displaying a positive sign. Societies witnessing a one-percentage-point augmentation in their population aged over 80 can anticipate an increase of 289 deaths per 100,000 inhabitants. This is congruent with the susceptibility of aging populations due to compromised immune systems and prevalent comorbidities, factors that amplify the risk of fatality. Conversely, the coefficients pertaining to "Physicians Density" and "GNI" do not attain statistical significance. Notably, the R^2 of this regression reaches 27.7%, mirroring the explanatory power observed when elucidating the "Relative Number of Deaths" through the HAQI variable. However, we have to admit that the number of observations in column 3 is lower, at 43, since physician density was only available for a few countries.

As an initial robustness assessment, we recalculated the "Relative Number of Deaths" over a 60-day interval, extending the observation period from 30 days. Notably, the estimated effects remain largely unaltered (refer to Appendix 3.A.1), except for anticipated changes attributed to the prolonged observation span. Consequently, the statistically significant variables exhibit enhanced precision and absolute magnitude. Conversely, the insignificance of the remaining variables remains consistent, and there is only a marginal increment in the adjusted R^2 to 30.7%.

Table 3.3: OLS regression results explaining the deaths per test.

	Deaths per Tests		
	(1)	(2)	(3)
HAQI	0.0001		
	(0.0001)		
GHSI		0.0003	
		(0.0001)	
Hospital Beds			-0.003^{***}
			(0.001)
Population 80			0.431^{**}
			(0.185)
Number of 1,000 Tests in 30 Days			-0.0019^{**}
			(0.00000)
OOPs			0.028
			(0.027)
PYLL Influenza			−0.0001
			(0.0005)
Physicians Density			−0.001
			(0.003)
Constant	0.003	−0.006	0.010
	(0.007)	(0.007)	(0.011)
Observations	58	58	32
R^2	0.012	0.080	0.404
Adjusted R^2	-0.006	0.063	0.261
Note:	*p<0.1; **p<0.05; ***p<0.01		

Table 3.3 presents the outcomes of our secondary regression analysis aimed at elucidating the "Deaths per Tests" ratio. For this regression, the indices HAQI and GHSI are introduced in a linear format rather than being squared. This adjustment is prompted by the earlier assumption in the initial regression that the quadratic effect could be attributed to testing capacity, which is now encompassed within the dependent variable. When the quadratic term is added, it appears insignificant,

which supports our hypothesis of dependency on test capacities. The coefficients of HAQI and GHSI are both statistically insignificant, and the explanatory power, as indicated by the R^2, is limited. The findings presented in column 3 indicate that a unit increase in the number of beds per 1,000 inhabitants leads to a statistically significant reduction of 0.3 percentage points in the mortality rate of those subjected to testing. Additionally, there exists a positive correlation between the proportion of the population aged over 80 years and "Deaths per Tests." Specifically, a 1 percentage point increase in this proportion corresponds to a ceteris paribus mortality rate elevation of 43.1 percentage points. The coefficient associated with the number of tests conducted within 30 days after the 50^{th} reported death is statistically significant, demonstrating that an increment of 1,000 tests contributes to a reduction of 0.19 percentage points in the mortality rate among those tested. This negative correlation can be attributed to the fact that while only a small fraction of those tested exhibit illness, each new test detects a greater number of healthy individuals. Furthermore, not all patients who are unwell succumb to COVID-19 related complications, further underscoring the negative relationship. To ensure adequate testing capabilities within a nation, financial backing is imperative (OECD, 2020a). Consequently, the variable per capita GNI was excluded from the model to obviate duplicating its effect. Additionally, "PYLL Influenza" was incorporated to enhance the analysis. By augmenting testing endeavors, it becomes feasible to delineate more distinctly between fatalities caused by COVID-19 and those resulting from other respiratory ailments such as influenza. Moreover, the variable "OOPs," reflecting the proportion of self-paying individuals in each country, was introduced. This variable was included due to the tendency for fully insured patients to undergo testing, which in turn impacts subsequent medical interventions and, consequently, mortality rates. Conversely, results pertaining to physician density, OOPs, and PYLL due to influenza do not significantly differ from zero. The R^2 is with 26.1% reasonably high.

Upon reviewing these findings, a certain degree of uncertainty persists regarding the extent to which these effects will endure or manifest themselves as additional data accumulates over time and more countries report more than 50 deaths. To provide an illustration, we undertook a robustness check by partitioning the existing dataset into distinct country groups. As displayed in Table 3.A.2, the first column encompasses the outcomes for the initial 10 countries that reported 50 deaths. Subsequent columns progressively incorporate more countries that surpass this threshold, increasing the number of observations and culminating in the fourth column that presents the results encompassing the entire dataset, as already presented in Table 3.2.

Notably, all coefficients consistently exhibit the same directionality as more countries are added, with the number of beds per 1,000 inhabitants and the proportion of individuals aged over 80 becoming statistically significant as the estimation encompasses 30 countries. Although the coefficient for physician density has yet to attain significance, a discernible reduction in standard errors with the accumulation of data is evident. This suggests the potential for its significance with further data incorporation. Conversely, for per capita GNI, the effect's direction and magnitude remain consistent, and it is unlikely that these coefficients will attain significance even with augmented data availability. The adjusted R^2 remains approximately constant at around 30%.

The same analytical approach, involving subgroup construction, was implemented for the "Deaths per Test" variable as a robustness check in Table 3.A.3. A parallel pattern, akin to the findings in Table 3.A.2, becomes evident for the coefficients related to the number of beds per 1,000 inhabitants and the percentage proportion of the population aged over 80 years. These coefficients consistently exhibit the same directionality and gain statistical significance with the incremental addition of data points. A similar trend holds true for the newly introduced variable "Number Tests In 30 Days." In the case of OOPs, the direction of the effect remains positive over time, albeit diminishing in magnitude. The reduction in standard error suggests that with an augmented dataset that includes more countires, this parameter can be estimated with greater precision. For PYLL Influenza, the standard error diminishes, consequently leading to a shift in the coefficient from positive to negative. Conversely, the coefficient of "Physicians Density" displays substantial oscillations between positive and negative values. It is plausible that both coefficients could eventually converge towards zero, thus potentially indicating insignificance in future analyses.

3.4 Discussion

In light of the unprecedented global disruption caused by the emergence of the COVID-19 pandemic, marked by complex challenges encompassing health, societal, and economic dimensions since 2020, this study seeks to address the substantial variation in mortality rates among nations through a cross-national comparison. Employing OLS regressions, we examine the effectiveness of healthcare systems and their contributing factors to mortality disparities. Our findings unequivocally demonstrate that a higher number of hospital beds per capita is associated with a significant reduction in mortality rates, while an elevated proportion of individuals aged over 80 in the population is linked to increased mortality. Additionally, the incorporation of an existing health economic index partially elucidates the divergent mortality rates. This research contributes to the understanding of COVID-19 mortality variations, offering insights into the effectiveness of healthcare systems and key demographic factors.

Contrary to initial expectations of a linear correlation, the HAQI exhibits a non-linear relationship with the Relative Number of Deaths, suggesting that countries not well-positioned on the HAQI scale initially experience a reduction in deaths, but this trend reverses for countries with higher HAQI scores, likely due to enhanced testing capabilities and more accurate reporting. In light of the imperative to fortify global preparedness for forthcoming pandemics, countries are urged to direct their attention to the determinants encapsulated within the HAQI. Enhancing these determinants holds the potential to elevate a nation's standing in the index, thereby bolstering its overall healthcare infrastructure and pandemic readiness. By strategically addressing factors that contribute to higher HAQI scores, countries can systematically bolster their healthcare systems, foster greater accessibility to quality medical care, and augment their resilience against future health crises. These proactive efforts not only promise to improve immediate pandemic response but also position nations on a trajectory of heightened preparedness, enabling them to navigate the intricate challenges posed by emerging infectious diseases with greater efficacy. In this pursuit, investing in areas highlighted by the HAQI not only elevates a country's ranking but also fortifies its capacity to safeguard the health and well-being of its populace in the face of unforeseen global health threats.

Despite the GHSI being meticulously designed to address the unique challenges posed by pandemics and epidemics, our analysis reveals a lack of significant correlation between the GHSI and COVID-19 mortality rates across countries. While the GHSI's specificity is tailored to exceptional health crises, its inability to demonstrate a substantial explanatory power in relation to pandemic outcomes suggests a complexity beyond its scope. This incongruity could reflect the multifaceted and nuanced nature of pandemic dynamics, wherein an interplay of intricate factors shapes the course of disease spread and mortality. The GHSI's emphasis on preparedness and response capacities may not fully encapsulate the diverse determinants influencing COVID-19 mortality disparities.

The empirical results of our study provide insights into the extent to which our initial expectations regarding specific determinants and their correlations with mortality rates were met. Our expectations were substantiated by the significant correlations observed in the case of hospital beds, physicians density, number of tests conducted in 30 days, and the proportion of the population aged over 80 years. These findings validate the anticipated negative correlation between hospital beds, physicians density, and the number of tests conducted in 30 days with mortality rates, reaffirming the critical role of healthcare capacity and testing efforts in pandemic management. Moreover, the positive correlation between the proportion of the population aged over 80 years and mortality rates aligns with the heightened vulnerability of older individuals to severe outcomes. However, it is noteworthy that some of our initial expectations were not empirically substantiated, as indicated by the lack of significant coefficients. Specifically, the anticipated positive correlations between mortality rates and OOPs, as well as PYLL due to influenza, did not manifest in our analysis. Similarly, the expected negative correlations between mortality rates and GNI per capita did not achieve statistical significance. These discrepancies emphasize the intricate and multifactorial nature of pandemic dynamics, where the influence of certain determinants might be more nuanced or heavily influenced by other contextual factors.

In conclusion, our study's empirical findings shed light on the complex interplay of various determinants with COVID-19 mortality rates. While some of our initial expectations were validated by significant correlations, the non-significant coefficients underscore the need for a comprehensive understanding that transcends simplistic assumptions. This nuanced perspective is essential for crafting effective policies and strategies that address the intricate web of factors contributing to pandemic outcomes.

The analysis, exemplified by the HAQI assessment, highlights two potential pathways through which an exceptionally robust healthcare system might influence the recorded mortality count. Firstly, a superior system could result in more identified deaths due to increased testing and well-trained medical staff. Conversely, it could lead to fewer deaths through effective prevention and mitigation measures. A similar perspective holds for physician density, where higher physician numbers can potentially treat a greater number of patients, potentially averting fatalities by providing timely medical interventions. Conversely, the greater expertise of more physicians might also lead to the identification of more COVID-19-related deaths. It is imperative to recognize that while correlations exist, causal relationships should not be prematurely inferred. Correlations can encompass opposing effects, with one outweighing the other and determining the observed direction of influence. Furthermore, exercising caution is essential when interpreting country group estimates (see Table 3.A.2 and 3.A.3). Effects initially significant in smaller samples might lose significance with additional data due to varying reasons. A learning effect could potentially explain such changes, whereby countries later affected by the pandemic could draw insights from those affected earlier, leading to better preparation and response strategies. To explore this, we introduced the number of days between the virus outbreak and the occurrence of the 50^{th} reported death in each country as a potential explanatory variable. However, the anticipated effect was not observed. The evolution of these estimates as the pandemic unfolds and more data accumulates remains an intriguing avenue of investigation. Notably, the coefficient of physician density in the first set of variables estimation is particularly noteworthy, and its potential significance in the future warrants observation.

Our study's findings can be situated within the context of previous research, shedding light on both similarities and distinctions with similar studies that investigated the determinants of COVID-19 outcomes. Studies like Lai, Wang, Wang, Hsueh, et al. (2020), Lai, Wang, Wang, and Hsueh (2020) and Numbeo (2020) also explored correlations between COVID-19 cases, deaths, and mortality rates with health indices, particularly the HAQI and the Health Care Index. They identified a notable and positive association between disease incidence and these health indices, implying that nations endowed with more robust healthcare systems demonstrate enhanced capacities for detecting confirmed cases. Nevertheless, their findings do not reveal a significant correlation between the HAQI and mortality rates, in contrast to our study's results. This disparity in outcomes could potentially stem from the divergence in data coverage, as their investigation encompassed a shorter temporal span until February 2020 and involved a smaller set of countries. In the realm of pandemic preparedness, Aitken et al. (2020) explored the association between the GHSI and COVID-19 outcomes. Their findings revealed a significant positive correlation between the GHSI and adjusted deaths per million people per day. While we also considered the GHSI in our analysis, our results differ, indicating a lack of significant correlation between the GHSI and COVID-19 mortality rates. This discrepancy could arise from the evolving nature of the pandemic, the inclusion of more recent and extensive data in our study, and the methodological differences employed.

Several studies have explored healthcare resource allocation in the context of previous influenza pandemics, aiming to estimate the required number of hospital beds and healthcare personnel for various disease severities (Nap et al., 2007; Sobieraj et al., 2007). For instance, Rudge et al. (2012) utilized this approach to identify deficiencies in healthcare resources, including hospital beds, equipment, nurses, and doctors, across six Asian regions, demonstrating the potential to prevent avoidable mortalities during influenza pandemics. In line with these findings, we incorporated *Hospital Beds* and *Physicians Density* in our model to assess whether the availability of these resources influences the varying COVID-19 mortality rates. Our analysis corroborated this relationship, particularly evident in the context of the number of hospital beds per 1,000 inhabitants. Another study by Ji et al. (2020), conducted during the early phase of the COVID-19 outbreak, suggested that regional disparities in healthcare resource availability could contribute to differing mortality rates among Chinese provinces, providing early evidence of the link between healthcare resources and pandemic mortality. Additionally, Jüni et al. (2020) employed a random-effects regression to examine variables such as climate and public health interventions in relation to epidemic growth. Although they also utilized the proportion of the older population as a variable, akin to our study, their focus remained on the epidemic growth, diverging from our mortality-oriented analysis.

A unique approach, the total interpretive structural modeling, was employed by Sathyabhama and Suresh (2020) to identify factors influencing the COVID-19 pandemic. Their study identified 11 factors, including the vulnerability of older populations, aligning with our findings. The presence of comorbidities, such as hypertension, cardiovascular diseases, diabetes, and obesity, as risk factors for severe COVID-19 outcomes, has been established in international research, paralleling earlier studies and our own observations. Moreover, higher patient age is consistently associated with elevated risk, in line with our study and previous research (Cummings et al., 2020; Docherty et al., 2020; Guan et al., 2020; Petrilli et al., 2020; Wang et al., 2020; Yang et al., 2020). Despite acknowledging the significance of these medical risk factors, we focused on health economic variables, as the medical field has extensively explored them. Studies by Sinha et al. (2020) and Roy and Khalse (2020) share similarities with our approach, as they examined similar variables.

Sinha et al. (2020) assessed correlation coefficients between COVID-19 infection rates, total deaths, gross domestic product (GDP), physicians, hospital beds, and testing rates across six countries, while Roy and Khalse (2020) explored the associations between COVID-19 deaths and cases, critical-care beds, median age, testing rates, population density, urban population percentage, and healthcare expenditure across 11 countries. Notably, they identified a significant negative correlation between critical care beds and the fatality rate, aligning with our findings. However, our study surpasses pure correlation analyses by incorporating a wider range of variables, adjusted explanatory factors, and an expanded set of countries.

Acknowledging the limitations of this study is imperative for a comprehensive understanding of its findings. One primary limitation pertains to the relatively limited number of observations within the range of 32 to 83, which could potentially constrain the robustness and generalizability of the results. Another crucial limitation arises from the dataset utilized for the explanatory variables. In an effort to encompass a broad spectrum of countries, we amalgamated partially incomplete datasets from different sources, introducing potential biases due to variations in data collection methods and years. While this approach ensured a larger and more up-to-date sample, it is crucial to acknowledge that the pandemic's evolving nature and exceptional circumstances may have altered healthcare capacities and resource allocation, potentially affecting the accuracy of the variables examined. Additionally, the accuracy of reported data, including the numbers of deaths and tests, is inherently influenced by a country's healthcare system, political stability, and economic status. As a result, variations in testing practices and categorization of COVID-19 related deaths across countries might lead to an underestimation or overestimation of actual COVID-19 mortality rates. Furthermore, the study does not account for non-pharmaceutical interventions that countries implemented, like social distancing rules or mask mandates, which undoubtedly influenced infection and death rates. It is vital to approach the results with caution, considering these limitations and the dynamic nature of the pandemic. The study's findings, while providing valuable insights, should be interpreted within the context of these inherent constraints.

The findings of this study offer valuable insights into the relationship between healthcare system factors and COVID-19 mortality rates. However, several avenues for further research emerge from the limitations and complexities identified within this study. Firstly, expanding the dataset to include a larger and more diverse set of countries could enhance the generalizability of the findings and provide a more comprehensive understanding of the relationship between healthcare system indicators and COVID-19 outcomes. Additionally, investigating the impact of non-pharmaceutical interventions, such as lockdowns, mask mandates, and travel restrictions, on COVID-19 mortality rates could shed light on the effectiveness of different strategies in mitigating the pandemic's impact. Furthermore, exploring the temporal dynamics of the relationship between healthcare system indicators and mortality rates as the pandemic evolves could yield insights into the changing patterns of COVID-19 impact on healthcare systems. Investigating the potential interactions between healthcare system factors and sociodemographic variables, such as income inequality and urbanization rates, could provide a more nuanced understanding of the underlying mechanisms driving COVID-19 mortality disparities.

Lastly, incorporating qualitative research methods to capture the perspectives of healthcare professionals and policymakers on the challenges and strategies related to COVID-19 response and resource allocation could offer valuable context and insights for improving healthcare system preparedness for future pandemics.

3.5 Conclusion

In conclusion, this study has underscored the critical role of healthcare system indicators in shaping COVID-19 mortality rates. The findings emphasize the importance of robust healthcare infrastructure, healthcare workforce density, and testing capacity in effectively managing the pandemic's impact. However, the complexities and limitations highlighted within the study underscore the need for proactive measures to address the evolving challenges posed by such health crises. Failure to address these challenges could lead to inadequate resource allocation, overwhelmed healthcare systems, and avoidable loss of life. To mitigate these risks, governments and policymakers should prioritize investments in healthcare infrastructure, bolster healthcare workforce capacity, and enhance testing capabilities. Moreover, fostering international collaboration in sharing best practices and resources is essential for a comprehensive response. The urgency of these actions is evident, as the potential consequences of unpreparedness extend beyond the current pandemic, affecting the overall resilience of healthcare systems to future health crises. As we navigate the ongoing challenges of the pandemic, it is imperative to heed the lessons learned and act decisively to build resilient healthcare systems that can effectively respond to unforeseen global health threats.

The key takeaway from this study is clear: Countries with a high proportion of elderly populations are particularly vulnerable and cannot alter this demographic in the short term. Instead, adopting a proactive approach to strengthening healthcare systems is not merely an option but an urgent imperative for safeguarding public health and ensuring global well-being.

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3.A Appendix

Table 3.A.1: Relative number of deaths for a period of 60 days.

	Relative Number of Deaths 60
Hospital Beds	-3.178^{***}
	(1.034)
Population 80	660.510^{***}
	(205.581)
Physicians Density	-0.642
	(3.362)
GNI per Capita	0.00004
	(0.0001)
Constant	3.723
	(8.036)
Observations	40
R^2	0.378
Adjusted R^2	0.307

*p<0.1; **p<0.05; ***p<0.01

Table 3.A.2: OLS regression results on subgroups of countries for relative number of deaths.

	Relative Number of Deaths			
	(1)	(2)	(3)	(4)
Hospital Beds	-1.687	-1.946^{*}	-1.921^{**}	-1.350^{**}
	(0.990)	(0.941)	(0.705)	(0.590)
Population 80	470.699	338.300	443.267^{***}	289.338^{**}
	(394.503)	(199.427)	(143.202)	(116.278)
Physicians Density	-2.735	-0.416	-0.908	-0.635
	(10.136)	(4.007)	(2.410)	(1.873)
GNI per Capita	0.0001	0.0001	0.0001	0.0001
	(0.0002)	(0.0002)	(0.0001)	(0.0001)
Constant	5.752	2.431	0.247	1.290
	(15.917)	(8.373)	(5.600)	(4.552)
Observations	10	21	32	43
R^2	0.653	0.379	0.420	0.346
Adjusted R^2	0.375	0.224	0.334	0.277

Note: Columns display the same estimation for the first 10, 21, 32, and 43 countries that have reported 50 deaths.

*p<0.1; **p<0.05; ***p<0.01

Table 3.A.3: OLS regression results on subgroups for deaths per tests.

	Deaths Per Tests		
	(1)	(2)	(3)
Hospital Beds	−0.002	−0.003**	−0.003***
	(0.003)	(0.001)	(0.001)
Population 80	1.591	0.389	0.431**
	(1.303)	(0.262)	(0.185)
Number Tests In 30 Days	−0.00000	−0.00001	−0.00000**
	(0.00002)	(0.00001)	(0.00000)
OOPs	0.074	0.035	0.028
	(0.145)	(0.051)	(0.027)
PYLL Influenza	0.003	0.001	−0.0001
	(0.004)	(0.001)	(0.0005)
Physicians Density	-0.017	0.0002	−0.001
	(0.024)	(0.005)	(0.003)
Constant	−0.023	0.005	0.010
	(0.091)	(0.022)	(0.011)
Observations	9	21	32
R^2	0.700	0.521	0.404
Adjusted R^2	-0.200	0.315	0.261

Note: Columns display the same estimation for the first 9, 21 and 32 countries that have reported 50 deaths.

*p<0.1; **p<0.05; ***p<0.01

Chapter 4

Causal Impact of Policy Measures and Behavior on the COVID-19 Pandemic in Germany

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Abstract

Critics protest loudly against restrictions imposed by politicians during the COVID-19 pandemic in Germany: Mandatory masks, lockdowns, school and business closures. This paper examines (1) the extent to which these policies have indirectly contributed to limiting the number of COVID-19 cases and deaths by forcing people to practice social distancing, and (2) the extent to which people have adjusted their social distancing behavior on their own based on information about national case and fatality numbers and therefore directly limited the number of COVID-19 cases and deaths. The panel analysis at the federal state level in Germany finds that substantial declines in COVID-19 case and death growth rates are attributable to private behavioral responses, but policies played an important role as well. A change in policies explains a large fraction of changes in social distancing behavior, which is why both policies and national information are important determinants of federal COVID-19 cases and deaths. Due to the lack of cross-sectional variation, there is uncertainty about the effect of mask mandates.

4.1 Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, emerged as a global health crisis in early 2020, rapidly transforming into an unprecedented challenge for public health systems worldwide. In response, governments and health authorities implemented a range of NPIs to control the virus' spread, including social distancing, lockdowns, mask mandates, and restrictions on public gatherings. Germany, like many other countries, adopted a multifaceted approach to pandemic management, tailoring policy measures to evolving epidemiological landscapes and public health needs. However, these interventions sparked significant public debate, with critics vocally opposing the restrictions imposed by politicians.

The literature on NPIs mitigating the spread of COVID-19 offers a rich tapestry of findings, revealing the multifaceted impacts of these interventions across different settings and methodologies. A core theme emerging from the literature is the conclusive efficacy of specific NPIs, such as mask mandates, social distancing measures, and lockdowns, in reducing COVID-19 transmission and mortality. Chernozhukov et al. (2021) and Bo et al. (2021) provide robust evidence from the US and a global dataset of 190 countries, respectively, highlighting the crucial role of these policies in curbing the spread of the virus. These findings are echoed in the work of Islam et al. (2020), which underscores the effectiveness of early lockdowns through a discontinuous time series analysis across 149 countries. Complementary analyses by Esra et al. (2020) further support the impact of household restrictions and compulsory mask-wearing in a multi-country context, including the US.

The diversity of methodological approaches in evaluating NPIs underscores the complexity of assessing their impacts. For example, Pleninger et al. (2022) utilize a vector autoregressive (VAR) model to study the effects of stringent measures in Switzerland, while Karaivanov et al. (2021) apply a panel susceptible-infected-removed (SIR) model to link rising caseloads with the easing of restrictions in Ontario, Canada. These methodological variations reveal the importance of context-specific analysis, as evidenced by studies like those of Ebrahim et al. (2020) and Wang et al. (2022), which examine workplace closures and early policy interventions across US counties and 121 countries, respectively.

The literature also points to the significant influence of socioeconomic factors and public compliance on the effectiveness of NPIs. Jalali et al. (2020) highlight the role of health disparities and noncompliance with stay-at-home recommendations in the US, suggesting that the success of NPIs is partially dependent on societal behaviors and inequalities. Similarly, studies by Chan et al. (2021) and Duhon et al. (2021) explore how socioeconomic determinants affect NPI outcomes. Chan et al. (2021) also highlights the variability in NPIs' effectiveness based on societal behaviors as well.

Insights into the comparative efficacy of different NPIs and their policy implications are provided by studies like those of Siedner et al. (2020) and Liu et al. (2021), which examine the impact of social distancing and school closures across the US. The research collectively suggests that while certain NPIs are universally effective, the optimal mix of interventions may vary based on local conditions and capacities. Furthermore, studies such as those by Amuedo-Dorantes et al. (2021) and Kovacs et al. (2020) use the Difference-in-Differences model to analyze the timing of lockdowns and the impact of mandatory masks, offering valuable insights for policymakers on the timing and implementation of NPIs to maximize their effectiveness.

In conclusion, the reviewed literature underscores the critical role of NPIs in controlling the COVID-19 pandemic, with a consensus on the general efficacy of measures such as mask-wearing, social distancing, and lockdowns. However, the impact of these interventions is modulated by factors including the timing of implementation, public compliance, and socioeconomic variables.

Despite the significant body of research on the effectiveness of NPIs in controlling the COVID-19 spread, a pressing need remains to examine the specific impact of policy measures and behavioral responses within the German context. While studies have explored the aggregate effects of NPIs on infection rates and mortality globally, the nuanced impact of such interventions, coupled with public adherence to guidelines in Germany, warrants closer examination. The variation in infection rates and outcomes across different regions within the country suggests that local factors, including policy implementation and community behaviors, may influence the pandemic's dynamics significantly.

This study aims to fill the gap in the literature by providing a comprehensive analysis of the causal impact of policy measures and public behavior on the COVID-19 pandemic in Germany by examining two critical dimensions: (1) the extent to which policy measures have indirectly influenced COVID-19 case and death rates through enforced social distancing, and (2) the degree to which individuals voluntarily modified their social distancing behaviors in response to information regarding national case and fatality trends, thereby directly impacting the pandemic's trajectory. By offering a comprehensive examination of the interplay between policy measures and public behavior in Germany's fight against COVID-19, this research aims to contribute valuable insights into the effectiveness of NPIs and the critical role of informed public compliance.

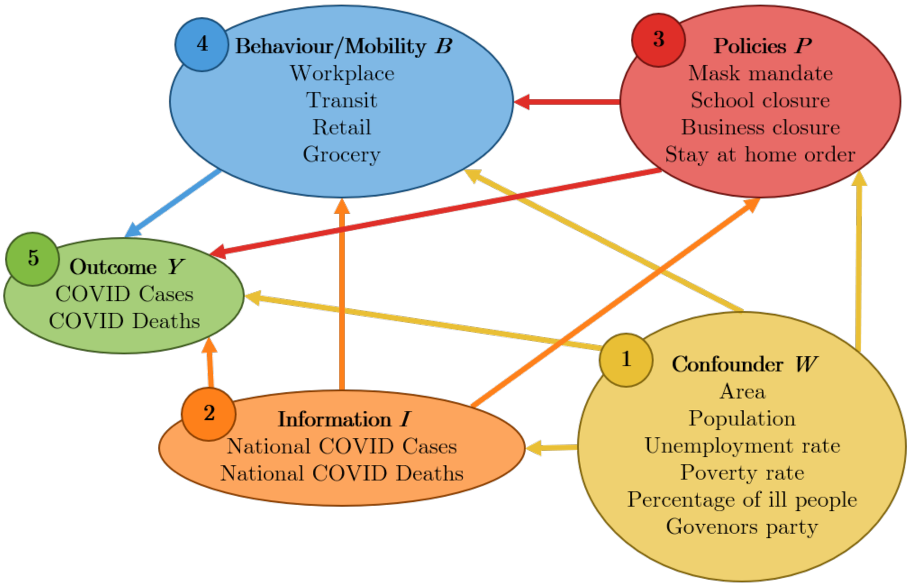
After setting the stage with a theoretical framework by Chernozhukov et al. (2021) in chapter 4.2, chapter 4.3 describes the data and methods for investigating the pandemic's dynamics. The empirical results in chapter 4.4 highlight how policies and individual behaviors impact COVID-19 cases and deaths, which is then discussed in relation to existing literature in chapter 4.5. The paper concludes in chapter 4.6 by summarizing findings, acknowledging limitations, and suggesting avenues for further research.

4.2 Framework

The objective of this study is to elucidate the impact of policy measures and changes in population behavior on COVID-19 case and death rates. I will use the causal model by Chernozhukov et al. (2021), introduced through the Wright-style causal diagram shown in Figure 4.1 that illustrates the conceptual framework for the estimation results presented later in Chapter 4.4. The policy measures (P) considered in this study include mandatory face masks, school and business closures, and domestic lockdowns. These measures are expected to have both direct and indirect effects on the spread of the virus, as they not only reduce transmission of the virus, but also influence social distancing behavior. Specifically, school and business closures as well as domestic lockdowns are expected to have a strong indirect effect on reducing the growth of cases and deaths by restricting gatherings and enforcing social distancing.

In contrast, mandatory use of face masks is expected to have a direct effect on reducing the transmission of aerosols, thereby slowing down the spread of the virus.

Figure 4.1: Interaction diagram.



Social distancing behavior (B) is determined by changes in the population's time spent at work, in public transit, retail shops, or supermarkets. By spending more time at home, the transmission of COVID-19 is limited, contributing to lower growth rates of cases and deaths. Moreover, information (I) on national case and death figures has an impact on political measures and the mobility of the population. In the past, some individuals isolated themselves voluntarily to avoid being infected with the virus, irrespective of the political regulations in place. This also contributes to lower case and death rates.

It is acknowledged that the effects of policy measures will vary across different federal states in Germany. In order to control for state-specific differences, various confounding factors (W) such as area, population, unemployment and poverty rates, proportion of people subject to illness, and the governing party are used as covariates.

As demonstrated in the numbered graph, policy measures (3) to contain the virus are initially adopted in each federal state based on confounding factors (1) and information on national case and death figures (2). The changes in the population's behavior (4) subsequently become apparent, and the overall impact on the number of cases and deaths (5) is observed.

4.3 Methods and Data

To express the contents of Figure 4.1 mathematically, the following equations 4.1 – 4.5 from Chernozhukov et al. (2021) are employed and subsequently estimated in Chapter 4.4.

$$\text{(BPI} \rightarrow \text{Y): } Y_{it+l} = \alpha B_{it} + \pi P_{it} + \mu I_{it} + \delta_Y W_{it} + \varepsilon_{it}^Y \tag{4.1}$$

$$\text{(PI} \rightarrow \text{B): } B_{it} = \beta P_{it} + \gamma I_{it} + \delta_B W_{it} + \varepsilon_{it}^B \tag{4.2}$$

Inserting Equation 4.2 into Equation 4.1 yields:

$$\text{(PI} \rightarrow \text{Y): } Y_{it+l} = (\alpha\beta + \pi) P_{it} + (\alpha\gamma + \mu) I_{it} + \bar{\delta} W_{it} + \bar{\varepsilon}_{it} \tag{4.3}$$

Therefore, the projection equation $Y \sim PI$:

$$\text{(Y} \sim \text{PI): } Y_{it+l} = a P_{it} + b I_{it} + \bar{\delta} W_{it} + \bar{\varepsilon}_{it} \tag{4.4}$$

should obey a and b as:

$$a = (\alpha\beta + \pi) \text{ and } b = (\alpha\gamma + \mu) \tag{4.5}$$

In the equations, B_{it} denotes variables for social distancing behavior in state i at time t, while P_{it} represents policies implemented in state i at time t. The outcome variable Y_{it+l} reflects either case growth with a 14-day lag or death growth with a 21-day lag. Additionally, I_{it} encompasses a set of information variables, and W_{it} collects all confounding variables. The primary focus is to explain the outcome variable Y after defining policies P and behavior B. For more detailed information on testable implications and identification, refer to Chernozhukov et al. (2021).

The panel dataset was constructed to estimate Equations 4.1 to 4.3. The dataset comprises daily observations from February 15, 2020, to December 31, 2021, across all 16 federal states in Germany, resulting in a total of 10,976 observations (n: 16 federal states; t: 686 days).

The information on COVID cases (C) and deaths (D) was sourced from the daily situation reports of the Robert Koch Institute for both individual federal states and Germany as a whole (Robert Koch Institut, 2022). Missing values on weekends or holidays were supplemented by interpolation or values from weekly reports (Robert Koch Institut, 2020). To measure the outcome variable for empirical analysis, Equations 4.6 and 4.7 transform the absolute number of cases and deaths into a weekly growth rate, where ΔC_t and ΔD_t represent the number of new cases within the last 7 days. Daily new cases and deaths are affected by the timing of reporting and testing. Focusing on weekly cases smooths out idiosyncratic daily fluctuations as well as periodic fluctuations associated with days of the week.

$$\Delta log(\Delta C_t) = log(\Delta C_t) - log(\Delta C_{t-7}) \tag{4.6}$$

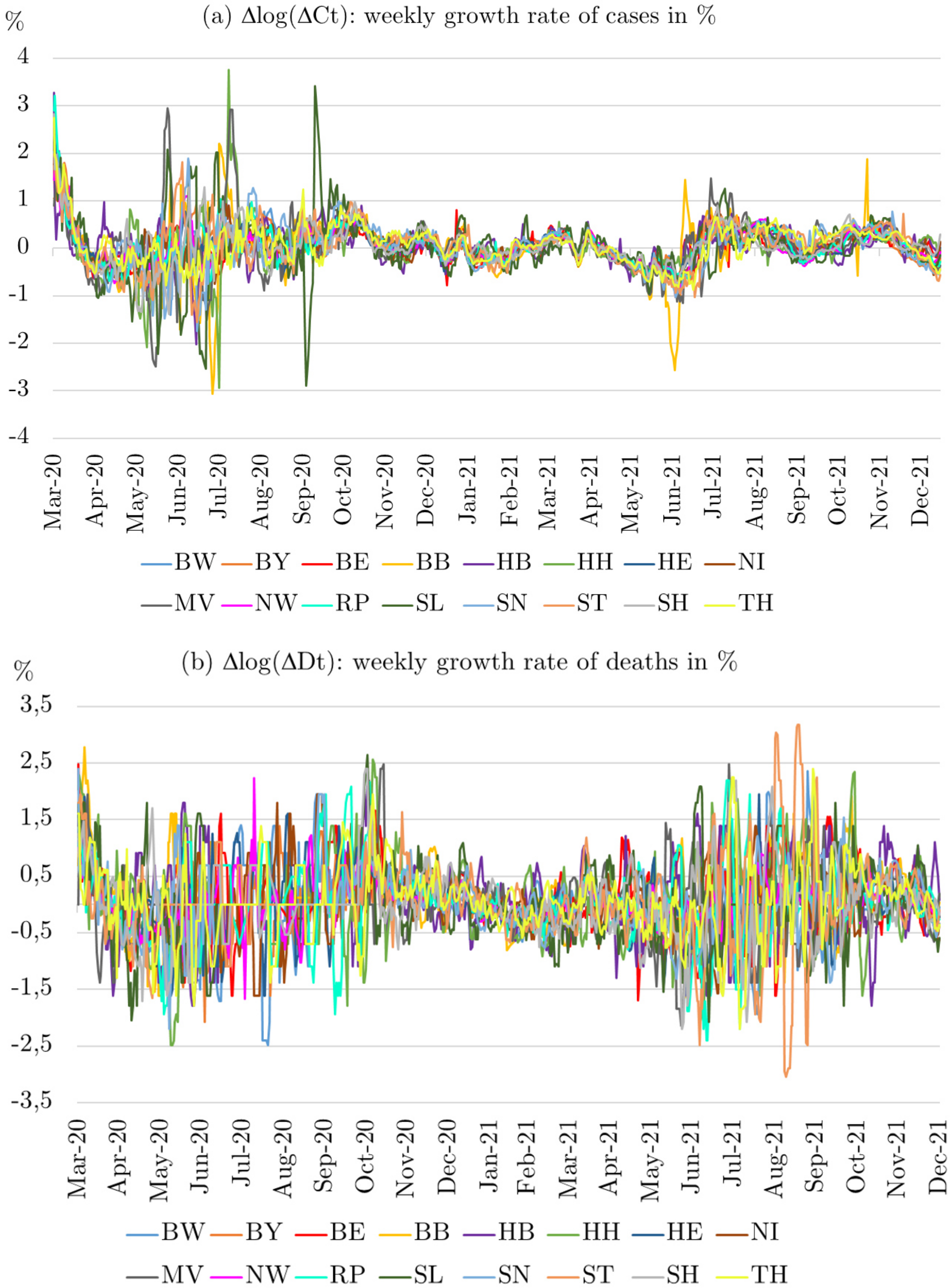
$$\Delta log(\Delta D_t) = log(\Delta D_t) - log(\Delta D_{t-7}) \tag{4.7}$$

Figure 4.2 displays the (a) case and (b) death growth over the entire period for all 16 federal states, illustrating different phases of volatility. From March to October 2020, the weekly growth rate of cases fluctuated between +3% and -3%, while the growth rate of deaths fluctuated between +2.5% and -2.5%. This was followed by a period of less volatile patterns until March 2021, when the volatility in the growth rate of deaths increased considerably again. These figures demonstrate noticeable differences, both across federal states and over time, that require further analysis.

To measure social distancing behavior B, Google COVID Community Mobility Reports (Google, 2020) based on Google Maps location data were utilized. The data in the categories of workplaces (*workplace*), retail and leisure (*retail*), grocery stores and pharmacy (*grocery*), and transit stations (*transit*) indicate the percentage change in visit intensity relative to the reference period between January 3, 2020, and February 6, 2020, when there was no evidence of COVID in Germany yet (Google, 2022). A moving average was constructed over one week to mitigate day-specific outliers. On Sundays, in particular, all the categories mentioned above are significantly less frequented than on weekdays.

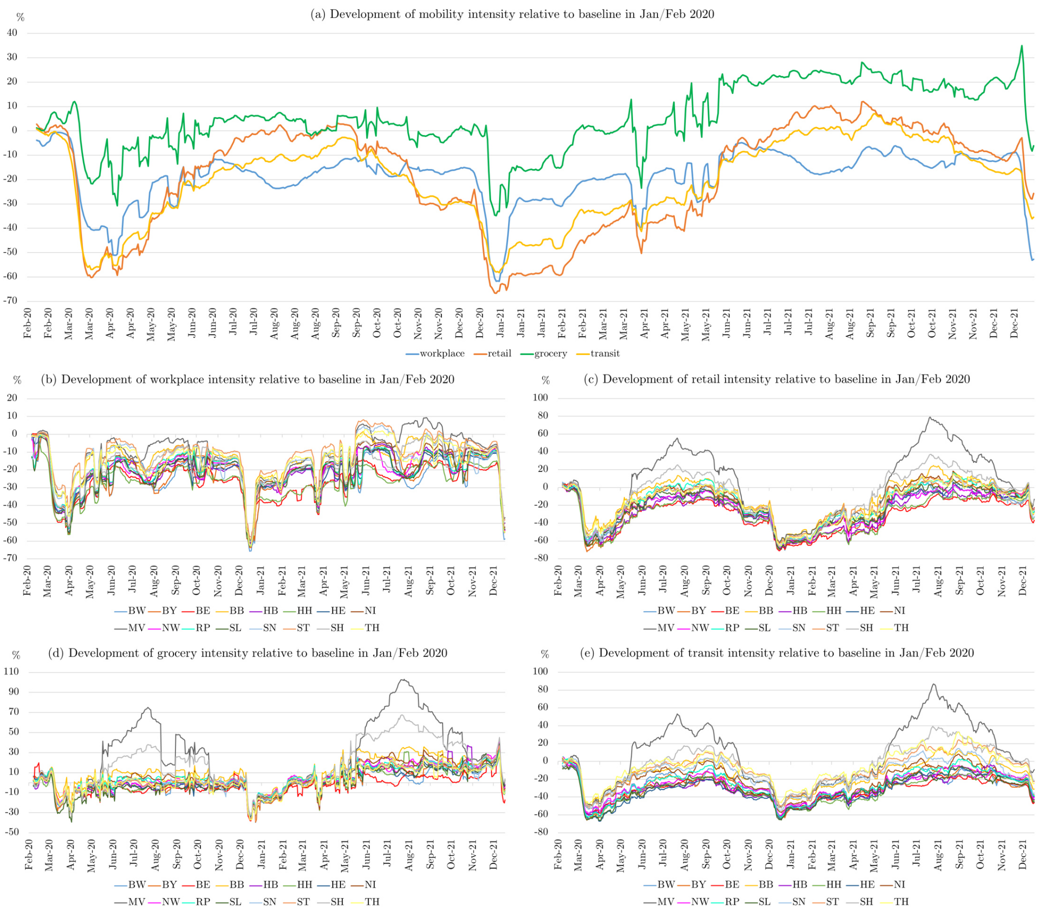
Figure 4.3 depicts the changes in (a) overall visit intensity and specifically for (b) *workplace*, (c) *retail*, (d) *grocery*, and (e) *transit* in each federal state of Germany for every date. The graphs exhibit a significant decrease in visit intensity in April

Figure 4.2: Evolution of case and death growth across federal states.



2020, when the country experienced its first surge in COVID-19 cases. Another sharp decline occurred around Christmas and New Year for both 2020 and 2021. However, the patterns between these two periods are not highly comparable. In most federal states, the frequency of visiting workplaces and transit remained permanently below the baseline level, while supermarkets were visited more frequently in 2021 than during the reference period of January 2020.

Figure 4.3: Evolution of google mobility reports across federal states.



Germany implemented several political measures (P) to contain the spread of COVID-19. These measures include a stay-at-home order (*stayathome*), mandatory face masks in stores, public transportation, and public buildings (*maskmandate*), mainly secondary school closures (*closedschool*), closures of non-essential stores above or below $800m^2$, closure of indoor dining areas in restaurants, but not for pick-up and delivery service, and movie theater closures. The corona ordinances, official press releases, and homepages of federal states and other governmental institutions were utilized to determine the policies imposed in each federal state[1]. All measures

[1](Authority for Health and Consumer Protection, 2020a, 2020b; Authority for Labor, Health,

were converted into dummy variables, with a value of 1 indicating that the measure was in effect, and a value of 0 indicating that it was not. To address issues with multicollinearity, an index was created by taking the average of closed non-essential stores above or below $800m^2$, restaurants, and movie theaters, resulting in a value between 0 and 1 ($businessclosureindex$).

Figure 4.4: Share of federal states with each policy in place.

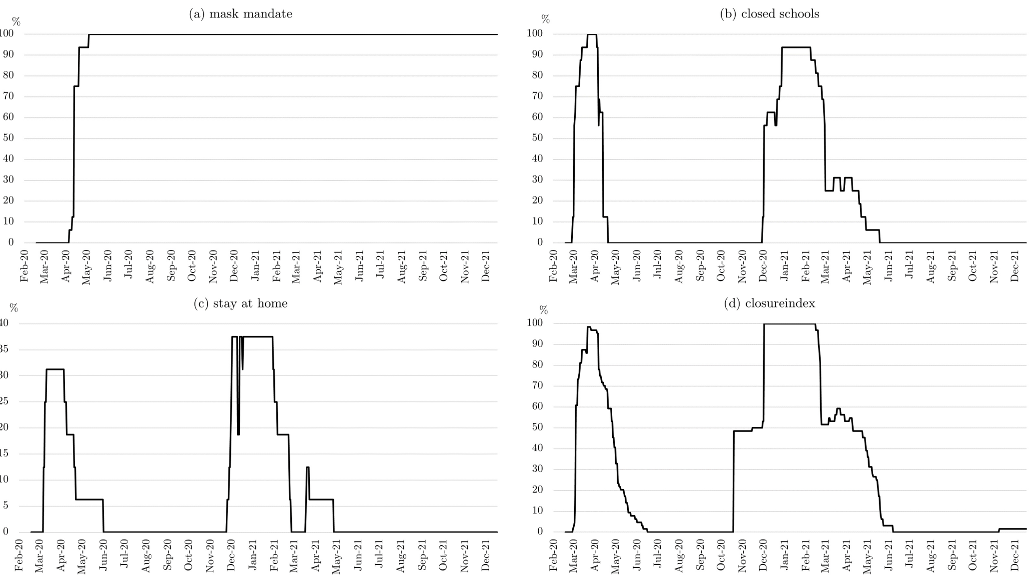


Figure 4.4 illustrates the percentage of states that implemented each of the remaining four policies at each date. There was considerable variation across states in terms of the duration during which the policies were active, with the exception of (a) mandatory face masks in stores, public transportation, and public buildings. All federal states implemented mandatory face masks within one month between April 20^{th} and May 18^{th} 2020 and retained this policy until the end of 2021. This makes it challenging to differentiate the impact of mandatory face masks from aggregate time

Social Affairs, Family and Integration, 2020; Bavarian State Ministry for Health and Care, 2022; dpa-infocom GmbH, 2020; focus.de, 2020; Government of the Saarland, 2022; Government of the State Baden-Württemberg, 2022; Hesse, 2020; Hessian Cabinet, 2021; Landesportal Schleswig-Holstein, 2020a, 2020b, 2021; Lower Saxony Ministry of Social Affairs, Health and Equality, 2020; Minister for Education, Science and Culture and Prime Minister and Minister for Social Affairs, Health, Youth Family and Seniors, 2021; Minister for Social Affairs, Health, Youth Family and Seniors, 2020; Minister of Labor, Heath and Social Affairs of the State of North Rhine-Westphalia, 2022; Minister of Social Affairs, Health and Sport, 2022; Minister of Social Affairs, Labor, Health and Demography, 2021; Ministry of Labor, Social Affairs, Health, Women and Family Affairs, 2022; Ministry of Lower Saxony for Social Affairs, Health and Equality, 2021; Ministry of Social Affairs, Health, Integration and Consumer Protection of the State of Brandenburg, 2022; Niedersächsisches Kultusministerium, 2020; Saxon State Ministry for Social Affairs and Social Cohesion, 2022; Senate of Berlin, 2022; Senate of Hamburg, 2022; Senator for Health, Women and Consumer Protection, 2022; State Gorvernment of Saxony-Anhalt, 2022; State Government of Rhineland-Palatinate, 2020; ZDFheute, 2020) series variation. The other three figures (b), (c) and (d) exhibit a seasonal effect, as there were no restrictive policy measures in any of the federal states during the summer months.

The confounding variables (W) included in the analysis were *area*, *population*, *unemploymentrate*, *povertyrate*, the proportion of people subject to illness (*percen– tageofillpeople*), and the governing party (*govenorsparty*). These were motivated by Wheaton and Kinsella Thompson (2020), who found that case growth is associated with factors such as residential density and per capita income. The data on area, population, and unemployment rates of the federal states were obtained from the Federal Statistical Office of Germany (Federal Statistical Office of Germany, 2020, 2022). Poverty rates were reported in the Poverty Report for Germany (Pieper et al., 2020). Population, area, and poverty rate were fixed over time as they were reported for 2019 only, while the unemployment rate was reported monthly. Information on the governing party was obtained from the respective official homepages and changed for some states (BE, BW, HH, MV, RP, and ST) due to federal state elections during the observational period[2].

Descriptive statistics for all variables can be found in Table 4.1.With this data, the equations are now estimated individually. All models are estimated as random effects models, with standard errors clustered at the federal state level, to account for heterogeneity and serial correlation within each state.

4.4 Results

The first estimation aims to investigate how policies and information affect social distancing behaviour ($PI \rightarrow B$). As outlined in Equation 4.2, there are a total of 16 estimations to be conducted, given the four behavioural variables (*workplaces*, *retail*, *grocery*, and *transit*) and four ways of including information (regional and national *logdC* as well as *dlogdC*). Specifically, cases C and deaths D can be used

[2](Bavarian State Government, 2022; Berlin State Centre for Political Education, 2022; Brandenburg State Portal, 2022; Country Portal of Mecklenburg-Western Pomerania, 2022; Hesse State Government, 2022; Saxony-Anhalt State Portal, 2022; Schleswig-Holstein State Portal, 2022; Senate Office of Hamburg, 2022; State Chancellery of Lower Saxony, 2022; State Chancellery of Saarland, 2022; State Chancellery of Saxony, 2022; State Chancellery Unesco World Heritage City Hall of Bremen, 2022; State Government of North Rhine-Westphalia, 2022; State Government of Rhineland-Palatinate, 2022; State Government of Thuringia, 2022; State Ministry of Baden-Württemberg, 2022)

Table 4.1: Summary statistics of underlying data set.

	Outcome Y:		*Policies P:*			
	COVID Cases C	COVID Deaths D	mask mandate	stayat home	closed schools	business closureindex
Min	0.000	0.000	0.0000	0.0000	0.0000	0.0000
Mean	139 228	3 224	0.9148	0.0667	0.1881	0.2919
Max	1 378 107	20 308	1.0000	1.0000	1.0000	1.0000

	Information I:		*Behavior B:*			
	National Cases C_{nat}	National Deaths D_{nat}	workplaces	retail	grocery	transit
Min	196	12	-65.714	-72.143	-39.571	-67.000
Mean	2 227 636.3	51 586.76	-18.901	-19.118	4.944	-20.528
Max	7 130 720.0	111 765.0	9.429	79.286	103.143	87.000

	Confounder W:					
	population	area	unemployment rate	poverty rate	percentageof illpeople	govenors party
Min	681 202	419.4	2.90%	11.90%	0.00%	1.00
Mean	5 197 919	22 348.8	6.59%	16.91%	2.24%	2.13
Max	17 947 221	70 541.6	12.00%	24.90%	15.98%	4.00

with federal data only or in combination with nation-wide values. Table 4.2 presents the results for the case information, while Table 4.3 presents the results for the death information.

Table 4.2 illustrates the impact of political measures on behavioral variables across the first four rows, and the effect of information dissemination through case numbers in rows four to eight. The differentiation between columns 1-4 and 5-8 lies in the employment of regional case numbers as information in the first block, and the inclusion of national case numbers in the second block. The primary focus of our analysis is the effect of political measures on behavior. Across all specifications, the anticipated negative impacts of school closures and business shutdowns are evident, indicating a reduction in public mobility. Conversely, the implementation of mask mandates exhibits positive behavioral effects. This can be partially attributed to an increased sense of safety amongst individuals wearing masks, leading to greater public presence, and also to the initial phase where activities were permitted, provided masks were worn. The outcomes of stay-at-home orders present a mixed picture. There is a negative impact on workplace attendance and positive effects on retail, although the impacts on grocery and transit appear to be insignificant. Given that grocery shopping was largely permitted, no significant change in visit intensity is noted. To exemplify the magnitude of these effects, consider the most evident scenario: the enactment of a business closure mandate led to a 34 percentage point decline in retail store visitation intensity compared to the pre-COVID-19 period. Regarding the information variables, the absolute case count exhibits a negative effect on behavior at both regional and national levels. Unexpectedly, the case growth rate over the past week shows a positive effect on behavior. In conclusion, variation in political measures and information variables account for between 47% and 82% of the variance in visit intensity, thus explaining a substantial portion of the behavioral changes. Comparing columns (1)-(4) with columns (5)-(8), the explanatory power of the model is marginally higher when national case numbers are included as information.

In Table 4.3, the information variables shift from case numbers to mortality numbers, both at regional and national levels. The outcomes do not significantly deviate from those observed in Table 4.2: there are negative effects from school closures and business shutdowns, and positive effects from mask mandates. For stay-at-home orders, previously insignificant effects on groceries and transit are now significant and positive. As mentioned, shopping was still permitted during lockdowns. While the direction of the effects of the information variables, specifically the death counts and their growth rate, mirrors that of the case numbers and their growth rate in Table 4.2, the magnitude of these effects is noticeably smaller. This suggests that the population was more influenced by reports on case numbers than by those on death counts in terms of altering their behavior. The explanatory power across all columns remains comparable to Table 4.2.

Table 4.2: Effect of policies and information on behavior ($PI \rightarrow B$) with cases as information.

	Dependent variable:							
	workplaces	retail	grocery	transit	workplaces	retail	grocery	transit
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
maskmandate	11.608***	17.003***	13.185***	21.997***	12.249***	18.528***	14.448***	23.251***
	(0.424)	(0.559)	(0.561)	(0.536)	(0.426)	(0.556)	(0.564)	(0.537)
closedschool	−1.408***	−2.724***	−1.465***	−0.572	−1.763***	−3.503***	−1.767***	−1.121***
	(0.327)	(0.399)	(0.398)	(0.380)	(0.327)	(0.393)	(0.396)	(0.377)
stayathome	−3.257***	1.621***	0.817*	0.641	−3.135***	1.725***	0.713	0.675
	(0.372)	(0.452)	(0.450)	(0.429)	(0.370)	(0.443)	(0.446)	(0.425)
businessclosureindex	−10.340***	−34.774***	−9.031***	−21.677***	−9.546***	−32.735***	−7.626***	−20.073***
	(0.381)	(0.473)	(0.472)	(0.451)	(0.388)	(0.476)	(0.480)	(0.457)
dlogdC	2.022***	6.790***	3.638***	4.745***	0.049	2.454***	1.387***	1.535***
	(0.194)	(0.235)	(0.234)	(0.224)	(0.261)	(0.313)	(0.315)	(0.300)
logdC	−0.699***	−3.562***	−2.609***	−2.786***	−0.781***	−1.939***	−0.519**	−1.227***
	(0.075)	(0.093)	(0.093)	(0.089)	(0.159)	(0.200)	(0.202)	(0.192)
dlogdCnat					4.316***	8.781***	3.971***	6.334***
					(0.368)	(0.440)	(0.444)	(0.422)
logdCnat					−0.005	−2.289***	−2.791***	−2.152***
					(0.183)	(0.233)	(0.235)	(0.224)
Constant	−32.266***	−6.153	−2.601	−30.482**	−32.671***	3.347	9.347	−21.442
	(1.438)	(6.825)	(12.042)	(14.479)	(1.658)	(6.902)	(12.090)	(14.512)
State variables	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	10,480	10,480	10,480	10,480	10,480	10,480	10,480	10,480
R^2	0.471	0.813	0.592	0.724	0.478	0.820	0.599	0.730
Adjusted R^2	0.470	0.813	0.591	0.723	0.477	0.820	0.598	0.730
F Statistic	9,309.803***	45,447.340***	15,167.000***	27,417.270***	9,583.011***	47,714.530***	15,604.790***	28,362.910***

Note: State variables include population, area, unemploymentrate, povertyrate, percentageofillpeople and govenorsparty   *p<0.1; **p<0.05; ***p<0.01

Table 4.3: Effect of policies and information on behavior ($PI \rightarrow B$) with deaths as information.

	Dependent variable:							
	workplaces	retail	grocery	transit	workplaces	retail	grocery	transit
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
maskmandate	12.768***	16.488***	10.451***	20.770***	13.134***	17.971***	10.608***	22.150***
	(0.477)	(0.534)	(0.595)	(0.530)	(0.480)	(0.467)	(0.586)	(0.474)
closedschool	−1.171***	−0.618*	−0.415	0.727**	−1.258***	−1.989***	−0.946**	−0.522
	(0.332)	(0.367)	(0.409)	(0.364)	(0.332)	(0.320)	(0.401)	(0.324)
stayathome	−3.070***	3.358***	1.394***	1.889***	−3.129***	2.156***	0.873*	0.775**
	(0.381)	(0.420)	(0.469)	(0.417)	(0.381)	(0.366)	(0.459)	(0.371)
businessclosureindex	−12.046***	−25.379***	−9.510***	−13.889***	−11.733***	−12.439***	−3.435***	−1.867***
	(0.464)	(0.513)	(0.572)	(0.509)	(0.514)	(0.501)	(0.628)	(0.508)
dlogdD	0.299**	2.859***	0.183	2.009***	−0.183	−0.485***	−0.679***	−1.047***
	(0.141)	(0.156)	(0.174)	(0.155)	(0.164)	(0.158)	(0.198)	(0.160)
logdD	−0.095	−6.403***	−2.219***	−4.980***	0.242	0.394***	0.656***	1.305***
	(0.098)	(0.108)	(0.120)	(0.107)	(0.155)	(0.151)	(0.190)	(0.153)
dlogdDnat					1.812***	2.439***	−1.948***	2.036***
					(0.301)	(0.290)	(0.364)	(0.294)
logdDnat					−0.430**	−9.635***	−4.163***	−8.915***
					(0.170)	(0.167)	(0.210)	(0.170)
Constant	−37.209***	−18.252*	−11.497	−39.055*	−36.062***	13.916	2.861	−9.309
	(3.065)	(9.973)	(14.358)	(20.794)	(3.121)	(10.014)	(14.387)	(20.812)
State variables	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	10,256	10,256	10,256	10,256	10,256	10,256	10,256	10,256
R^2	0.461	0.845	0.578	0.747	0.463	0.883	0.596	0.801
Adjusted R^2	0.461	0.845	0.577	0.747	0.462	0.883	0.596	0.801
F Statistic	8,766.409***	55,794.220***	14,001.470***	30,279.480***	8,835.235***	77,228.970***	15,122.350***	41,191.580***

Note: State variables include population, area, unemploymentrate, povertyrate, percentageofillpeople and govenorsparty *p<0.1; **p<0.05; ***p<0.01

The interplay between political measures, info dissemination, and social distancing behavior has become apparent from the estimates presented above. Table 4.4 presents the estimation results from the next step, examining the relationship among these three factors – policy, behavior, and information – and the outcome variables, namely case and death growth ($BPI \rightarrow Y$). Given the temporal lag between infection and the confirmation of a COVID-19 case or death, the outcome variables are lagged by 14 days for case numbers and 21 days for death counts (Chernozhukov et al., 2021). The rows in the table first display the four political measures, followed by the four behavioral variables, and then the four potential information variables. Columns 1 and 2 focus on case growth as the outcome, while columns 3 and 4 concentrate on death growth. Columns 2 and 4 additionally incorporate national case and death numbers, alongside regional figures. Overall, the table reveals that all these variables together account for merely 17% and 20% of the variance in case growth and a notably lower 4% and 3% of the variance in death growth, respectively.

Among the individual variables, positive effects of mask mandates, school closures, and business shutdowns on the growth of case numbers are identified. This suggests that while the population may not have congregated in schools or businesses, gatherings occurred elsewhere, leading to infections. Stay-at-home orders have been found to decrease the growth of death numbers; specifically, the measures have led to a reduction in the case growth rate by 7.6%. Regarding behavioral variables, an increase in visit intensity in retail and transit logically corresponds with more people congregating in close quarters, leading to higher infection rates and thus case growth. Conversely, an increase in visit intensity at groceries and workplaces shows a negative effect, meaning that as visit intensity in these areas rises, the growth of cases decreases. This is likely because access to these locations was permitted only when the risk of infection was low or when overall national case numbers were low. The effects on the death rate growth are smaller and, in some instances, insignificant.

The analysis thus far has illustrated the complexity of concurrently examining political measures and behavioral changes. Consequently, Table 4.5 focuses solely on the effect of political measures and information on the outcome variables of case and death growth, excluding the modeling of behavior. The impact of behavioral variables is encapsulated within the policy variables.

Table 4.4: Direct effect of behavior and policies on lagged case and death growth ($BPI \to Y$).

	Dependent variable:			
	dlogdC14		dlogdD21	
	(1)	(2)	(3)	(4)
maskmandate	0.346***	0.339***	0.211***	0.056*
	(0.021)	(0.021)	(0.034)	(0.032)
closedschool	0.093***	0.070***	−0.023	−0.023
	(0.015)	(0.015)	(0.023)	(0.023)
stayathome	−0.076***	−0.070***	−0.046*	−0.042
	(0.017)	(0.017)	(0.027)	(0.026)
businessclosureindex	0.061**	0.063***	0.173***	0.148***
	(0.024)	(0.023)	(0.037)	(0.036)
workplaces	−0.005***	−0.005***	−0.0001	−0.0003
	(0.001)	(0.001)	(0.001)	(0.001)
retail	0.010***	0.007***	0.009***	0.011***
	(0.001)	(0.001)	(0.001)	(0.001)
grocery	−0.007***	−0.005***	−0.006***	−0.008***
	(0.0005)	(0.0005)	(0.001)	(0.001)
transit	0.0005	0.001**	−0.001	−0.001
	(0.001)	(0.001)	(0.001)	(0.001)
dlogdT	−0.088***	−0.151***		
	(0.024)	(0.024)		
logdC	−0.008***			
	(0.003)			
dlogdC	0.169***			
	(0.010)			
logdCnat		−0.020***		
		(0.004)		
dlogdCnat		0.398***		
		(0.017)		
logdD			−0.011*	
			(0.007)	
dlogdD			0.081***	
			(0.010)	
logdDnat				0.015*
				(0.009)
Constant	−0.215***	−0.088*	−0.058	0.015
	(0.042)	(0.050)	(0.064)	(0.068)
State variables	Yes	Yes	Yes	Yes
Observations	10,048	10,048	9,941	10,053
R^2	0.173	0.198	0.043	0.032
Adjusted R^2	0.172	0.197	0.041	0.031
F Statistic	2,098.157***	2,475.671***	440.843***	331.688***

*p<0.1; **p<0.05; ***p<0.01

Note: State variables include area, unemploymentrate and povertyrate

The first two columns present the effect of policy and information variables on case growth with a reporting lag of 14 days. Both columns show positive effects of mask mandates and school closures on case growth and negative effects of stay-at-home orders and business closures on case growth, as well as negative effects regarding the increasing testing rate. When national information variables are included in Column 2, the explanatory power of the model increases to 17.4%, and the coefficients are estimated with greater precision. Columns 3 and 4 examine death growth as the outcome variable. Apart from the positive effect of mask mandates, no significant effects of political measures can be observed. In this context, the inclusion of national information variables does not lead to a higher explanatory power.

The estimated effects of policies on behavior presented in Tables 4.2 and 4.3, as well as the effects of policies and behavior on case and death growth in Table 4.4, can be used to calculate the total effect of policies on the outcome variables. Given that one can observe fewer significant or insignificant effects on death rates across all specifications, the following comparison will focus only on case numbers, although the procedure for death rates will remain the same.

The results of estimating ($PI \to Y$) are largely consistent with the approach of separately estimating direct and indirect effects and then combining them. Table 4.6 provides an overview of the comparison of estimated coefficients, with the last column indicating the differences between the two methods of estimating the effect of policies on case and death rates. Column "Average" in Table 4.6 displays the average of the "Total" and "$PI \to Y$" columns. This average serves as a simple and appealing way to combine the two estimates of the total effect, with one based on the causal structure and the other obtained from a direct estimation of the equation $PI \to Y$. The average estimate could be utilized in generating counterfactuals in subsequent analyses.

The interpretation of the results in Table 4.6 proceeds row by row. For mask mandates, one can observe that approximately 90% of the effect of this policy on case growth can be attributed to the direct effect, while only 10% is due to the indirect effect via behavioral change. The overall effect is significant at a magnitude of 0.3767, indicating that the implementation of the mask mandate results in an increase in the case growth rate by 37 percentage points. Similarly, for school closures and

Table 4.5: Total effect of policies on case and death growth ($PI \rightarrow Y$).

	Dependent variable:			
	dlogdC14		dlogdD21	
	(1)	(2)	(3)	(4)
maskmandate	0.335***	0.325***	0.256***	0.131***
	(0.021)	(0.020)	(0.032)	(0.030)
closedschool	0.094***	0.066***	−0.022	−0.034
	(0.015)	(0.015)	(0.023)	(0.023)
stayathome	−0.040**	−0.040**	−0.019	−0.016
	(0.018)	(0.017)	(0.027)	(0.026)
businessclosureindex	−0.188***	−0.102***	0.035	0.016
	(0.017)	(0.018)	(0.031)	(0.034)
logdC	−0.027***			
	(0.003)			
dlogdC	0.229***			
	(0.010)			
logdCnat		−0.042***		
		(0.004)		
dlogdCnat		0.496***		
		(0.016)		
dlogdT	−0.134***	−0.207***		
	(0.024)	(0.024)		
logdD			−0.051***	
			(0.006)	
dlogdD			0.105***	
			(0.010)	
logdDnat				−0.043***
				(0.007)
Constant	−0.058	0.147***	−0.112**	0.136**
	(0.039)	(0.049)	(0.056)	(0.060)
State variables	Yes	Yes	Yes	Yes
Observations	10,048	10,048	9,941	10,053
R^2	0.139	0.175	0.035	0.022
Adjusted R^2	0.138	0.174	0.034	0.021
F Statistic	1,619.373***	2,124.021***	364.562***	228.641***

*p<0.1; **p<0.05; ***p<0.01

Note: State variables include area, unemploymentrate, povertyrate, percentage ofillpeople and govenorsparty stay-at-home orders, the primary impact is seen in the direct effect. However, the direction of the effects between the direct and indirect components differs for both policies. A fundamentally positive direct effect of school closures on case growth is mitigated by the indirect behavioral effect. Conversely, an initially negative effect of stay-at-home orders is also mitigated by the behavioral effect, resulting in a reduced overall magnitude. Unfortunately, for all three variables, the calculated total effects and the estimated total effects differ significantly (see the "Difference" column). The large differences may be due to the difficulty in identifying the effect of e.g. mask mandates given a lack of cross-sectional variation. The only variable for which the effect can be estimated correctly and without significant deviation is business closures. Here, one can observe that the indirect effect via behavior constitutes the main component and is moderated in magnitude by the direct effect. Overall, the closure of businesses results in a reduction of the case growth rate by 18.27 percentage points. This is the only effect that can be reliably and plausibly estimated.

Table 4.6: Direct and indirect policy effects without national variables.

	Direct	Indirect	Total	$PI \rightarrow Y$	Average	Difference
	π	$\alpha * \beta$	$\pi + \alpha * \beta$	a		
	(1)	(2)	(3)	(4)	$\frac{(3)+(4)}{2}$	(3)-(4)
maskmandate	0.346***	0.0307***	0.3767***	0.335***	0.3559	0.0417***
	(0.021)	(0.015)	(0.014)	(0.021)		(0.003)
closedschool	0.093***	−0.0102***	0.0828***	0.094***	0.0884	−0.0112***
	(0.015)	(0.005)	(0.008)	(0.015)		(0.002)
stayathome	−0.076***	0.0271***	−0.0489***	−0.040**	−0.0445	−0.0089**
	(0.017)	(0.013)	(0.015)	(0.018)		(0.003)
businessclosureindex	0.061***	−0.2437***	−0.1827***	−0.188***	−0.1854	0.0053
	(0.024)	(0.014)	(0.012)	(0.017)		(0.003)
logdC	−0.008***	−0.0153***	−0.0233***	−0.027***	−0.0252	0.0037***
	(0.003)	(0.007)	(0.003)	(0.003)		(0.0002)
dlogdC	0.169***	0.0347***	0.2037***	0.229***	0.2164	−0.0253***
	(0.010)	(0.017)	(0.014)	(0.010)		(0.002)

*p<0.1; **p<0.05; ***p<0.01

Note: Direct effects capture the effect of policy on case growth holding behavior, information, and confounders constant. Direct effects are given by π in equation $(BPI \rightarrow Y)$ (see Tab. 4.4). Indirect effects capture how policy changes behavior and behavior shift case growth. They are given by α from $(BPI \rightarrow Y)$ (see Tab. 4.4) times β from $(PI \rightarrow B)$ (see Tab. 4.2 and 4.3). The total effect is $\pi + \beta\alpha$. Column $PI \rightarrow Y$ shows the coefficient estimates from $(PI \rightarrow Y)$ (see Tab. 4.5). Column Difference and Average refer to column Total and $(PI \rightarrow Y)$.
Standard errors are computed by bootstrap and clustered on state level.

4.5 Discussion

With the onset of the COVID-19 pandemic, many governments implemented a range of political measures in an effort to slow or halt the pandemic's progression, thereby reducing both case and death numbers. This study investigated the effectiveness of these political measures in Germany, incorporating, for the first time, the indirect effects via voluntary or involuntary behavioral changes in the population. Additionally, the study explored whether individuals modify their behavior in response to information about local or national case and death numbers.

Methodologically, the study was based on Chernozhukov et al. (2021)'s causal model, adapted from his analysis of 50 US states to the 16 German federal states. Data included daily observations of cases, deaths, policy implementations, and movement patterns from Google Mobility as a proxy for behavior from the beginning of the pandemic in 2020 until the end of 2021.

The panel analysis revealed that substantial declines in COVID-19 case and death growth rates are directly attributable to policies, with private behavioral responses playing a significant role. Changes in any given policy accounted for a large fraction of changes in social distancing behavior, indicating the effectiveness of the measures. Furthermore, both regional and national information emerged as important determinants of behavior, as well as cases and deaths. Overall, the effect of business closure policies on case growth could be reliably estimated, resulting in an 18.27 percentage point reduction in case growth rate.

It was observed that all political measures influenced behavior, which is valuable information for policymakers, validating that their efforts were not in vain. However, the direction of these effects was contentious. Specifically, mask mandates showed positive effects on behavior, indicating that people exhibited less social distancing behavior when wearing masks, possibly due to a false sense of security. In contrast, school and business closures showed expected negative effects, reducing social gatherings by closing places where people could congregate. The effect of stay-at-home orders was less clear; while one would expect these measures to restrict behavior as measured by Google Mobility, the actual effects were mixed. Nevertheless, the direction of the effects of policies on behavior aligned with their effects on case growth, with stay-at-home orders reliably reducing case growth.

A major part of this study aimed to replicate Chernozhukov et al. (2021)'s analysis for the US using data for Germany. The primary difference lies in the number of federal states (16 for Germany versus 50 for the US), leading to greater variability in political measures in the US and limited covariate inclusion for Germany. Despite this, the causal model was adaptable to a different setting like Germany. However, parallel results between the two countries are limited. Chernozhukov et al. (2021) found no significant results for school closures in the US, attributed to a lack of variability across states, a situation that in Germany pertains more to the nationwide mask mandates. Since education policy is a state matter in Germany, there is sufficient variation in school closures.

Chernozhukov et al. (2021)'s US analysis suggested that keeping all businesses open would have led to 17 to 78% more cases, and not implementing stay-at-home orders would have increased cases by 6 to 63%. Our findings similarly indicate that business closures reduce case growth by 18 percentage points and stay-at-home orders by 4 percentage points. Both studies agree that individuals voluntarily reduce visits to workplaces, retail stores, grocery stores, and public transit in response to higher numbers of new cases and deaths.

Our study's differences from the US results may stem from several factors. At the time of data collection, there was no comprehensive database in Germany documenting when and where specific political measures were implemented. These data were manually compiled, introducing potential errors. While case and death numbers were quickly available after the pandemic's onset, reporting issues, especially early in the pandemic, posed challenges. Debates over whether to count deaths "with" COVID-19 or "from" COVID-19, along with temporal discrepancies in reporting, were addressed through lag structures in the model, yet the chosen 14- and 21-day lags might not fully capture all effects.

Given these limitations, it may be prudent to incorporate Germany-specific characteristics into the model and vary the political measures to include only those independently decided by federal states. Additionally, fundamental critiques of Chernozhukov et al. (2021)'s methodology, such as the use of moving averages and the loss of information on absolute case numbers, suggest that alternative metrics like the R-Factor might offer more valid outcome variables.

Practically, the study shows that Chernozhukov et al. (2021)'s model can be applied to different countries and settings, provided there are enough observational units or sufficient variability in the variables across states. However, the effects and effect sizes are not universally comparable, highlighting the need for tailored approaches in pandemic response. Regional characteristics play a significant role, as seen in the varying responsibilities for schools and the nationwide mask mandate in Germany compared to state-level decisions in the US. The significant impact of social distancing behavior in both nations suggests that individuals voluntarily limit contact in response to higher transmission risks, an important feedback mechanism influencing future cases and deaths. Ignoring this voluntary response in model simulations could lead to over-predictions of future case and death numbers.

Overall, this paper provides an initial insight into the interplay of political measures, social distancing behavior, and their impact on case and death growth. However, due to limitations, only the effect of business closures could be reliably estimated, preventing a comprehensive understanding of the efficacy of NPIs. It remains crucial to determine the effectiveness of political measures and to what extent they are needed if individuals also change their behavior without enforcement.

4.6 Conclusion

This paper provides an initial insight into the interplay of political measures, social distancing behavior, and their impact on COVID-19 case and death growth. The study, employing a panel analysis at the federal state level in Germany, reveals that both policy interventions and private behavioral adjustments have significantly contributed to the observed declines in COVID-19 case and death growth rates. The findings indicate that policy changes account for a considerable portion of the variations in social distancing behaviors, underscoring the importance of both governmental policies and accessible national health information as pivotal determinants of COVID-19 outcomes.

However, limitations in the data meant that only the effect of business closures could be reliably estimated, preventing a comprehensive understanding of the efficacy of NPIs. The analysis also highlights a degree of uncertainty regarding the specific impact of mask mandates due to a lack of cross-sectional variation, pointing to an area requiring further investigation.

It remains crucial to determine the effectiveness of political measures and to what extent they are needed if individuals also change their behavior without enforcement. This study's insights emphasize the significant role of informed and strategic policy-making, while also suggesting that further research is needed to fully comprehend the nuances and long-term impacts of various NPIs.

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Chapter 5

Survey of Drug Use and its Association with Herd-level and Farm-level Characteristics on German Dairy Farms

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Abstract

The use of veterinary drugs is of similar importance to that of human drugs in addressing health challenges. In this context, pharmaceuticals and their metabolites inevitably enter soil and water in unknown quantities. Therefore, this study collects and analyzes drug data from 2020 for 50 dairy farms located in Germany. The most frequently used substance group is antibiotics (40.13%), followed by antiphlogistics (18.86%), antiparasitics (13.09%), and hormones (9.29%). Treatment frequencies record the number of days per year on which an average animal on a farm was treated with a substance. The calculated values range from 0.94 to 21.69 d/yr and are distributed heterogeneously across farms. In this study, on average, a cow was treated on 6 days (d) in 2020: 2.34 d with antibiotics, 1.07 d with antiphlogistics, 0.76 d with antiparasitics, and 0.41 d with hormones. In addition to individual farm management practices, other factors are related to treatment frequency. Farms with a veterinary care contract used more hormonal substances than farms without a care contract. In addition, higher milk yield coincides with more frequent treatments

with antiphlogistic or hormonal substances. Other related factors include grazing, longevity, farm size, and use of a claw bath. Our study represents an important first step in describing the amounts and determinants of veterinary drugs used in livestock farming. Such insights on magnitudes and farm parameters are essential to estimate potential environmental effects and derive strategies to reduce veterinary drug use.

5.1 Introduction

Pharmaceuticals are an indispensable and fundamental part of public health. In particular, advancements in pharmaceutical therapy have enhanced the ability to effectively address health challenges, including various infectious diseases. In this context, not only is the use of human medicines is important, but also the use of veterinary medicines. The latter contribute not only to animal well-being, but also to food safety.

Various substances are used for the treatment and prevention of diseases. However, their detection in soils and waters has been raising concerns for years (Barra Caracciolo et al., 2015; Maculewicz et al., 2022; Mesa et al., 2018; Zuccato et al., 2006). These concerns encompass the effects of drugs and their metabolites on non-target organisms in the environment as well as the development of resistance. Antibiotic resistance is recognized by the World Health Organization (WHO) as one of the top 10 threats to global health (World Health Organization, 2019). In addition to human pharmaceuticals, veterinary drugs also have a substantial effect on the emergence of resistance (Bártíková et al., 2016). Resistance to both antibiotics and antiparasitic agents is a growing concern in the therapy of livestock (Charlier et al., 2022). Furthermore, substances such as moxidectin, which are excreted in substantial quantities by cattle after treatment, exhibit lethal toxicity to numerous invertebrates (Mesa et al., 2018). Within the realm of anti-inflammatory agents, Parolini (2020) demonstrates, through various in vitro experiments, that a mixture of different compounds resembling those found in natural aquatic environments significantly heightens the toxicity to aquatic invertebrates in comparison to individual components. When hormonal agents find their way into the environment, their effect is primarily observed in vertebrates. Kidd et al. (2007) conducted a study in Canada revealing that estrogenic compounds in water bodies had such a profound influence on fish reproduction that they neared extinction. Furthermore, the use of anti-inflammatory drugs has been subject to critical discourse. Oaks et al. (2004) illustrated that the administration of diclofenac to cattle in Pakistan nearly eradicated vulture populations. In the European Union (EU), diclofenac is only approved for use in cattle in Estonia and Spain (European Medicines Agency, 2022), with the first vulture fatality attributed to diclofenac documented in 2020 (Herrero-Villar et al., 2021).

It is essential to note that all the aforementioned studies encompass only a limited perspective of the ecological consequences of the application of specific pharmaceuticals within particular regions. In Germany, veterinary drugs are used in livestock farming on cattle, pigs, and poultry. Consequently, pharmacologically active substances and their metabolites primarily enter soil and water through farm manure (Hamscher & Bachour, 2018; Hamscher & Mohring, 2012). To assess the actual environmental input of veterinary drugs, comprehensive data are required, differentiated by animal species and farm characteristics (Wöhler et al., 2020).

In the EU, the use of veterinary drugs is regulated by law. In addition to the EU-wide antibiotic minimization concept (European Union, 2022), national efforts are also underway in Germany to record and reduce the use of antibiotics in animal husbandry. Since 2014, certain fattening farms in Germany have therefore been required to report the quantities of antibiotics used to the competent authority every 6 month (mo) (Federal Ministry of Food and Agriculture, 2021a). This system will be further expanded in the upcoming years. Despite these efforts, limited data are available for Germany documenting the use of veterinary drugs in general (i.e., substances other than antibiotics). In Germany, veterinarians themselves are required by law to document all drugs applied and dispensed for livestock, not just antibiotics. However, this is usually only done locally in offices and on farms (Federal Ministry of Food and Agriculture, 2009, 2015). In contrast to fattening farms, dairy farms have not been required to report any drug data until 2023. The annually published pharmacological industry sales figures for antibiotics to veterinarians in Germany indicate the absolute quantity and the sales region (Federal Office of Consumer Protection and Food Safety, 2021). However, those figures do not include information on the actual use of antibiotics in specific animal species. In particular, the type of production system and the kind of species are important for assessing potential emissions into the environment (Wöhler et al., 2023).

Studies in Germany and the EU have mostly been limited to the use of antibiotics in farm animals for fattening, or have only included the application frequency of other drugs (Mitrenga et al., 2020; van der Laan et al., 2021). On the other hand, in human medicine, surveys which provide information beyond the pure use of antibiotics already exist (Ludwig et al., 2022). However, to assess the input and environmental effects of veterinary drug use, it is particularly important to know the application quantities (not only frequencies) of all substance groups (not only antibiotics) for all kinds of animal species, not only fattening animals (Bártíková et al., 2016).

Our study contributes to closing this research gap by recording all drugs used in 2020 in a first step via a nationwide survey on dairy farms. Based on the legally required documentation on the farms, drug use was evaluated with regard to both the quantity applied and the frequency of application. In addition, other farm parameters were collected to investigate their relationship on drug usage. From this, potential strategies for reducing the use of certain substance groups can be derived in further steps to minimize their environmental effects.

5.2 Materials and Methods

The data in this study come from a nationwide survey on 50 dairy farms. We collected general farm data by a questionnaire and combined it with drug data from the application and dispensing receipts. For protection of data privacy, we collected and anonymized all data in 2021/22 for the entire year 2020. Institutional Review Board approval was not necessary because data collection was anonymous, precluding any identification of individuals, and did not involve animal experimentation.

The questionnaire listed in Supplemental Figures 5.S.1 and 5.S.2 (http://dx.doi.org/10.22029/jlupub-18392) was filled out by the farm manager during the farm visit and was used to collect data about the farm, farm managers, animals, and the production parameters in the year 2020. It is based on the farm surveys by Alvåsen et al. (2018) and Dickhaus (2010). The standardized questionnaire used in this study meets the requirements for objectivity, reliability, and internal validity (Moosbrugger & Kelava, 2020) . Its comprehensibility was tested on 2 test farms before the survey. To answer questions on animal numbers, farmers relied on the official animal database of the federal states (Herkunftssicherungs- und Informationssystem für Tiere (HI-Tier)) and for performance data, they relied on documentation from the local control associations on the farms (Bavarian State Ministry of Food Agriculture and Forestry, 2023).

For the collection of pharmaceutical data, we retrieved existing data. According to the legal situation for the survey year 2020, veterinarians and farmers were required to document the application or prescription of pharmaceuticals by the Veterinary Home Pharmacy Regulation (Federal Ministry of Food and Agriculture, 2009) and required to keep the receipts for 5 year (yr) by the Regulation on the Application and Documentation of Veterinary Medicinal Products by Animal Keepers (Federal Ministry of Food and Agriculture, 2015). We accessed the supporting documents, handwritten or machine-generated on paper, onsite at the farms as part of the survey and supplemented the drug data on the receipts with manufacturer information regarding active substances and concentrations contained.

The entire survey took place on a selection of the approximately 54,000 dairy farms in Germany (Federal Statistical Office of Germany, 2022a). Some of the farm managers volunteered after calls in journals and via associations. We actively recruited others via lists of training farms. To assess the regional representativeness of our sample, we mapped the regional location of the 50 farms in our sample to official statistics on the regional frequency of dairy farms in Germany (Federal Statistical Office of Germany, 2021). The overall survey is not representative, so its external validity is not entirely ensured. However, it does provide a valuable reference point for Germany, as the means of our sample closely resemble those reported in German statistics for many variables (see Supplemental Tables 5.S.1 and 5.S.2; http://dx.doi.org/10.22029/jlupub-18392).

First, we examined the collected drug data descriptively for the quantity applied and the application frequency, independently of the farm surveyed. Then, farm-specific treatment frequencies were calculated from the drug data. equation (Eq.) 5.1 shows the treatment frequency, which is a metric introduced by the German legislature originally intended to solely depict the utilization of antibiotics in animal husbandry (Federal Ministry of Food and Agriculture, 2013):

$$T_j = \frac{\sum_{i=1}^{N}(X_{ij} \times D_{ij})}{A_j} \tag{5.1}$$

To calculate the general treatment frequency (T_j) per farm (j), we sum over all substances used (i). The number of animals treated with a substance (X_{ij}) is multiplied by the number of treatment days (D_{ij}). The application frequency in the numerator ($X_{ij} \times D_{ij}$) is an absolute value that indicates how often a substance is used. The sum over all substances used is then divided by the average number of animals kept per farm (A_j). The treatment frequency thus represents a farm specific and relative value describing how often an animal is treated with any substance on average per yr.

In our study, we not only calculated the treatment frequency for antibiotics (TAB), but the overall treatment frequency (TO) and, in addition, separate the treatment frequency for antiphlogistics (TAPH), the treatment frequency for antiparasitics (TAP), and the treatment frequency for hormones (TH).

As an example, a farmer has 50 animals, which received medications in the year 2020 as follows: 15 cows received 3 d of penicilin each, 10 cows received 1 d of tetracycline each, and 8 cows received 1 d of prostaglandin each. According to Eq. 5.2, this results in a total therapy frequency of 1.26, specific to this farm. Additionally, therapy frequencies for certain groups of substances can be calculated. For animals on this farm, the therapy frequency is 1.1 for antibiotics (Eq. 5.3), and 0.16 for hormones (Eq. 5.4). In other words, on average, each animal on his farm received medication on 1.26 d in 2020, including 0.16 d with hormone treatment and 1.1 d with antibiotic treatment.

$$TO_j = \frac{15 \times 3 + 10 \times 1 + 8 \times 1}{50} = 1.26; \tag{5.2}$$

$$TAB_j = \frac{15 \times 3 + 10 \times 1}{50} = 1.1; \tag{5.3}$$

$$TH_j = \frac{8 \times 1}{50} = 0.16. \tag{5.4}$$

Using regression analysis, part of the variation in treatment frequencies can be explained by differences in farm characteristics. The selection of explanatory variables is based on a recent approach using machine learning. The LASSO method is a supervised machine learning algorithm that identifies the variables that are correlated with the variable being explained. Variables that have less influence or no influence at all are set to zero, and LASSO finds groups or correlations among the explanatory variables and removes all but one of the variables that measure the same effect. This means LASSO only selects the truly important ones from a plethora of variables to reduce overfitting by irrelevant variables (Ranstam & Cook, 2018; Tibshirani, 1996). Because LASSO still considered a multitude of farm characteristics to be important, and to avoid the issue of multiple testing, we selectively examined only a handful of parameters from those generated by LASSO, guided by the relevant literature (Arnott et al., 2017; Heringstad et al., 2007; Koeck et al., 2014; van der Laan et al., 2021).

We regressed the explanatory variables individually on treatment frequencies using OLS regression. The R^2 shows in percentage terms how much variation in treatment frequencies can be explained by variation in the parameters studied. The performed *t*-tests provide information on the significance of the estimated parameters for continuous variables. For binary dummy variables, the *t*-test indicates whether the means of the 2 groups differ significantly from each other. For categorial variables, we used analysis of variance (ANOVA) to compare multiple groups. For heterogeneous groups, the Games-Howell test indicates which groups are significantly different from each other (Ruxton & Beauchamp, 2008). In the results section, we present the direction, the relevance as an absolute value, and the significance of the effects.

5.3 Results

A total of 50 dairy farms from 8 different federal states with a total of 13,565 cattle participated in the study. For later analysis, we divided them into smaller farms (farm size = 0) with less than 88 lactating cows and larger farms (farm size = 1) with more than 88 lactating cows based on the median. In addition, we subdivided the farms into the regions south (region = 0), middle (region = 1) and north (region = 2). Within these groups, 58% of farms are located in the southern region, followed by 26% the in northern region and 16% in the middle region, which roughly corresponds to the regional distribution of all dairy farms in Germany (Federal Statistical Office of Germany, 2021). Supplemental Table 5.S.3 (http://dx.doi.org/10.22029/jlupub-18392) provides more detailed information on the classification and distribution of farms across federal states.

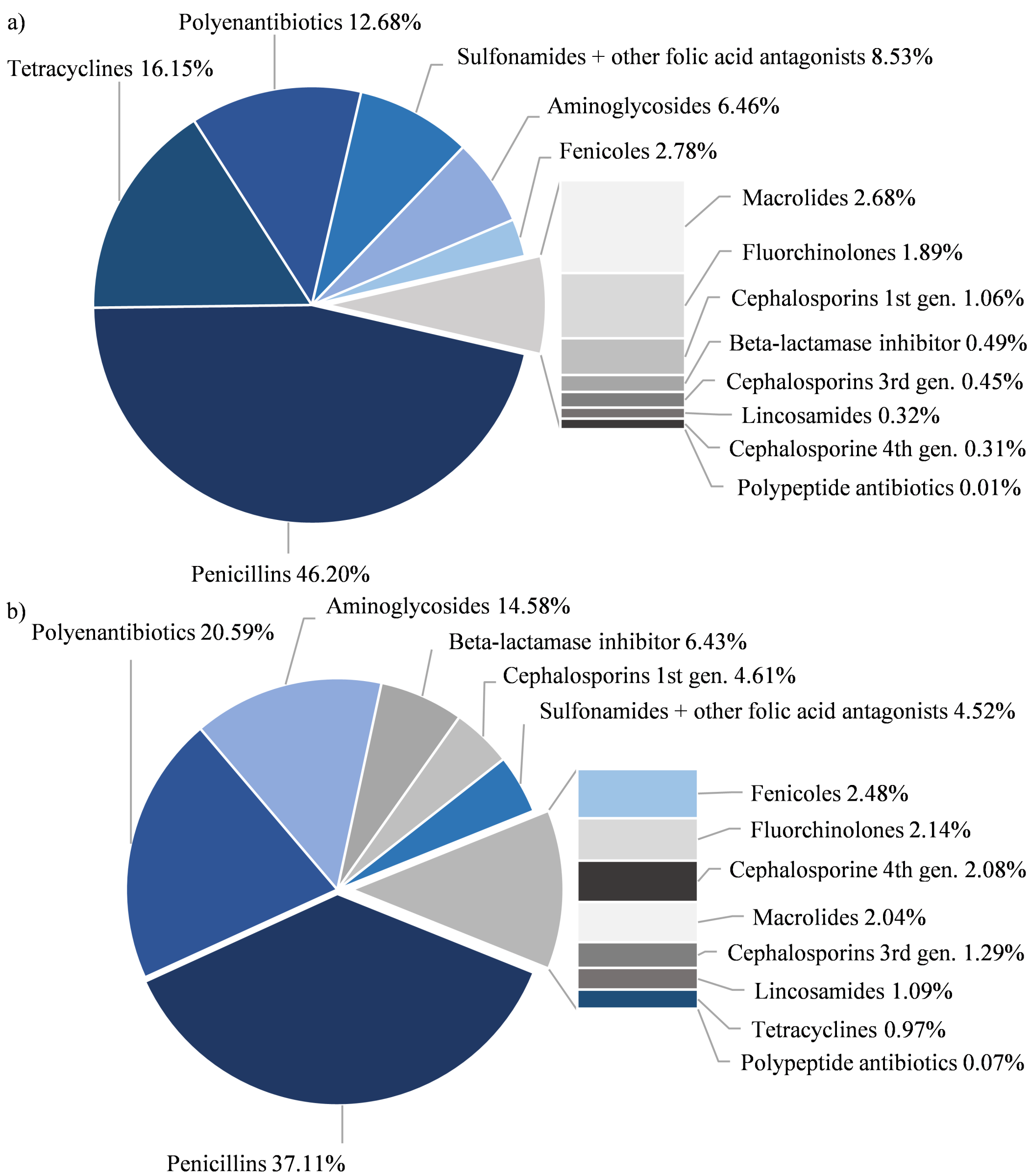
For a better overview of farm characteristics in the sample, we present a farm with mean values as follows: The mean farm in our sample was built in 1996 and is managed by a 45-yr-old person with a title of master craftsman. On 150 hectare (ha), the managing person and their 3 workers take care of 270 cattle, 128 of which are lactating cows that give approximately 9,360 kg of milk per yr. The alley ways of the freestalls are equipped with a slatted floor, and the cows from own breeding are milked in the milking parlor. In 2020, 204 drug receipts were issued for the mean farm. Of these, 40% of the drugs were applied directly by the veterinarian, 65% were dispensed to the farmer, and some technically belonged to both categories. Within the entire group of farms, 6% are certified organic, 74% have a veterinary care contract, and 26% use a claw bath. Supplemental Tables 5.S.1 and 5.S.2 (http://dx.doi.org/10.22029/jlupub-18392) show more detailed information on the individual variables.

In this survey, we were able to collect an overall active ingredient quantity of 956.47 kg, which can be classified into 26 active ingredient groups based on 91,126 individual applications. In terms of quantity, electrolytes with a share of 44.56% (426.52 kg) of the total quantity and carbohydrates with 35.16% (336.59 kg) were used the most on the dairy farms visited. According to EU Regulation 2019/06 in Europe (European Union, 2022), electrolytes and carbohydrates are also classified as drugs. These are, for example, glucose infusions for cattle with metabolic diseases. They are followed by antibiotics (9.37%, 89.71 kg) and antiphlogistics with (6.77%, 64.84 kg). If, on the other hand, the frequency of application is considered instead of the quantity applied, antibiotics are in the lead, as expected, with a share of 40.13% of all applications, as they usually must be applied for several days in a row. They are followed by antiphlogistics (18.86%), antiparasitics (13.09%), and hormones (9.29%), as they are mostly applied just once. Supplemental Table 5.S.4 (http://dx.doi.org/10.22029/jlupub-18392) shows all other substance groups and their share of quantity and frequency applied.

Antibiotics

Figure 5.1a shows the application quantities and Figure 5.1b shows the application frequencies of antibacterial substances, categorized by substance subgroups. Penicillins are the antibiotics used the most in terms of quantity (46.20%, 41.45 kg) and frequency (37.11%). Tetracyclines are important in terms of quantity (16.15%, 14.49

Figure 5.1: (a) Proportional application quantity and (b) proportional application frequency of the substance group antibiotics used on 50 dairy cow farms in Germany in 2020, categorized by antibiotic subgroups.

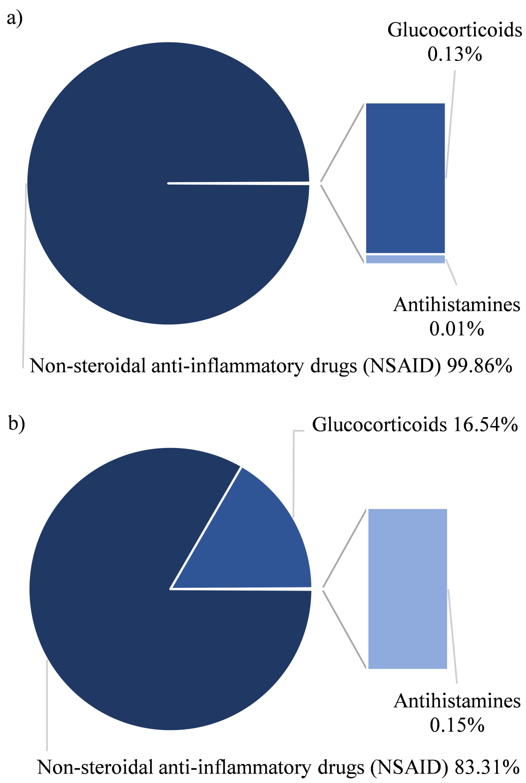


kg), but are used rather rarely, with 0.97% relative application frequency. In contrast, polyene antibiotics, aminoglycosides, first generation cephalosporins, β-lactamase inhibitors (usually combined with penicillins), and fourth generation cephalosporins are used relatively frequently compared with the quantity applied. The fourth generation cephalosporins in particular, which represent highest priority critically important antimicrobials, are used more frequently (2.08%) than tetracyclines, but have a minimal effect in terms of the quantity applied (0.31%, 0.28 kg).

Antiphlogistics

Figure 5.2 shows 3 substance subgroups for antiphlogistics. Non-steroidal anti-inflammatory drug (NSAID)s are the most relevant group, accounting for 99.86% (64.74 kg) of the quantity of antiphlogistics applied. Glucocorticoids are used relatively frequently (16.54%) among the antiphlogistics, but are of lesser importance in terms of their quantity applied (0.13%, 0.09 kg). Antihistamines are of little importance in terms of quantity (0.01%, 0.006 kg) and application frequency (0.15%).

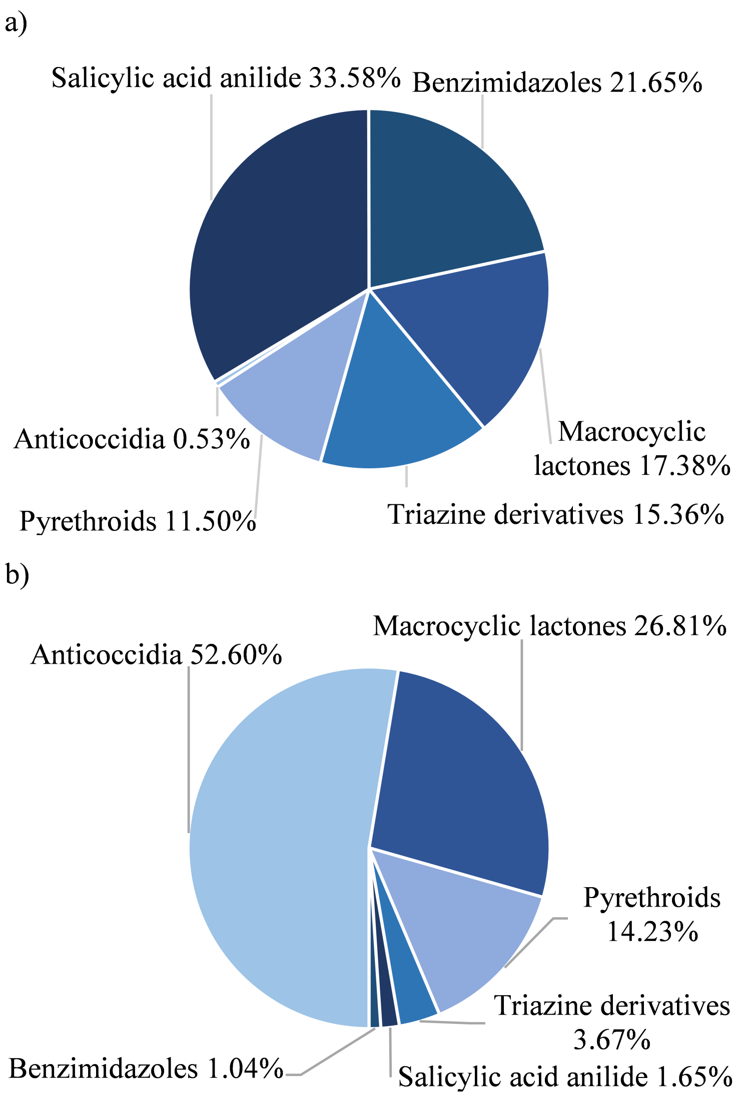
Figure 5.2: (a) Proportional application quantity and (b) proportional application frequency of the substance group antiphlogistics used on 50 dairy cow farms in Germany in 2020, categorized by antiphlogistic subgroups.



Antiparasitics

In the group of antiparasitics, salicylic acid anilides (1.65%) are used very rarely along with benzimidazoles (1.04%). However, due to the high concentration required for oral application form, they have the greatest importance in terms of quantity (33.58%, 1.5 kg; 21.65%, 0.97 kg), as shown in Figure 3. Anticoccidials are applied the most frequently with 52.6%. Because they are only used in calves at low concentrations, the quantitative importance is low (0.53%, 0.02 kg).

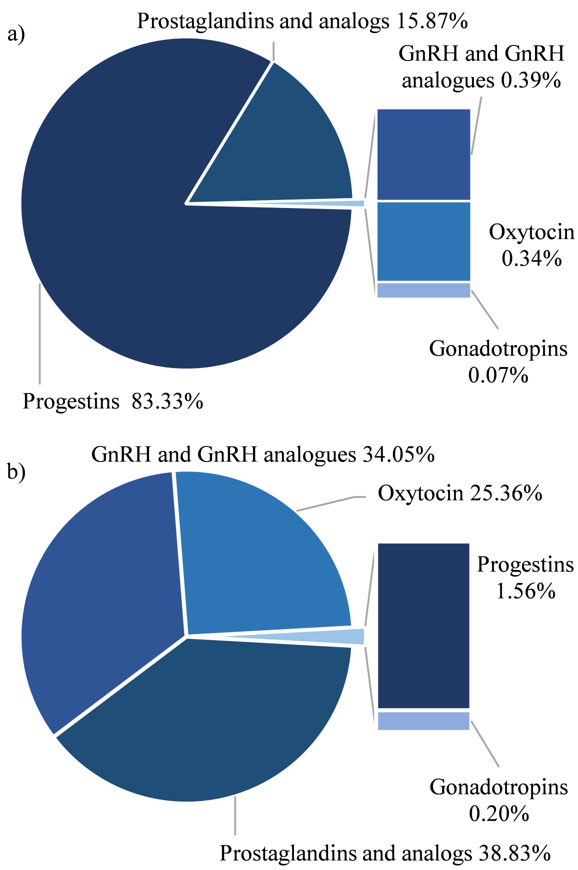
Figure 5.3: (a) Proportional application quantity and (b) proportional application frequency of the substance group antiparasitics used on 50 dairy cow farms in Germany in 2020, categorized by antiparasitic subgroups.



Hormones

Figure 5.4 shows the substance subgroups of hormones and their application quantity and frequency. Progestins are used very rarely (1.56%) as a local long-term preparation but have the greatest importance in terms of quantity (83.33%, 0.06 kg) due to their high concentration. Prostaglandin, GnRH, and oxytocin preparations are used relatively frequently (38.83%; 34.05%; 25.36%) in very low concentrations (15.87%, 0.01 kg; 0.39%, 0.0003 kg; 0.34%, 0.0003 kg).

Figure 5.4: (a) Proportional application quantity and (b) proportional application frequency of the substance group hormones used on 50 dairy cow farms in Germany in 2020, categorized by hormone subgroups.



Farm Characteristics

To examine the correlation of the farm characteristics with drug use in more detail, we used the treatment frequencies. Table 5.1 provides an overview of TO and the treatment frequency of each substance group (TAB, TAPH, TAP, TH). The mean shows that an average cow in this survey is treated with a substance on approximately

6 d/yr: on 2.34 d with antibiotics, on 1.07 d with antiphlogistics, on 0.76 d with antiparasitics and on 0.41 d with hormones. Sixteen of 50 farms do not use any antiparasitics and 10 farms do not use any hormones. We found a wide range in TO from a minimum of 0.94 d to a maximum of 21.69 d in 2020.

Table 5.1: Summary statistics of treatment frequencies measured in d/yr.

Variable[1]	N[2]	Mean	SD	Minimum	Maximum
TO	50	5.82	3.79	0.94	21.69
TAB	50	2.34	1.59	0.25	8.72
TAPH	50	1.07	0.86	0.14	4,74
TAP	50	0.76	1.30	0.00	6.03
TH	50	0.41	0.518	0.00	2.15

[1] TO = overall treatment frequency;
TAB = treatment frequency with antibiotics;
TAPH = treatment frequency with antiphlogistics;
TAP = treatment frequency with antiparasitics;
TH = treatment frequency with hormones.
[2] N = number of dairy farms in study.

Due to the large number of farm characteristics, not all of them were examined for their influence on treatment frequencies. Subsequently, we confine our focus to a subset of parameters whose effects are documented in the existing literature and have been further identified as pertinent through LASSO regression analysis with $\alpha = 1$, as the number of potential covariates exceeds the number of observations. The result of a 10-fold cross-validation, with the objective of minimizing the mean squared error, is $\lambda = 0.086$. Supplemental Table 5.S.5 (http://dx.doi.org/10.22029/jlupub-18392) displays all the variables that LASSO has deemed relevant but which, based on the literature, are not included in our regression analysis.

Table 5.2 shows the results of simple regressions of selected farm characteristics on respective treatment frequencies. Farm size in line 1 shows a significant ($P = 0.04$) correlation with TO. On average, large farms with a TO of 6.9 d/yr used drugs on roughly 2 more days than small farms (TO = 4.7 d). The treatment frequency of antibiotics (TAB = 0.77 d, $P = 0.088$) and antiparasitics (TAP = 0.7 d, $P = 0.057$) is higher for large farms. Large farms have a significantly ($P = 0.005$) higher TH by 0.4 d. Small farms used hormonal substances on average on 0.2 d and large farms on 0.6 d. A veterinary care contract in line 2 comes along with a 0.346 d higher TH ($P = 0.037$).

Table 5.2: Effects of farm-specific characteristics on dairy herd treatment frequencies; OLS estimates.

	Dependent variables[1,2]				
Explanatory variables	TO	TAB	TAPH	TAP	TH
Farm size	2.106 **	0.769 *	0.213	0.696 *	0.399 ***
(0 = small; 1 = large)	(1.037)	(0.441)	(0.244)	(0.358)	(0.136)
	4.739 ***	1.957 ***	0.965 ***	0.415	0.210 **
	[0.083]	[0.060]	[0.016]	[0.073]	[0.151]
Vet. care contract	1.679	0.387	0.260	0.474	0.346 **
(0 = no; 1 = yes)	(1.210)	(0.516)	(0.278)	(0.418)	(0.161)
	4.577 ***	2.055 ***	0.879 ***	0.412	0.154
	[0.039]	[0.012]	[0.018]	[0.026]	[0.087]
Milk yield	0.001 ***	0.0002*	0.0001 **	0.0001	0.0001 ***
(annual average in kg)	(0.0003)	(0.0001)	(0.0001)	(0.0001)	(0.00004)
	-1.379	0.299	-0.130	-0.431	-0.669*
	[0.149]	[0.068]	[0.080]	[0.035]	[0.178]
Region	0.686	0.257	0.073	0.041	0.299 ***
(0 = south; 1 = middle; 2 = north)	(0.623)	(0.262)	(0.143)	(0.216)	(0.075)
	4.667 ***	1.910 ***	0.949 ***	0.694*	-0.093
	[0.025]	[0.020]	[0.005]	[0.001]	[0.251]
Grazing	-1.360	-0.478	-0.456*	0.430	-0.264*
(0 = no; 1 = yes)	(1.111)	(0.469)	(0.247)	(0.382)	(0.150)
	6.309 ***	2.514 ***	1.235 ***	0.608 **	0.505 ***
	[0.030]	[0.021]	[0.066]	[0.026]	[0.061]
Longevity	-0.763 **	-0.312 **	-0.110	-0.111	-0.140 ***
(average period in years)	(0.368)	(0.155)	(0.086)	(0.131)	(0.049)
	9.282 ***	3.759 ***	1.569 ***	1.266 **	1.043 ***
	[0.082]	[0.078]	[0.033]	[0.015]	[0.147]
Claw bath	2.876 **	1.671 ***	0.361	0.161	0.696 ***
(0 = no; 1 = yes)	(1.163)	(0.459)	(0.275)	(0.423)	(0.136)
	5.072 ***	1.907 ***	0.977 ***	0.721 ***	0.228 ***
	[0.113]	[0.216]	[0.035]	[0.003]	[0.354]

[1]Note: Coefficients of simple linear regression are listed in the first line for each variable. Std. errors are indicated in parentheses, constants in curly brackets, and R^2 in square brackets.
[1] TO = overall treatment frequency; TAB = treatment frequency with antibiotics; TAPH = treatment frequency with antiphlogistics; TAP = treatment frequency with antiparasitics; TH = treatment frequency with hormones.
* p<0.1; ** p<0.05; *** p<0.01.

Milk yield in line 3 has an effect on all treatment frequencies in the simple regression. Thus, a 500 kg higher average annual milk yield correlates with an increase in TO by 0.5 d (P = 0.007). For TAB, treatment frequency increases by 0.1 d when average annual milk yield increases by 500 kg (P = 0.067). A similar effect is observed for TH (P = 0.002) and TAPH (P = 0.046). The effect size is lower with a 0.05 d increase in TH and TAPH for the same milk yield increase of 500 kg. According to line 4 in Table 5.2, the regional distribution of farms has an influence solely on use of hormones. We found a significant increase in TH by 0.3 d in the northern direction when compared with the south, center, and north regions (P = 0.02). If farmers offer their cows outside grazing (line 5), this leads to a tendential reduction in treatment frequency. If grazing is offered, the treatment frequency is 0.46 d (P = 0.07) lower for antiphlogistics and 0.26 d (P = 0.08) lower for hormones. A longer utilization period in line 6 comes along with a significantly reduced treatment frequency. Thus, TO decreases by 0.76 d when the average duration of use increases by one year (P = 0.04). This decrease is mainly driven by the associated decrease in treatment frequency of antibiotics (TAB = -0.312 d, P = 0.04) and hormones (TH = -0.14 d, P = 0.006). Farms using a claw bath (line 7) showed 2.876 d higher TO (P = 0.02) and a 1.671 d significantly higher TAB (P = 0.00), as well as a 0.696 d higher TH (P = 0.00) as seen in line 7.

5.4 Discussion

To the authors' knowledge, this study first describes the use of all substance groups applied on dairy farms in Germany. Previous studies, such as Hommerich et al. (2019) or Preine and Krömker (2022) focused exclusively on the use of antimicrobial substances.

On the 50 dairy farms in the study, antibiotics were the most frequently applied substance group, followed by antiphlogistics, antiparasitics, and hormones. The quantity applied in part differed greatly from the application frequency. By calculating treatment frequencies, it is possible to determine how many times per year an average animal on a farm was treated with a particular substance. For the overall treatment frequency, values ranged from 0.94 to 21.69 d/yr and were highly heterogeneous. On average, a cow in the study was treated on about 6 d, including 2.34 d with antibiotics, 1.07 d with antiphlogistics, 0.76 d with antiparasitics, and 0.41 d with hormones. In addition to individual farm management, other factors are also related to treatment frequency, such as a veterinary care contract, milk yield, grazing, longevity, farm size, and use of a claw bath.

The data from our study were obtained from a convenient sample, as participation in the study was voluntary. To better estimate the extent of voluntary response bias, we compared the characteristics of participating farms with all farms in Germany, displayed in Supplemental Tables 5.S.1 and 5.S.2 (http://dx.doi.org/10.22029/jlupub-18392). By relying on voluntary participation following announcements in journals, we predominantly reached farmers who are self-motivated and proactive in seeking information. Additionally, through targeted phone calls to training farms, we were able to include a higher proportion of farms with younger (year of birth in study: 1974, in Germany (GER): 1986) and better-educated (master craftsmen in study: 58%, GER = 37%) farm managers, as one must possess a master's title to be eligible for training apprentices. In our study, very small farms are underrepresented (area in study: 151 ha, GER = 101 ha; small farm size in study: 50%, GER = 60%), but we captured the regional distribution across Germany (see Supplemental Table 5.S.3 for details; http://dx.doi.org/10.22029/jlupub-18392). Unfortunately, we cannot definitively state whether the values in our study statistically differ from those in Germany, and we therefore acknowledge a bias. We can only argue that very small farms, which are predominantly part-time operations in Germany, are becoming less common, and their effect on the quantities of pharmaceuticals used is minimal due to their small livestock numbers. Despite this minor bias, our unique data set provides added value because it combines pharmaceutical data with farm and animal characteristics for Germany for the first time.

The data quality in this study profits from the extraction of information exclusively from books, thereby ensuring the exclusion of subjective opinions or assessments. Farms in Germany are required by law to keep their veterinary drug records on the farm for 5 yr, which is why we were able to review all drugs prescribed and applied by a veterinarian on site in 2020 (Federal Ministry of Food and Agriculture, 2009). It is reasonable to assume that every drug sold by a veterinarian to a farm is documented and that we can rely on the stated quantities, given the stringent controls in place in Germany. A questionnaire used to collect different farm parameters in addition to the data about drug use was completed by the farm manager or herd manager. For animal numbers and performance measures, we relied on the official animal database of the federal states (HI-Tier) and on the local control associations for the farms (Bavarian State Ministry of Food Agriculture and Forestry, 2023).

The official regulatory treatment frequency is determined per 6-mo period (Federal Ministry of Food and Agriculture, 2021a) and the number of animals kept enters the formula on the exact day matching the application period. However, animal number recording to the exact date is prone to error (Hemme et al., 2017). The associated data were not available to us due to data protection rights, which is why the treatment frequency in this study was calculated on an annual basis using the average number of animals kept over the entire year from the HI-Tier database.

On average, a cow in our study has a treatment frequency for antibiotics of 2.34 d. This is comparable to the survey by Hommerich et al. (2019), in which the treatment frequency for antibiotics on 474 farms averaged 2.1 d from 2011 to 2015. Despite the smaller sample size compared with that of the aforementioned papers, we are able to contribute meaningful results which are comparable to other studies and rely on high-quality data.

The use of antibiotics is heavily discussed. Nevertheless, particularly in cows on dairy farms, limited data are available on the actual quantities applied per species and year so far. Our data show that in terms of quantity, penicillins and tetracyclines are the antibiotic groups used the most in cows on dairy farms. The same is shown by Hajek et al. (2010), van Rennings et al. (2014) and the German sales surveys according to the regulation on the database-supported information system on medicinal products of the German Institute of Medical Documentation and Information (DIMDI-AMV) (Federal Office of Consumer Protection and Food Safety, 2021). However, the first 2 studies include beef cattle in addition to cows on dairy farms. The sales survey includes all antibiotics sold to veterinarians in Germany, irrespective of animal species, and thus does not show animal species-specific consumption. The study of van Rennings et al. (2014), comparable to our study, found large differences between the application frequency and the application quantity of substance subgroups. Again, cephalosporins and aminoglycosides are used relatively frequently in comparison to the quantity applied. The difference between application quantity and frequency for tetracyclines seen in our study is not shown in the survey by van Rennings et al. (2014). This could be because fattening animals integrated therein are treated more frequently with tetracyclines (Mitrenga et al., 2020). Polyene antibiotics were used in fairly high quantities (12.7%) and frequencies (20.6%), and monensin is the only active substance approved in Germany as a veterinary drug for cows. In light of the EU's antibiotic reduction concept, its use for ketosis prophylaxis is viewed critically because it is not used to treat infections, but rather to influence the metabolic state.

For antiphlogistics and antiparasitics, our collected data are unique for Germany in this form, so no comparable data are available. Anti-inflammatory drugs (antiphlogistics) account for only 6.77% of the total quantity of administered agents, yet they play a significant role with an application frequency of 18.86%. Farmers and veterinarians are obliged under German animal welfare legislation to treat animals and alleviate pain, and in this context, anti-inflammatory drugs play a crucial role. It is well established that the early use of anti-inflammatory drugs reduces systemic inflammation (Schmitt et al., 2023), thereby contributing to antibiotic conservation. Quantitatively, glucocorticoids have a limited presence among anti-inflammatory drugs, as their high activity necessitates administration in very low concentrations. Nevertheless, they are frequently employed, comprising 16.54% of the total usage.

The use of antiparasitic agents is highly farm specific. Within our sample, 16 farms do not use antiparasitics at all. The most common application of antiparasitics is for young calves against Cryptosporidia. However, the largest quantity of active ingredients is used in cattle that have access to pasture. This is because the parasite pressure is significantly higher in grazing conditions (Vanderstichel et al., 2012) compared with pure confinement housing. Despite the lower quantity of active ingredients compared with other groups, the environmental effects of antiparasitics should not be underestimated.

Data on hormone use in German cows are not yet available. In the Netherlands, van der Laan et al. (2021) surveyed the application frequency of reproductive hormones on 760 farms. They show a frequency of hormone use (prostaglandin 62.9%;

gonadotropin-releasing hormone (GnRH) 33.1%; progesterone 4.0%) comparable to the one in our study (prostaglandin 38.83%; GnRH 34.05%; progesterone 1.56%). Progestins (progesterones) were used very rarely in both studies. However, our study shows that progestins are by far the most important in terms of quantity. Again, substantial differences exist between the application frequency and quantity of drugs.

Our regression results show that, among other characteristics, farm size and the overall treatment frequency, as well as the treatment frequency of hormones, are correlated. Accordingly, the large farms in our study use drugs such as hormones more frequently compared with smaller farms. Additionally, a veterinary care contract is associated with a change in hormone use. In the study by van der Laan et al. (2021) from the Netherlands, it also was shown that farms with a veterinary care contract used hormones more frequently. A possible explanation could be the more regular rectal examination of the animals on the farms (Derks et al., 2013), which results in a more frequent diagnosis of fertility disorder and an accompanying therapy with hormones. In addition, farms with veterinary care contracts often have higher performance levels. According to a study by Ries et al. (2022), they achieve higher performance levels as measured by milk yield than farms without a care contract. The increased focus on performance parameters could be a reason for more active fertility management as well. Among the farms that did not use hormones at all, the majority were smaller farms (< 88 lactating cows). However, in the Netherlands, farm size was not correlated with hormone use according to van der Laan et al. (2021). Ries et al. (2022) showed that smaller farms were more likely to not have a veterinary care contract. In our study, we see a tendency that large farms are 20% more likely to have a care contract than small farms ($P = 0.1$). Thus, it seems reasonable to assume that the increased use of hormones is correlated with the existence of the veterinary care contract and the associated stronger veterinary monitoring with regard to fertility disorders, rather than by farm size, as initially posited.

As discussed in detail in many studies, milk yield and health traits are negatively correlated with breeding (Heringstad et al., 2007; Koeck et al., 2014). In our study, farms with high milk yield show a higher treatment frequency. The effect is large, with an increase in overall treatment frequency of 0.5 d per 500 kg more milk per year. In addition to overall treatment frequency, milk yield is also related to treatment frequencies of antiphlogistics, hormones and antibiotics. Conditions associated with high milk yield include mastitis, ketosis, lameness, ovarian cysts, and retained placenta (Heringstad et al., 2007; Koeck et al., 2014; Simianer et al., 1991). Mastitis, lameness, and retained placenta are usually treated with antibiotics and antiphlogistics, and ovarian cysts are most often treated with hormones (Taktaz et al., 2015), which is mirrored by the increased treatment frequencies. In general, estrus detection is essential for reproductive performance (Gordon, 2011). In a study of 267 lactating cows, Lopez et al. (2004) showed that increasing milk yield reduced the duration of estrus, making it less detectable. This could be an additional explanation for the more frequent use of hormones when milk yield increases. Because in our study large farms with more than 88 lactating cows showed a significantly higher milk yield ($P = 0.00$, mean = 8,187.2 kg vs. 10,533.8 kg), it can be suspected that farm size has an indirect influence on treatment frequency.

In this survey, the region has an influence on the treatment frequency of hormones. Farms from the southern region used hormones significantly less frequently than farms from northern regions. Southern Germany is mainly home to small traditional farms (Merle et al., 2012), which use a different fertility strategy. As mentioned before, small farms usually do not have a veterinary care contract and have a lower milk yield, which could explain our present findings.

Hygiene has a major influence on biosecurity and thus on the health of animals in the herd. Animals kept permanently indoors are dirtier than animals that have pasture access (Nielsen et al., 2011). In addition, animals with pasture access are less likely to be affected by lameness (Haskell et al., 2006; Olmos, Boyle, et al., 2009), mastitis (Washburn et al., 2002), and uterine disease (Olmos, Mee, et al., 2009). Overall, grazing has a positive effect on animal health (Arnott et al., 2017). In our survey, farms with grazing options used antiphlogistics and hormones slightly less often than farms without that option. In contrast, a significant increase in the use of antiparasitics would have been expected on farms with grazing options, as animals are exposed to greater parasite pressure when grazing (Vanderstichel et al., 2012). We could not prove this with respect to all animals on a farm. However, when considering treatment frequency excluding applications to calves younger than 6 mo, which often do not have access to pasture, farms with pasture access tend to have a higher treatment frequency of 0.32 d for antiparasitics compared with farms without pasture access ($P = 0.03$). Calves have a strong influence on the treatment frequency of antiparasitics, as they are significantly more likely to receive antiparasitic treatment, and treatment frequency is not about the quantity applied, but the application frequency.

Farms with a longer utilization period treat their animals less often in this study. This is mainly related to the less frequent use of antibiotics and hormones. Older animals tend to fall ill more often (Abebe et al., 2016; Gernand et al., 2012),but are thus discarded more quickly. In Germany, cows are most often discarded due to fertility problems and udder diseases (Heise et al., 2016). It can be speculated that a longer life of milking cows could speak for a farm management with optimal general conditions for the animals, in a way that they are generally healthier, require less treatment, and grow older as well. However, in this study, only drug data were collected, which is why it is not possible to draw any direct conclusions about the overall health of animals studied.

In Germany, claw baths cannot be used for the therapy of claw diseases (European Union, 2022)because no products are available for therapeutic use. However, precautionary care measures to reduce germ pressure are possible. Therefore, one might assume that farms that use a claw bath for prevention would have a lower treatment frequency than farms that do not. Our results, however, present a contrasting picture: Farms with a claw bath have a 2.9 d higher overall treatment frequency ($P = 0.016$). The treatment frequencies with antibiotics and hormones with 1.7 d and 0.7 d are significantly higher than in farms without claw bath ($P = 0.00$). Studies on the efficacy of claw baths in cattle are limited (Jacobs et al., 2019). In addition, the design and management of the claw bath is critical to its success (Cook, 2017). In our study, the use of a claw bath is positively correlated with the amount of diagnosis concerning the musculoskeletal system ($P = 0.008$). Supplemental Table 5.S.6 (http://dx.doi.org/10.22029/jlupub-18392) provides an overview of the frequency of diagnoses recorded in our study, sorted by diagnosis group. Dobson et al. (2008) showed that lame cows had significantly reduced estrus behavior. In addition, lame cows are 3.5 times more likely to have delayed cyclicity (Garbarino et al., 2004) and lower ovulation rates (Melendez et al., 2018). Omontese et al. (2020) found a lower proportion of cyclic cows in cows with claw lesions compared with healthy cows. This could explain why farms with a claw bath used hormones more frequently than farms without a claw bath.

Wet and manure-soiled areas promote potential claw disease (Stanek, 2005) and negatively affect udder health (Dohmen et al., 2010), resulting in more frequent mastitis (Firth et al., 2019). Animals with claw problems lie down more than healthy animals (Ito et al., 2010). The increased ground contact of the udder when lying down results in poorer udder hygiene (DeVries et al., 2012), and thus may contribute to increased infection of the udder by environmental germs. Farms that used a claw bath were more likely to have a diagnosis of mastitis in our study ($P = 0.08$). This could explain why farms with a claw bath used antibiotics significantly more often than other farms.

Dairy livestock operations in central European countries such as Germany and the Netherlands are structured in a similar way, with a large number of familyrun dairy operations that keep small- to medium-sized herds, depending on the region. On average, German farms keep about 72 dairy cows (Federal Statistical Office of Germany, 2022b), and Dutch farms keep about 110 dairy cows (Statistics Netherlands, 2022). Legal regulations on animal husbandry and the use of medicines are at a comparable level as well, despite country-specific laws through EU regulations. On the contrary, dairy livestock operations in the US have a different structure, as a US farm keeps an average of 316 dairy cows (United States Department of Agriculture, 2022). In addition, the legal framework is different compared with the EU. For these reasons, our data can only be transferred very cautiously to countries with different agricultural and legal structures.

When looking at the substances applied, large differences between the application frequency and the application quantity of substance subgroups are noticeable. In Germany, treatment frequencies are used as a key figure in the field of antibiotic minimization to document the use of antibiotics in livestock farming. However, this indicator only represents the application frequency of drugs, but not the application quantity (van Rennings et al., 2013). In addition, our study shows an excerpt of multiple parameters which are related to the application frequency of veterinary drugs, but refrains from making assumptions about herd management, the different sensitivity of farmers to detect diseases, or the role of prophylaxis. Hence, to comprehensively capture and assess the utilization of veterinary drugs on farms, it is imperative to consider more than just a singular frequency-based application statistic.

5.5 Conclusion

Our study has shown that cows on dairy farms are treated with antibiotics and other substances with high environmental risk probability, such as antiphlogistics, antiparasitics, and hormones. However, our study shows that the treatment frequency per animal is very heterogeneously distributed between farms. In addition to individual farm management, factors such as the presence of a veterinary care contract, farm size, milk yield, grazing, longevity, and the use of a claw bath correlate with treatment frequency. With regard to the recording and minimization of environmental inputs by veterinary drugs, we see that the monitoring of a single substance group (antibiotics) is not sufficient and can only provide initial aspects for further regulation across all substance groups. A first enhancement would entail the centralized provision of comprehensive veterinary drug data across all animal species, given their current high-quality existence but limited local accessibility on farms. Further studies are needed to evaluate the specific release into the environment and consequences for the ecosystem.

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5.S Supplemental Material

Figure 5.S.1: Questionnaire part 1.

GENERAL INFORMATION ON THE INTERVIEW

A	GENERAL		
A-1	Interview identifier		
A-2	Interviewee's position		
A-3	Farm managers age		
A-4	Farm managers education level		
A-5	Date of interviews		
A-6	Duration of interview	Start:	End:

GENERAL INFORMATION ON THE FARM

B	FARM Data						
B-1	Farms post code						
B-2	Farmed area in ha						
B-3	Number of workers						
B-4	Does your farm have an organic certificate?	☐ Yes Certificate:		☐ No			
B-7	Number of animals kept	Animal species	Group	01	01.04.	01.08.	01.12.
		Cattle I	Cattle				
			Calves				
B-8	Veterinary care contract	☐ Yes		☐ No			
B-9	Type of stock book	☐ electronic	☐ hand written	☐ Prints from vet			

SPECIAL INFORMATION ON THE FARM

C	HUSBANDRY CONDITIONS					
C-1	Construction year of barn					
C-2	Husbandry					
C-3		Calves (14d)	☐ Igloo	☐ Warm stall	☐ Group	
C-4	Continuous occupancy	☐ Yes		☐ No		
C-5	In-Out procedure	☐ No	☐ Stable	☐ Compartment	☐ Stock	
C-6	Soil condition	☐ fully slatted floor	☐ partly slatted floor	☐ paved	☐ bedding	
C-7	Grazing	☐ No	☐ Yes		☐ Grazing	
C-8	Lying pens	☐ High pens	☐ Low pens		☐ Other	
C-9	Milking system	☐ Milking parlor	☐ Pipe milking system		☐ Milking robot	
C-10	Animal Origin	☐ own farm	☐ 1 other farm		☐ 2 other farms	☐ >2 other farms
C-12	hygienical sluice	☐ Yes	☐ No		☐ loose room	
D	VACCINATIONS					
D-1	Dairy cows	☐ Newborn diarrhea	☐ Bronchopneumonia		☐ Schmallenberg virus	
D-2	Suckler cow	☐ Newborn diarrhea	☐ Bronchopneumonia		☐ Schmallenberg virus	
Other vaccinations:						

Figure 5.S.2: Questionnaire part 2.

E	PERFORMANCE INFORMATION				
E-1a	Dairy cows:	Average milk yield in kg			
E-2a		Average utilization in years			
E-3a		Annual average of fat and protein in kg			
F	EXCREMENT				
F-1	Manure removal	☐ Manually	☐ Robot	☐ Muck pusher	
F-2	Slurry storage	☐ Open	☐ Closed	☐ Outside	☐ in barn
F-3	Amount of manure per year in m^3				
F-4	Slurry treatment	☐ None	☐ Biogas plant	☐ Other:	
F-5	Slurry use	☐ Own land only	☐ Partial external land		
F-6	Solid manure storage	☐ paved	☐ temporarily not paved		
F-7	Amount of solid manure per year in t				
F-8	Solid manure use	☐ Own land only	☐ Partial external land		
G	VENTILATION				
G-1	Ventilation type	☐ active	☐ passive		
G-2	Air filtration	☐ Yes	☐ No		
H	CLEANING AND DISINFECTION				
H-1	Cleaning	☐ without disinfection	☐ with disinfection		
H-2	Frequency of cleaning				
H-3	Frequency of disinfection				
H-4	Disinfectant				
H-5	Disinfectant whereabouts				
H-6	Claw bath	☐ Yes	☐ No		
H-7	Calving box	☐ Yes	☐ No		
J	SOURCES OF DRUG SUPPLY				
J-1	Source 1				
		Documentation:	Share in %:		
J-2	Source 2				
		Documentation:	Share in %:		
K	STORAGE OF DRUGS AND RESIDUALS				
K-1	Storage				
K-2	Use of residual quantities	☐ Yes how:	☐ No		
K-3	Residual quantities in %				
K-4	Drug disposal				
K-5	Times per year				
K-6	Knowledge on drug disposal				
L	COMMENTS				
Z	Evaluation requested?	☐ Yes	☐ No		

Table 5.S.1: Summary of descriptive statistics of all continuous variables studied.

Variable	Description	N	Mean	Std. Dev.	Min.	Max.	Mean GER
Age	Farm manager's y.of birth	50	1974	9.95	1954	1992	1968[1]
Area	Farmed area (in ha)	50	150.81	155.22	18	870	101.4[2]
Calves	Numb. of avg. calves kept	50	45.83	41.29	2	193	-
Cattle	Numb. of avg. cattle kept	50	225.48	201.35	34	930	-
CattleCalves	Numb. of avg. cattle and calves kept	50	271.31	238.00	37	1,064	-
CY	Construction year of barn	50	1996	14	1960	2015	-
Longevity	Avg. utilisation period in y.	50	4.54	1.42	2.000	9.500	3.34[3]
Milk yield	Avg. annual milk yield in kg	50	9,360.50	1,899.23	6,000	13,399	8,457[4]
Papp	Number of applied pharmaceutical agents	50	85.82	88.65	0	445	-
Pused	Number of used pharmaceutical agents	50	265.40	216.09	14	973 -	
Pdisp	Number of dispensed pharmaceutical agents	50	190.420	191.95	1	958	-
PerPapp	Percentage of applied pharmaceutical agents	50	0.40	0.27	0.000	0.960	-
PerPdisp	Percentage of dispensed pharmaceutical agents	50	0.65	0.23	0.040	1.000	-
Pused	Number of used pharmaceuticals	50	204.40	158.76	7	742	-
Lcows	Number of lactating cows	50	128.48	112.77	25	541	68,41[2]
Staff	Number of workers	50	3.96	4.09	1	22	-

[1]Federal Statistical Office of Germany (2021), based on all agricultural farms in Germany.
[2]Federal Statistical Office of Germany (2021)
[3]Regional Control Association North Rhine-Westphalia (2021)
[4]Federal Ministry of Food and Agriculture (2021b)

Table 5.S.2: Summary of descriptive statistics of all categorial variables studied.

Variable	Description	N	Value	n	%	cum. %	% GER[1]	cum. % GER
Organic	Organic certificate	50	0: no	47	94	94	91	91
			1: yes	3	6	100	91	100
Claw bath	Claw bath	50	0: no	37	74	74	-	-
			1: yes	13	26	100	-	-
Edu	Farm manager's education	50	0: career changer	2	4	4	-	-
			1: fellow	14	28	32	26	26
			2: master craftsmen	29	58	90	371	63
			3: university degree	5	10	100	16	79
			4: other				21	100
Farm size	Farm size in lactating cows	50	0: small ($\leq$ 88)	25	50	50	60	60
			1: big (> 88)	25	50	100	40	100
Grazing	Grazing	50	0: no	32	64	64	571	57
			1: yes	18	36	100	431	100
Husb	Husbandry cows	50	0: tie-stalls	4	8	8	381	38
			1: free-stall	46	92	100	661	104
HusbCalve	Husbandry calves	50	0: igloo	0	0	0	-	-
			1: warm stall	35	70	70	-	-
			2: group	15	30	100	-	-
Milksys	Milking system	50	0: pipe milking system	4	8	8	-	-
			1: milking parlour	29	58	66	-	-
			2: milking robot	17	34	100	-	-
Muck	Muck removal	50	1: manual	24	48	48	-	-
			2: robot	11	22	70	-	-
			3: muck pusher	15	30	100	-	-
Origin	Animal origin	50	1: own farm	46	92	92	-	-
			2: one other farm	0	0	92	-	-
			3: $\geq$ one other farm	4	8	100	-	-
Region[2]	Region in Germany	50	0: South	29	58	58	60[1]	60
			1: Middle	8	16	74	18[1]	78
			2: North	13	26	100	22[1]	100
SB	Type of stock book	50	0: none	0	0	0	-	-
			1: electronic	25	50	50	-	-
			2: handwritten	23	46	96	-	-
			3: printed	2	4	100	-	-
Soil	Soil condition	50	1: fully slatted floor	31	62	62	-	-
			2: partly slatted floor	0	0	62	-	-
			3: paved	16	32	94	-	-
			4: bedding	3	6	100	-	-
Vet. care contract	Veterinary care contract	50	0: no	13	26	26	-	-
			1: yes	37	74	100	-	-

[1]Federal Statistical Office of Germany (2021)
[2] For more detailed information, see Table 5.S.3.

Table 5.S.3: Classification of the variable "Region" based on farm location.

Variable Value	Descr.	Federal States	Share of farms GER[4]	Share of farms sample
Region = 0	South	BW, BY[1]	60.20%	58%
Region = 1	Middle	RP, HE, NW, SN, SL, TH[2]	17.47%	16%
Region = 2	North	NI, ST, BB, BE, HH, HB, MV, SH[3]	22.33%	26%

[1]BW: Baden-Württemberg, BY: Bavaria
[2]RP: Rhineland-Palatinate, HE: Hesse, NW: North Rhine-Westphalia, SN: Saxony, SL: Saarland, TH: Thuringia
[3]NI: Lower Saxony, ST: Saxony-Anhalt, BB: Brandenburg, BE: Berlin, HH: Hamburg, HB: Bremen, MV: Mecklenburg-Vorpommern, SH: Schleswig-Holstein
[4]Federal Statistical Office of Germany (2021)

Table 5.S.4: Substance groups with application quantity and application frequency.

Substance group	Application quantity in kg	Application quantity in %	Total applications	Application frequency in %
Electrolytes	426.519	44.56%	5742	6.40%
Carbohydrates	336.585	35.16%	1607	1.79%
Antibiotics	89.710	9.37%	36011	40.13%
Antiphlogistics	64.835	6.77%	16924	18.86%
Bismuth compounds	22.255	2.32%	2609	2.91%
Dermatologics	6.400	0.67%	113	0.13%
Antiparasitics	4.458	0.47%	11746	13.09%
Boric acid compound	1.994	0.21%	80	0.09%
Anesthetics/Narcotics	1.761	0.18%	409	0.46%
Vitamins	0.961	0.10%	2026	2.26%
Disinfectants	0.417	0.04%	66	0.07%
Others	0.413	0.04%	301	0.34%
Roborants	0.370	0.04%	103	0.11%
Muscle relaxants	0.112	0.01%	46	0.05%
Antimycotics	0.100	0.01%	3	0.00%
Sedatives	0.093	0.01%	2558	2.85%
Hormones	0.077	0.01%	8336	9.29%
Expectorants	0.070	0.01%	550	0.61%
Parasympatholytics	0.040	0.00%	232	0.26%
Diuretics	0.034	0.00%	141	0.16%
Antitympanika	0.014	0.00%	1	0.00%
Antithrombotics	0.013	0.00%	5	0.01%
Hyperaemics	0.002	0.00%	5	0.01%
Proton pump inhibitor	0.001	0.00%	27	0.03%
Parasympathomimetics	0.001	0.00%	28	0.03%
Sympathomimetics	0.000	0.00%	59	0.07%
Total	957.233	100 %	89728	100 %

Table 5.S.5: Additional variables identified as relevant by LASSO.

Dependent variable	Relevant explanatory variables
TO[1]	Edu. Cattle. Cattle Calves. CY. Origin. Muck. Pused. Latitude. Longitude. Pdisp. PerPdisp
TAB[2]	Area. Soil. Milksys. Origin. Claw bath.
TAPH[3]	Age. HusbCalve. Milksys. Origin. Pdisp
TAP[4]	Pdisp
TH[5]	Age. Edu. Bio. Cert. Calves. SB. HusbCalves. Soil. Grazing. Milksys. Origin. Longevity. Muck. Pused. Longitude. PerPdisp.

Note: See Table 5.S.1 and 5.S.2 for a description of variables.
[1] Overall treatment frequency
[2] Treatment frequency with antibiotics
[3] Treatment frequency with antiphlogistics
[4] Treatment frequency with antiparasitics
[5] Treatment frequency with hormones

Table 5.S.6: Frequency of diagnoses recorded in our study sorted by diagnosis group.

Diagnosis group	Frequency of occurance
Mastitis and teat disease	5026
Metabolic and deficiency disease	1759
Urinary and reproductive tract disease	1076
Respiratory disease	998
Digestive tract and abdominal disease	793
Skin disease	679
Musculoskeletal disease	655
Anaesthesia and analgesia	639
Oestrus cycle modulation	629
Infectious disease	391
Circulatory disease	216
Parasitics	103
Other	91
Nervous system	28
Muscous membranes and eye	8

Chapter 6

Pharmaceutical Consumption in Human and Veterinary Medicine in Germany: Potential Environmental Challenges

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Abstract

Pharmaceutical usage in both human and veterinary medicine contributes substantially to societal well-being. However, concerns regarding its environmental impacts are increasing. Despite global awareness, a substantial knowledge gap exists in Germany and several other countries regarding pharmaceutical residues, hindering comprehensive environmental risk assessments. This study aims to bridge this gap by analyzing veterinary pharmaceutical consumption in livestock farming in Germany and comparing it with human pharmaceutical usage, subsequently correlating these findings with environmental data on pharmaceutical residues to conduct a straightforward analysis of the environmental risk. Data from 129 agricultural farms were utilized to comprehensively analyze veterinary pharmaceutical usage. Extrapolation to national levels estimates a substantial quantity of active substances used, particularly antibiotics and electrolytes. Comparison with human pharmaceutical usage highlights differences in substance prevalence and usage patterns. Environmental correlations indicate a considerable presence of pharmaceutical residues in Germany,

with notable distinctions between human and veterinary sources. In the environmental risk analysis, significant differences are evident between individual active substances within the same substance group. The study underscores the importance of addressing pharmaceutical residue impacts on the environment and emphasizes the necessity of comprehensive data for informed decision-making and environmental management strategies.

6.1 Introduction

Pharmaceuticals are undeniably integral to our daily lives. Beyond the evident benefits of disease eradication, healing, therapy, and prevention in both humans and animals, they also contribute to food safety. However, concerns about their usage have emerged as well (Barra Caracciolo et al., 2015; Maculewicz et al., 2022; Zuccato et al., 2006). Some adverse effects are widely known, such as the development of antibiotic resistances, recognized by the WHO as one of the top ten threats to global health (World Health Organization, 2019). Not only do antibiotic resistances represent a growing concern in the treatment of both humans and animals, but resistance to antiparasitic agents is on the rise as well (Charlier et al., 2022). In addition, the consumption of pharmaceuticals such as hormones or anti-inflammatory drugs and the resulting residues in soil and water lead to negative effects on non-target organisms in the environment (Kidd et al., 2007; Parolini, 2020). However, most of the effects on non-target organisms are still not well understood or partially unknown (Boxall et al., 2003; Hamscher & Bachour, 2018).

Despite global awareness of the issue, there exists a significant knowledge gap regarding discharges of pharmaceuticals into the environment in Germany. Accurate estimation of environmental consequences necessitates a comprehensive understanding of the pharmaceuticals in use, including the quantity of each active substance employed (Wöhler et al., 2020). Official data on consumption quantities from veterinary medicine are, in Germany, only available for antibiotics, but even this information is incomplete, as presently, veterinarians are obliged to report usage data for certain animal categories only (Federal Ministry of Food and Agriculture, 2021), and the pharmaceutical industry merely provides aggregated figures on the sales of antibiotics to veterinarians only (Federal Office of Consumer Protection and Food Safety, 2021). For all other substance groups and individual compounds, consumption data are lacking. Research conducted in Germany and the European Union has primarily focused on the utilization of antibiotics in livestock purposes, with some studies only examining the frequency of use and not the quantity used (Hemme et al., 2018; Hommerich et al., 2019; Kasabova et al., 2021; Kuipers et al., 2016; Mitrenga et al., 2020; Olmos Antillón et al., 2020; van der Laan et al., 2021).

In human medicine, the annual pharmaceutical report (Ludwig et al., 2022) only provides information on daily doses of medications, making it nearly impossible to calculate the absolute quantity used. Without comprehensive data on the types and quantities of pharmaceuticals used, assessing their impact on the environment is challenging. Moreover, apart from the difficulty in identifying, quantifying, and tracing the origin of environmental inputs, for most substances the consequences of residues on humans, animals, and the environment have not been fully explored yet.

In response to this knowledge gap, we have collected and extrapolated veterinary pharmaceutical consumption data, specifically in the context of livestock farming, to estimate national levels. By comparing human and veterinary pharmaceutical substances, our study aims to elucidate which substances and substance groups are prevalent in different sectors. Furthermore, we correlate our findings with data on pharmaceutical residues in the German environment to establish connections between usage patterns and environmental presence to conduct a straightforward analysis of the environmental risk.

6.2 Materials and Methods

For this study, we have combined three data sources for Germany. Firstly, we utilized data from a nationwide survey[1] conducted on 129 agricultural farms (summary statistics in Supplemental Table 6.S.1), covering the entire year 2020. These farms are categorized into 50 dairy farms, 15 cattle fattening farms, 16 piglet producers, 33 pig fattening farms, 10 laying hen farms, and 5 broiler producers from nine different federal states. From their official application and dispensing receipts, we obtained medication data, providing an overview of the veterinary drugs used, including their quantities in kg, the active substances contained, the duration of medication, and the number and category of treated animals.

In a subsequent step, we expanded our study from the 129 surveyed farms to a national scale by estimating the total usage of veterinary drugs across Germany, categorized by animal category. To ensure accurate comparisons between different animal categories, which may vary in live weight, we computed the usage of each active substance per livestock unit using the conversion factors provided by Eurostat

[1]More detailed information about the survey can be found in the paper by Abdallah et al. (2024)

(2021) in Supplemental Table 6.S.2. For the extrapolation, we divided the amount of each active substance used by the livestock units in the study, and then multiplied these figures by the total number of livestock units in Germany (variable LU_DE in Supplemental Table 6.S.1)as recorded in the 2020 Agricultural Census (Federal Statistical Office of Germany, 2021a). As part of a robustness assessment in Supplemental Table 6.S.8, for each active substance, the quantity utilized per PCU was computed in accordance with the methodology prescribed by the European Medicines Agency (EMA). This computation entailed dividing the active substance quantity documented in the study by the estimated live weight of the livestock cohort maintained or slaughtered within the respective year (European Medicines Agency, 2011, 2018).

As a second dataset, we incorporated aggregated consumption data for human pharmaceuticals obtained by the German Environment Agency from the following source: IQVIA MIDAS® quarterly data Germany), Update 4Q22 for the calendar year 2020 reflecting estimates of real-world activity. The data refer to human medical use only and comprise 2,813 active substances with a total sales quantity of 38.921 t.

To establish comparability between humans and livestock, we subsequently present the administered dosage of active substance in milligrams per kg body weight. For this purpose, the extrapolated amounts of active substances were divided either by the total mass of livestock (Bavarian Academy for Nature Conservation and Landscape Management, 2018) or by the mass of the population of Germany (Federal Statistical Office of Germany, 2023a, 2023b).

As a third dataset, we utilized data on environmental findings of pharmaceutical residues. In a meta-analysis, the German Environmental Agency compiled studies worldwide between 1988 and 2020 that identified pharmaceutical residues in the environment, such as soils and waters, creating a publicly accessible database (German Environment Agency, 2022). The database includes information on the source study, the location of the findings, and the detected active substances. For further analysis, we employed 295 publications with 34,001 environmental findings specific to Germany until the year 2020. In the evaluation, we aligned the active substances used in veterinary and human medicine in 2020 with environmental findings. Detected transformation products that could be clearly attributed to an original active substance were assessed accordingly.

To ascertain the environmental risk posed by identified substances in veterinary and human medicine, we calculated PEC values for each substance and compare these with PNEC values.

According to European Medicines Agency (2016), predicted environmental concentration in soil (PECsoil) of an active substance of a veterinary medicinal product, expressed in micrograms per kg ($\mu g/kg$), is determined through Equation 6.1, where D represents the daily dose of the active substance, measured in milligrams per kg body weight per day ($mg/(kg_{bw} * d)$). Ad is the number of days the treatment is administered. BW denotes the body weight of the animal in kg_{bw}, and P is the annual turnover rate of animals per place, both variables given in European Medicines Agency (2016), Table 3. The constant 170 $(kg_N)/ha$ refers to the EU limit for nitrogen application on fields. Fh is the fraction of the herd that receives treatment, a value ranging between 0 and 1, given in European Medicines Agency (2016), Table 2. The value 1500 kg/m^3 is the bulk density of dry soil, the value 10000 m^2/ha represents the area of entry per hectare, while 0.05 meters indicates the depth of soil penetration considered in the model. Ny is the amount of nitrogen produced per place per year, H is the housing factor, which is 1 for animals housed year-round and 0.5 for animals housed for only 6 months, both detailed in European Medicines Agency (2016), Table 3 as well. In the end, the term is converted into micrograms.

$$PEC_{soil}(\mu g/kg) = \left(\frac{D * Ad * BW * P * 170 * Fh}{1500 * 10000 * 0.05 * Ny * H}\right) * 1000 \tag{6.1}$$

For subsequent comparability, we first convert PECsoil values for each active substance to PECgroundwater using Equation 6.2, with RHO_{soil} representing the bulk density of fresh soil (1700 kg/m^3). $K_{soil-water}$ is the partition coefficient between solids and water in soil (volume/volume), defined as 1 as worst case assumption due to a lack of data, and 1000 is a conversion factor to adjust to liters (European Medicines Agency, 2016).

$$PEC_{groundwater}(\mu g/l) = \frac{\frac{PEC_{soil}}{4} * RHO_{soil}}{K_{soil-water} * 1000} \tag{6.2}$$

In a subsequent step, we convert PECgroundwater into predicted environmental concentration in surfacewater (PECsurfacewater) using Equation 6.3 (European Medicines Agency, 2016).

$$PEC_{surfacewater}(\mu g/l) = \frac{PEC_{groundwater}}{3} \tag{6.3}$$

For human medicine data, we can directly calculate a PECgroundwater using Equation 6.4 (European Medicines Agency, 2024), where A in kg/year represents the total amount of active substances consumed in humans in Germany in the year 2020. R denotes the percentage rate at which substances are eliminated through absorption, evaporation, decomposition by water, or natural degradation in disposal systems. Due to the absence of precise data for R, we follow Fass (2012) in setting this value to 0. P represents the number of inhabitants in Germany. Consequently, V in l/day is the average wastewater volume per capita, amounting to 200 liters. The dilution factor of wastewater by surface water flow, D, is set to 10 (European Medicines Agency, 2024). Supplemental Table 6.S.3 gives an overview of calculated and transformed PEC values per substance.

$$PEC_{surfacewater}(\mu g/l) = \frac{A * 1,000,000,000 * (100 - R)}{365 * P * V * D * 100} \tag{6.4}$$

Now that we have calculated the PEC values, we proceed to determine the PNEC values. Various metrics assess the hazard of substances: no observed effect concentration (NOEC), EC10, and EC50 (the concentrations causing 10% and 50% inhibition of growth in exposed organism, respectively), and LC50 (the concentration at which 50% of the exposed organism perish). The values and sources of metrics pertaining to each specific substance can be found in Supplemental Table 6.S.4. The PNEC value in Equation 6.5 standardizes these diverse metrics, rendering the values comparable across all substances. This is achieved by dividing the respective metric by a safety factor. The safety factor is set at 100 for NOEC and EC10, and 1000 for EC50 and LC50 (European Chemicals Agency, 2008).

$$PNEC(\mu g/L) = \frac{Metric}{Securityfactor} \tag{6.5}$$

For a subset of substances, the PNEC value can be calculated, thereby enabling risk assessment through the division of PECsurfacewater by PNEC as per Equation 6.6. For this purpose, the PEC values from human and veterinary medicine are summed. If the resulting value exceeds 1, the concentration of the substance in the environment is greater than the concentration deemed safe. Accordingly, risk quotients are categorized based on their significance into high (> 10), moderate (≥ 1), low (> 0.1), and insignificant (≤ 0.1) (Fass, 2012).

$$RiskQuotient = \frac{PEC_{surfacewater}}{PNEC} \tag{6.6}$$

6.3 Results

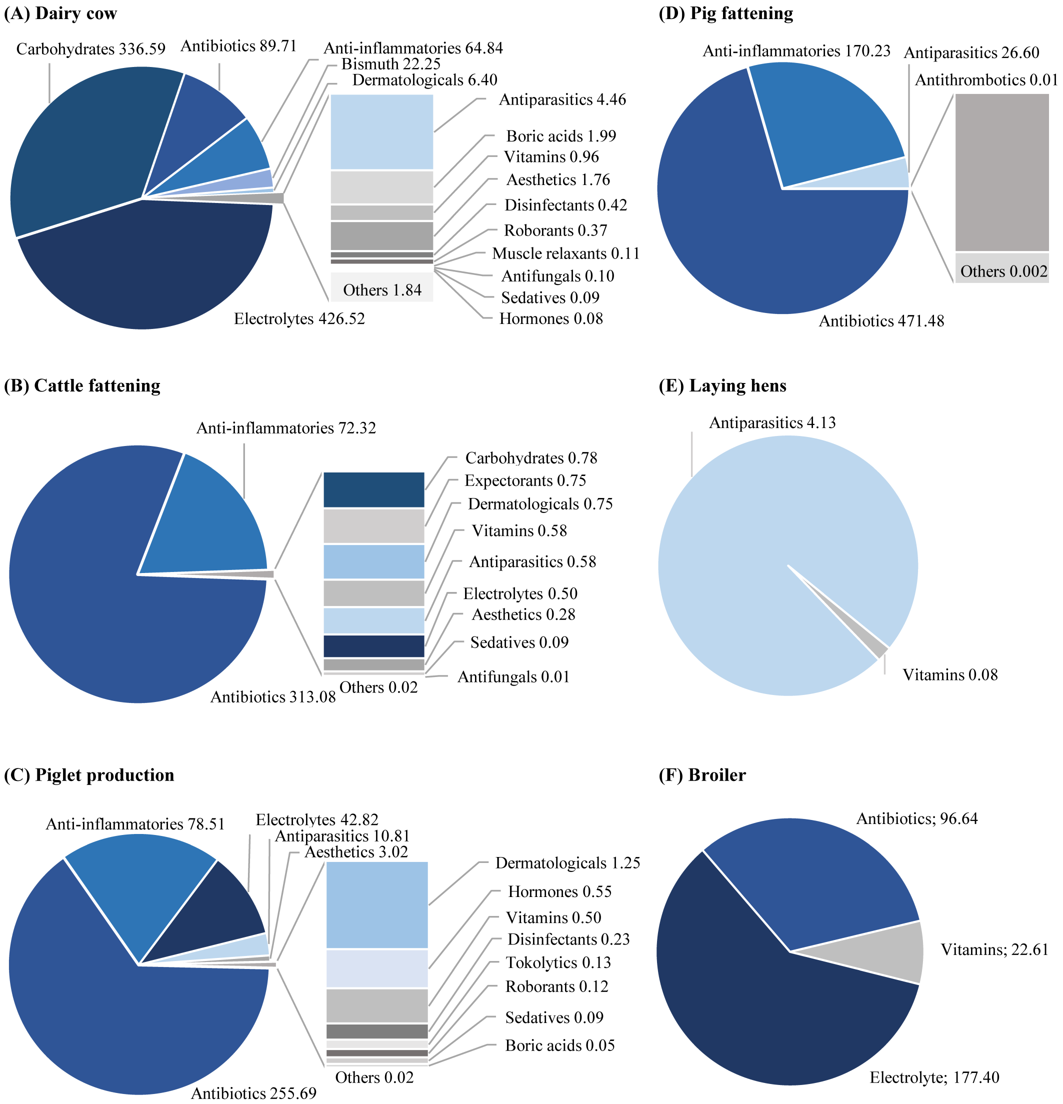
6.3.1 Active Substances Used in Livestock Farming

Within the scope of this study, a comprehensive analysis was conducted on a total of 15,502 veterinary prescriptions from 129 farms. Segmented across 29 substance groups, we were able to identify 162 distinct active substances with a cumulative consumption of 2709.95 kg. Antibiotics predominate in terms of quantity, constituting 1226.61 kg. The amount of antibiotics per PCU was 83.1 mg/PCU. Following are electrolytes (647.24 kg), categorized as pharmaceuticals according to EU regulations (European Union, 2022), anti-inflammatory agents (385.90 kg), and carbohydrates (337.36 kg). Antiparasitics, with a quantity of 46.57 kg, and hormones (0.63 kg) hold a quantitatively subordinate significance. More detailed figures for additional substance groups are available in Supplemental Table 4.6.S.5.

Figure 6.1 depicts, in six pie charts, the use of pharmaceutical agents per animal category in kg, partitioned by active substance groups. The values for dairy cows (A) are based on 13,565 animals across 50 farms. On average, each farm issued 204 drug prescriptions in 2020. In total, substances from 26 out of 29 substance groups were employed in dairy farms, amounting to a total quantity of 957.23 kg. Electrolytes possessed the highest quantitative importance at 426.52 kg, followed by carbohydrates at 336.59 kg. Subsequently, antibiotics (89.71 kg), anti-inflammatory drugs (64.84 kg), and bismuth (22.25 kg), utilized for teat sealing, are of note. Antiparasitics and hormones were administered at 4.46 kg and 0.08 kg of active substance, respectively.

For cattle fattening (B), the values were derived from 15 farms managing a total

Figure 6.1: Surveyed drug consumption quantity per animal category in kg, partitioned by substance groups for the year 2020. (A) dairy cow, (B) cattle fattening, (C) piglet production, (D) pig fattening, (E) laying hens, (F) broiler.



of 5,765 animals, partly through extensive cow-calf operations on pasture and partly through intensive bull or calf fattening in barns. On average, each farm issued 70 drug prescriptions in 2020. Among the 18 utilized active substance groups in cattle fattening, totaling 389.74 kg, antibiotics with 313.08 kg and anti-inflammatory drugs with 72.32 kg were the most common. Other substance groups, such as antiparasitics (0.58 kg), electrolytes (0.50 kg), and anesthetics (0.28 kg), occurred only in minimal quantities.

For piglet production (C), the pharmaceutical data were sourced from 16 farms, typically involved in breeding sows and raising the piglets they give birth to until they reach a weight of approximately 30 kg. The pharmaceutical data were derived from 31.615,5 animals. On average, each farm issued 198 drug prescriptions in 2020. Of the 18 active substance groups utilized, totaling 393.78 kg, antibiotics (255.69 kg) and anti-inflammatory drugs (78.51 kg) occupied a central position, similar to cattle fattening farms. Electrolytes (42.82 kg), antiparasitics (10.81 kg), anesthetics with 3.02 kg, and hormones with 0.55 kg were also used in substantial quantities.

The data for pig fattening (D) come from 33 farms with 30,127.76 animals. On average, each farm issued 27 drug prescriptions in 2020. Of the 8 active substance groups employed, totaling 668.33 kg, antibiotics were by far the most utilized (471.48 kg), followed by anti-inflammatory drugs (170.23 kg) and antiparasitics (26.60 kg). Antithrombotics (0.013 kg), hyperemic agents (0.002 kg), anaesthetics (0.0005 kg) and sedatives (0.0002 kg) had a substantially lower importance.

For laying hens (E), the data were derived from 10 farms with a total of 105,750 laying hens participating in the sample. On average, each farm issued 4 drug prescriptions in 2020. Besides antiparasitics (4.13 kg), this sample only recorded the use of vitamins at 0.08 kg. The five broiler farms (F) with a total of 206,800 animals received 34 drug prescriptions on average per farm in 2020. In addition to electrolytes (177.40 kg) and antibiotics (96.64 kg), vitamins (22.61 kg) were utilized as well.

6.3.2 Extrapolation

For the extrapolated quantities of active substances for Germany, the sample's treated livestock units served as the basis, the target variable being the total number of livestock units in Germany. The extrapolation revealed that for 15,723,673 livestock units in Germany, approximately 1,368.33 t of active substances were utilized. Of this total, nearly 70%, equivalent to 587.58 t, comprised antibiotics, followed by 347.61 t of electrolytes mainly used in dairy cows and broilers. The amount of antibiotics per PCU was 83.3 mg/PCU for the extrapolation. Carbohydrates (187.8 t) used in dairy cows and anti-inflammatory drugs (187.48 t) were utilized in nearly equal amounts. Antiparasitics followed with a significantly lower quantity of 22.91 t. Hormones were amounting to 232 kg of active substances. More detailed information for additional substance groups is available in Supplemental Table 6.S.6.

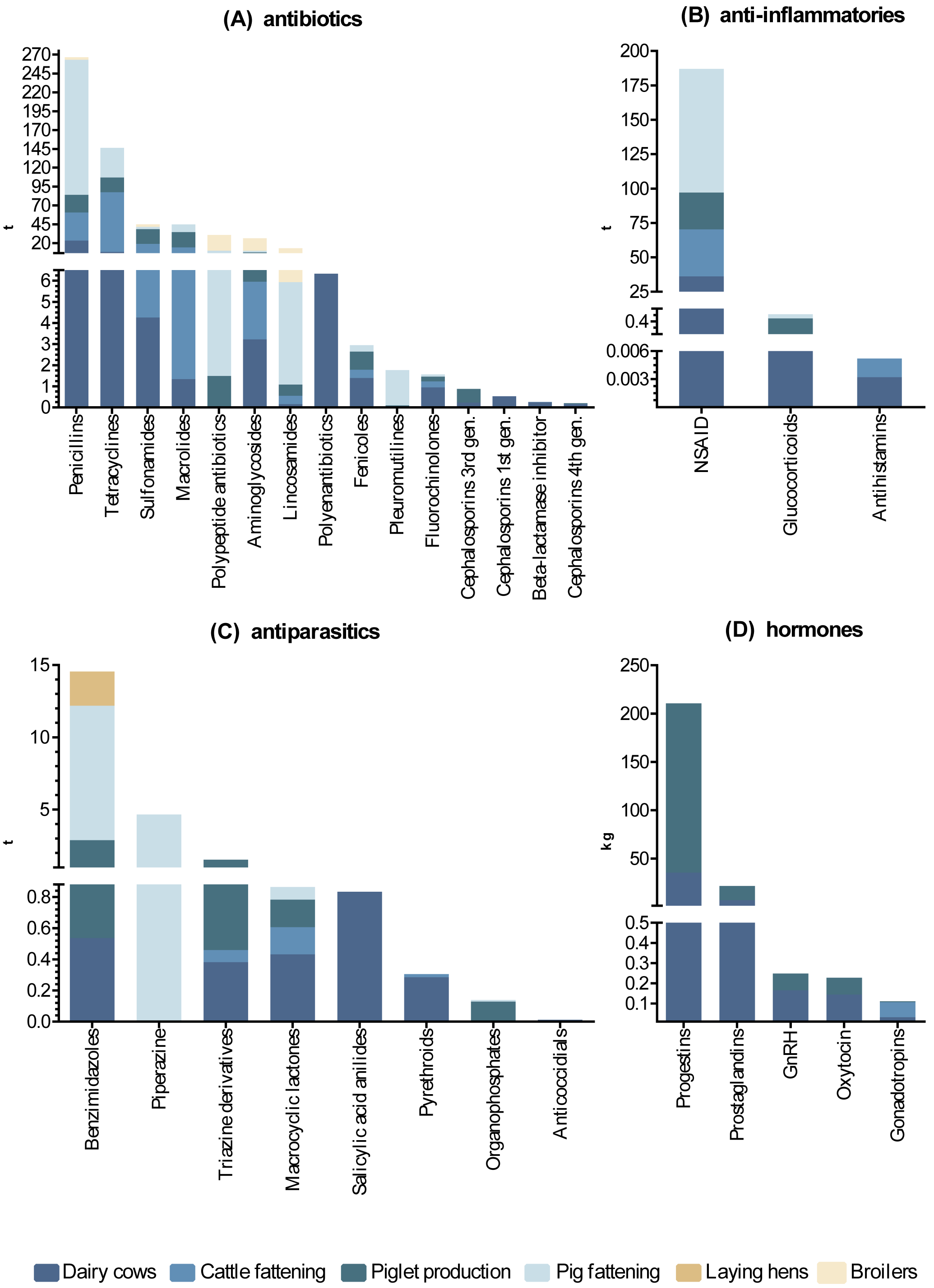
Figure 6.2 displays the active substance groups of antibiotics (A), anti-inflammatory drugs (B), antiparasitics (C), and hormones (D), along with the individual active substances within them. The bars indicate the consumption quantity in t, and the colors indicate the animal category for which the substances were used.

In the upper part of Figure 6.2, the antibiotic group (A) is further broken down. Penicillins, totaling 266.49 t, and tetracyclines, amounting to 146.47 t, constituted 70% of the overall antibiotic quantity. Penicillins are primarily used in pig fattening, while tetracyclines are predominantly employed in cattle farming. However, both subgroups of antibiotics also have significant importance in other animal categories, except for laying hens. In broiler production, polypeptide antibiotics and aminoglycosides play a major role. Polyene antibiotics are exclusively used in dairy cows for ketosis prophylaxis (VETIDATA, 2024). Medically important antimicrobials for human medicine (MIA), such as fluoroquinolones (1.56 t) and third (0.87 t) and fourth (0.20 t) generation cephalosporins, are used in limited quantities. Fluoroquinolones and fourth-generation cephalosporins are primarily used in dairy cows, while third-generation cephalosporins are mainly employed in piglet production.

As shown in the upper-right part of the figure on anti-inflammatory drugs (B), these were only used in cows and pigs in our sample. Quantitatively, only NSAIDs were significant with 187.01t. Glucocorticoids amounted to 0.46 t, and antihistamines were at 4.9 kg, used exclusively in cows.

Antiparasitics (C) are depicted in the bottom-left diagram and were used in all categories except for broilers. Benzimidazoles (14.55 t), constituted the largest group and were primarily used in pig fattening, piglet production, and laying hens. In our

Figure 6.2: Extrapolated consumption quantities of active substances in the substance groups of (A) antibiotics, (B) anti-inflammatories, (C) antiparasitics, and (D) hormones for Germany in 2020, partitioned by animal category.



sample, no other antiparasitics were used in laying hens. Piperazine (4.67 t) was exclusively used in pig fattening. Triazine derivatives (1.54 t) rank third and were predominantly used in piglet production and dairy cows. Macrocyclic lactones and pyrethroids were mainly used in dairy cows. Salicylanilides and anticoccidials were used exclusively in dairy cows, and organophosphates were used in pigs only.

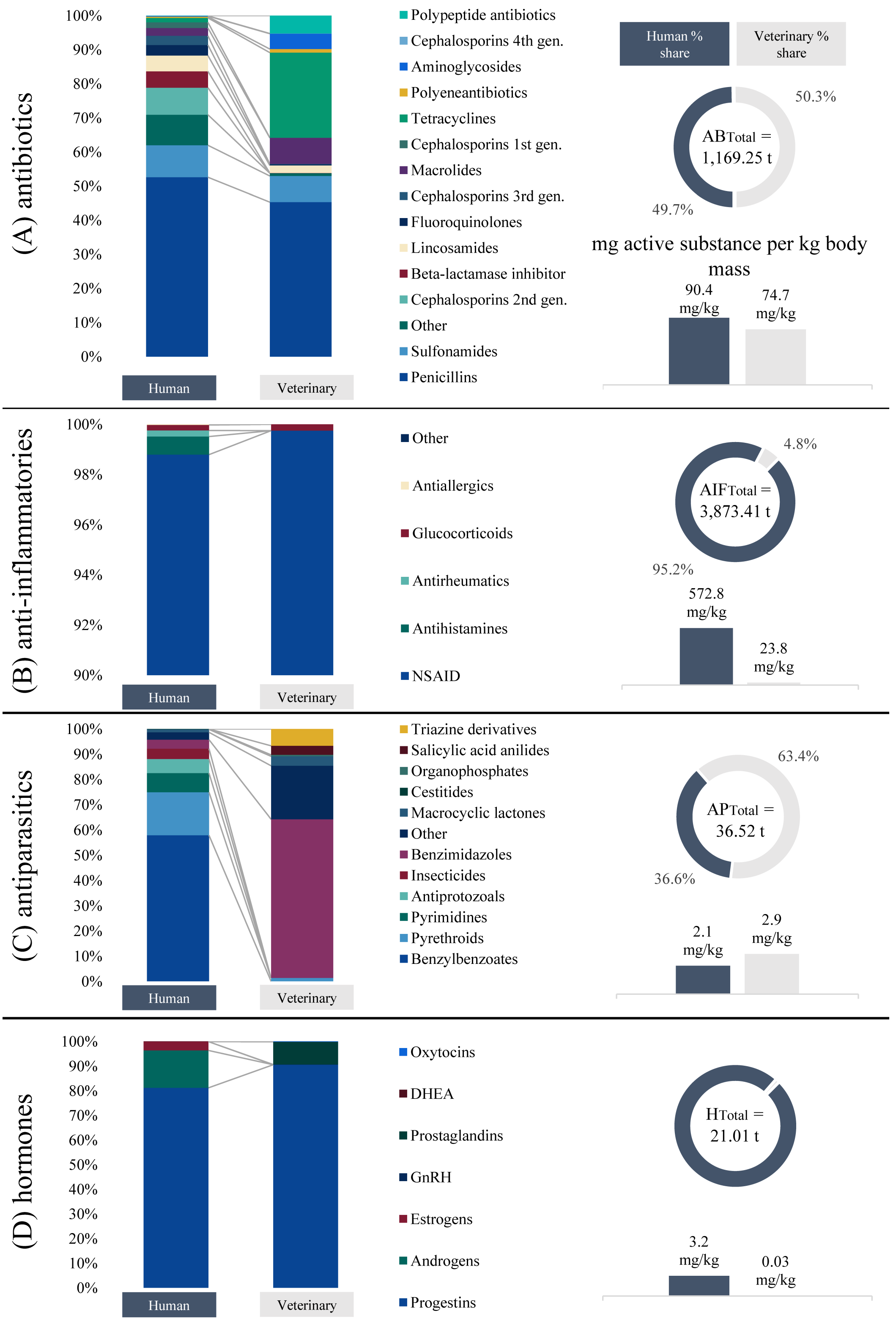
In the graph at the bottom-right, hormones (D) exhibit a small quantity, totaling only 232 kg, as they are administered in very small doses. Among the sex hormones, progestins were the most prominent (210 kg) and were used in sows and dairy cows. Prostaglandins and their analogues were much less frequently used, totaling 20 kg. Finally, GnRH (0.25 kg), as well as oxytocin (0.23 kg) and gonadotropins (0.11 kg) were applicated in lower kg amounts. In our survey, sows were treated with equine chorionic gonadotropin (eCG) as well, however, no quantity of active substance in kg could be determined as there was insufficient information provided by the manufacturer regarding the concentration of the active substance in the preparation.

6.3.3 Comparison of Human and Veterinary Pharmaceutical Use

Utilizing consumption data derived from human medicine, we were able to delineate the comprehensive utilization of pharmaceuticals across human and veterinary medicine in Germany. Figure 6.3 comprises four segments, representing the substance groups of antibiotics (A), anti-inflammatory drugs (B), antiparasitics (C), and hormones (D). Within these classifications, as adapted from Schröder et al. (2020), the bar charts on the left illustrate the relative consumption of individual substances within each substance group. The left bar signifies pharmaceutical usage in human medicine, while the right bar conveys extrapolated values for veterinary medicine. The right segment further provides insights into the proportion of the overall drug quantity attributed to human versus veterinary medicines. Lastly, the estimated application of these drug categories per kg in humans and animals is outlined. For an assessment of the average utilized drug quantity per person or animal, the indicated milligram value necessitates multiplication by the respective body mass.

In the case of antibiotics (A), it is evident that in both human and veterinary medicine, penicillin was the most extensively used antimicrobial, followed by sulfonamides for human and tetracyclines for veterinary use. In livestock farming,

Figure 6.3: Comparison of the use of veterinary and human pharmaceuticals, categorized by active substance groups of (A) antibiotics, (B) anti-inflammatories, (C) antiparasitics, and (D) hormones for Germany in 2020. Illustrated in the bar charts on the left is the comparison of the consumed active substances. Shown in the top right is the consumption share of the total quantity and in the bottom right, the amount of active substances used per kg of body mass.



tetracyclines and macrolide antibiotics were employed more frequently than in human medicine. However, in human medicine, second-generation cephalosporins and MIA, i.e. cephalosporines of the third and fourth generations, as well as fluoroquinolones, were more prevalent. The consumption of approximately 1,169 t of antibiotics was divided roughly equally between human and veterinary medicine. Regarding the quantity used per kg, human medicine surpassed veterinary medicine with 90.4 mg/kg compared to 74.7 mg/kg body mass.

Concerning anti-inflammatory drugs (B), it is evident that in both human and veterinary medicine, NSAIDs were utilized in more than 90% of cases. The consumption of approximately 3,873 t of anti-inflammatory drugs was predominantly attributed to human medicine, accounting for 95.2%. Additionally, the calculated quantity of active substance per kg in human medicine, at 572.8 mg/kg, was substantially higher than the corresponding value in veterinary medicine, which stood at 23.8 mg/kg.

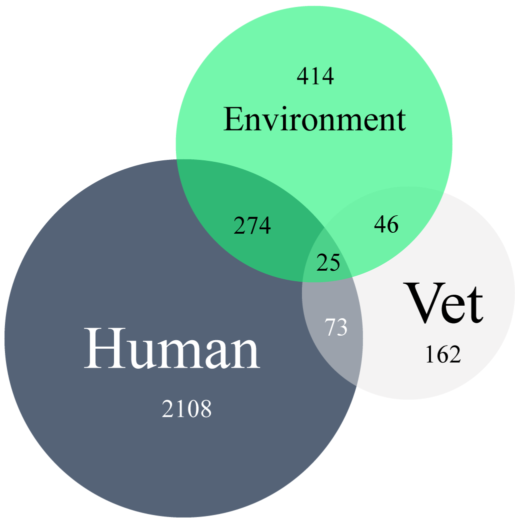
A diverse pattern is evident in the bar chart for antiparasitics (C). While scabicides agents and antiprotozoals dominated in human medicine consumption, they were scarcely applied in veterinary medicine. In contrast, benzimidazoles prevailed in veterinary medicine, while they played a minor role in human medicine. The consumption of 36.5 t of antiparasitics in Germany was attributed to approximately 63.4% in veterinary medicine. Additionally, the quantities of active substances used per kg were at a similar level, with 2.1 mg/kg in human medicine and 2.9 mg/kg in veterinary medicine.

In the lower part of the figure, hormones (D) are depicted. Both in human and veterinary medicine, progestins were predominantly used. In human medicine, androgens were additionally utilized, while in veterinary medicine, prostaglandins were employed. Of the approximately 21 t of hormones consumed, 98.9% were attributed to human medicine. Moreover, the consumption in human medicine, at 3.2 mg/kg, was a hundred times higher than in veterinary medicine, which stands at 0.03 mg/kg.

6.3.4 Environmental Findings

From the previous results, it is now evident which active substances from which substance groups were used in the field of human medicine and in livestock farming within our study. As depicted in the Venn diagram in Figure 6.4, a total of 2,108 different active substances were identified in the human domain, and 162 different active substances in the field of livestock farming veterinary medicine. 73 active substances were utilized in both domains; illustratively, amoxicillin and acetylsalicylic acid can be mentioned.

Figure 6.4: Number of active substances and derivatives found in the environment and their association with human and/or veterinary pharmaceuticals.



We correlated this information with environmental findings of active substances and derivatives. In total, 414 active substances and derivatives were identified in the environment in Germany by the end of the year 2020 (German Environment Agency, 2022). Comparing the active substances used in our study in 2020 with those found in the environment up to 2020, approximately 66% (or 274 substances) can be attributed to human medicine, while about 11% (or 46 substances) originate from the veterinary medicine domain. 25 active substances, constituting 6% of all identified substances, were used in both domains, including penicillin G and metamizole. A total of 119 environmental findings did not correspond to data on human pharmaceuticals used in 2020 or appear in the study conducted on agricultural farms. For 1834 active substances from human medicine and 116 active substances from our veterinary medicine sample, no environmental match could be identified.

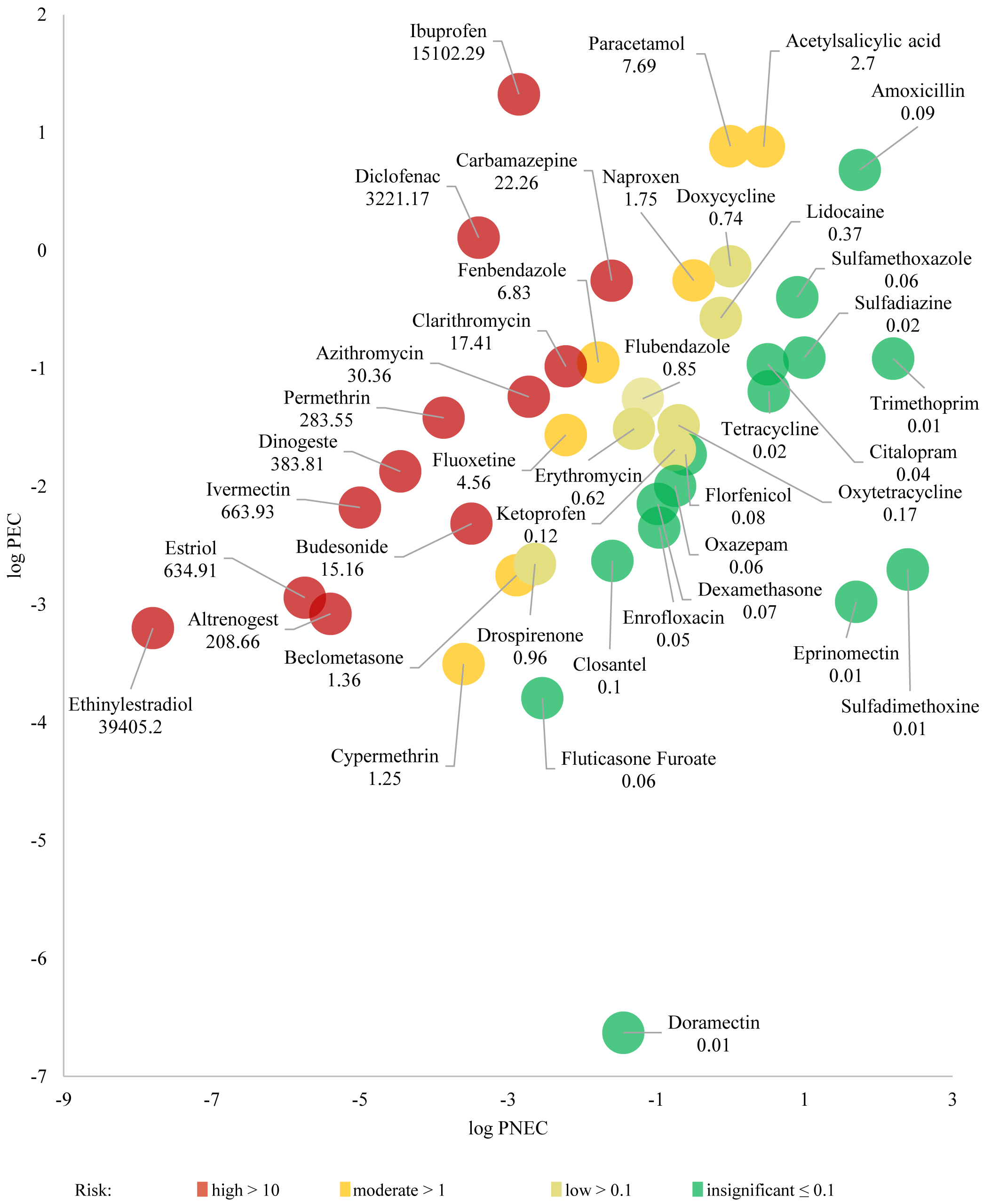
The majority of various active substances in the environment were derived from the group of antibiotics, such as sulfonamides (sulfamethoxazole, sulfadiazine, sulfadimidine) (human sector 42, veterinary sector 29, both sectors 11). Following antibiotics, active substances from the group of anti-inflammatory agents emerged, with diclofenac and ibuprofen taking precedence (human 44, vet 6, both 6) and being the most represented individual active substances in the database as well. Subsequently, clotrimazole, sulfamethoxazole and carbamazepine ensued as important individual substances. Following antibiotics and anti-inflammatory agents, active substances from the group of antidepressiva (human 19, vet 0, both 0), antiypertensiva (human 15, vet 0, both 0) and hormones (human 10, veterinary 0, both 0) emerge, such as estradiol. Antiparasitics (human 2, vet 2, both 0) did not rank among the top ten identified groups of active substances.

6.3.5 Risk calculation

For 41 substances used in livestock farming and human medicine, we were able to calculate PNEC values, thereby enabling the assessment of environmental risk.

Figure 6.5 illustrates the logarithmically scaled PECsurfacewater values on the ordinate against the logarithmically scaled PNEC values on the abscissa. Each circle in the diagram represents a substance, with its risk quotient value determining the color of the circle. At first glance, a trend from the bottom left to the top right becomes evident, indicating that high PECsurfacewater values are associated with high PNEC values. A horizontal comparison of substances reveals that those with a similar amount used, hence a similar high PECsurfacewater value, such as altrenogest (left) and eprinomectin (right), can have very different PNEC values, resulting in a wide range of risk quotient values from 39,405.20 (ethinylestradiol) to 0.000007 (doramectin). The vertical comparison clearly demonstrates that for substances of similar environmental hazard levels, the quantity used significantly influences the risk, driving it upwards (compare, for example, carbamazepine (top) with doramectin (bottom)). According to our calculations, the substances posing the greatest risk are ethinylestradiol, ibuprofen and diclofenac with values between 39,405.20 and 3,221.17, followed by ivermectin, estriol, dinogest, permethrin, and altrenogest with still high values around 663.93 and 208.65. Ethinylestradiol has the highest risk quotient with 39,405.20, indicating that the concentration of the active substance in the environment is approximately forty thousand times higher than the concentration deemed to be safe. Substances like paracetamol, fluoxetine and acetylsalicylic acid

Figure 6.5: Environmental impact assessment based on PECgroundwater and PNEC values.



present moderate risk, whereas substances like doxycycline, lidocaine and flubendazole have a low risk. Antibiotics like amoxicillin, tetracycline, and antiparasitics such as eprinomectin and doramectin pose insignificant risk. Therefore, the risk assessment depends on the individual substance, as no clear pattern emerges within substance groups, with e.g. antibiotics represented almost across all risk categories.

6.4 Discussion

The first dataset of our study contains data on the use of veterinary pharmaceuticals on farms, encompassing the main categories of animals kept in Germany: cattle, pigs, and poultry. To the best of our knowledge, it is the first survey of all substance classes used in livestock farming in Germany that is not restricted to antibiotics. The pharmaceutical consumption of other livestock, like sheep and goats, as well as companion animals was not considered. When official data on animals kept or slaughtered in Germany in 2020 are considered, the animal categories included in our survey represent approximately 90% of all animals (Central Association of Zoological Specialist Companies e.V., 2023; Federal Statistical Office of Germany, 2021a, 2021b; Fédération Equestre Nationale, 2023). Additionally, our sample of farms is based on voluntary participants due to the absence of legal reporting requirements. The farms participating in our study are distributed across 9 of the 16 federal states in Germany, with a notable aggregation in both the northwest and southern regions, mirroring the national distribution. Our data show that approximately 90 percent of the farms are located in these regions, compared to about 80 percent reported in the 2020 Agricultural Census (Federal Statistical Office of Germany, 2021a). The representation of farms from Eastern Germany is marginally lower in our study. Consequently, we anticipated a slight underestimation of the quantity of pharmaceuticals used, reflected in the extrapolation from a sample to the entire population.

Regarding antibiotics, there exist official statistics that can be compared with our study. The sales figures of antibiotics to veterinarians in 2020 (Federal Office of Consumer Protection and Food Safety, 2021) and the antibiotic quantities from this survey show a very similar distribution for some groups, with penicillins and tetracyclines ranking first and second, respectively (see Supplemental Table 6.S.7). Additionally, the annual indicator published by the EU for antibiotic use per PCU slightly exceeds that of this survey, with 83.8 mg/PCU (European Medicines Agency, 2021d) compared to 83.1 mg/PCU, (see Supplemental Table 6.S.8) and 83,3 mg/PCU for the extrapolation. Although the extrapolation is derived from a sample of only 129 farms, it is deemed plausible due to the comparable PCU values. For other substance groups, there are no official comparison values in veterinary medicine. Furthermore, there are hardly any studies available that go beyond antibiotic use and address other substance groups (Hemme et al., 2018; Hommerich et al., 2019; Kasabova et al., 2021; Kuipers et al., 2016; Olmos Antillón et al., 2020; Sawant et al., 2005). Regarding hormone use, van der Laan et al. (2021) demonstrate in their study with 760 Dutch farms a similar distribution of hormonal agents used in dairy cows. Although our data are based on a sample rather than a full census, they provide initial important insights into pharmaceutical use in livestock in Germany.

Differences in the number of pharmaceutical prescriptions or the amount of active substances used are evident across various animal categories. For instance, in dairy cows or breeding sows, the focus often lies on individual animal treatment, whereas in group-housed fattening pigs or laying hens, treatment is administered to subgroups or the entire group. In the case of antiparasitics, the leading substances in terms of quantity are typically administered orally or as pour-on preparations, necessitating higher concentrations than injections (Otranto et al., 2005). Some groups of active substances are not used in all animal species, either due to the absence of approved drugs for the respective animal category or because the disease profile does not occur in a specific husbandry system or animal category. In this study, no antiparasitic agents are used in broilers, although most broilers are infected with Eimeria species (Andreopoulou et al., 2022). Farmers often combat these parasites using substances approved as feed additives, which are available without veterinary prescription and do not require explicit documentation (Dalloul & Lillehoj, 2006; European Union, 2003). All these reasons could account for the occasionally substantial differences in drug utilization among animal categories.

In comparing active substances used in human and veterinary medicine, it becomes apparent that a similar quantity of antibiotic agents is employed, although the distribution among substances varies. Penicillins, as first-line antibiotics, hold significant importance in both human and veterinary medicine. Alongside penicillins, tetracyclines are predominantly utilized in veterinary medicine, particularly in pig and cattle fattening (Federal Ministry of Food and Agriculture, 2019). Since entire groups are typically treated metaphylactically in these cases, the quantities of active substances used are markedly higher. Tetracyclines are less prominent in human medicine, where there is generally greater variability among substances compared to veterinary medicine. One reason for this is that newly approved antibiotics are used exclusively in human medicine. Furthermore, in Germany, there are legal regulations in veterinary medicine that restrict the use of MIA or subject their use to distinct conditions (Federal Ministry of Food and Agriculture, 2009). This could explain why the use of third-generation cephalosporins and fluoroquinolones in livestock is tremendously lower than in human medicine.

The importance of another group of active substances, anti-inflammatory agents, also varies markedly between human and veterinary medicine. In human medicine, for instance, tablets or gels containing anti-inflammatory agents such as ibuprofen, paracetamol, acetylsalicylic acid, and diclofenac are frequently purchased over the counter in pharmacies without a prescription (Sarganas et al., 2015). All of the mentioned substances belong to the group of NSAIDs and ranked among the top 7 anti-inflammatory agents used in human medicine in our study. In veterinary medicine, the situation differs as drugs or active substances cannot be obtained without a prescription for livestock (VETIDATA, 2024). Moreover, ibuprofen and diclofenac are not approved for use in animals due to their potential for adverse effects (Federal Institute for Drugs and Medical Devices, 2024; Scherkl & Frey, 1987). While there are approved drugs for animals containing acetylsalicylic acid and paracetamol, the latter appears to play a minor role according to our findings. We can only speculate that anti-inflammatory agents, like meloxicam, are more frequently used in companion animals compared to livestock, as companion animals generally live longer and are often regarded as family members with different medical expectations. On the other hand, companion animals account for only about 10% of the animal population in Germany (Central Association of Zoological Specialist Companies e.V., 2023; Federal Statistical Office of Germany, 2021a, 2021b; Fédération Equestre

Nationale, 2023) and, due to their lower body weight, require smaller individual doses. Therefore, conclusions on the change in the distribution between human and veterinary medicine by including companion animals cannot be drawn, as published data on consumption in companion animals does not exist.

The differences in the use of antiparasitic substance groups between human and veterinary medicine reflect the treatment goals in both fields. In livestock, animals are often kept in close quarters in contact with their excretions. Depending on hygiene management, endo- and ectoparasites can be easily transmitted (Roepstorff & Nansen, 1994). Animals with access to pastures are even more exposed to parasitic pressure (Vanderstichel et al., 2012). Therefore, antiparasitics are used in livestock for reasons of animal welfare and food safety. The objectives of antiparasitic treatment in animals include preventing disease transmission to the animal itself, such as vector borne diseases, and also controlling the zoonotic potential of transmission from pets to humans (Baneth et al., 2016). In human medicine, the primary goal is to combat parasites directly affecting humans, such as mites (Sunderkötter et al., 2019). This is reflected in the most commonly used substances as well, such as benzyl benzoate and pyrethroids, which are used against ectoparasites.

The objectives of hormone use differ between human and veterinary medicine as well. Progestins are corpus luteum hormones and primarily used in human medicine for contraception. Nearly 70% of German women prefer hormonal contraception, with hormonal preparations being taken for up to 36 weeks per year in some cases (Balakrishnan et al., 2023). In veterinary medicine, the focus lies less on contraception and more on treatment of fertility problems or on synchronizing the sexual cycle in female animals for the issue of herd management. Progestins are therefore primarily used in sows for estrus synchronization over approximately 18 days (Federal Institute for Drugs and Medical Devices, 2024; Wang et al., 2018). Besides contraception, human medicine encompasses a variety of other indications for hormone use, such as prostate cancer and menopausal symptoms (Armeni et al., 2021; Sweeney et al., 2015), which are not relevant in livestock medicine. In Germany, hormonal substances are prohibited in all fattening animals (Federal Ministry of Food and Agriculture, 2009), and since 1996, certain hormonal growth promoters have been banned for use in all livestock throughout the EU as well (European Union, 1996). In our study, hormone use, like the use of all pharmaceuticals, could be likely underestimated. In addition to the overlooked hormonal treatment of animals, technically, the amount of active substance could not be calculated for drugs containing the natural hormone eCG, which is used in sows to influence the weaning-to-first-service interval and litter size (Sechin et al., 1999). In our study, eCG accounted for less than 5% of all hormone preparations used, which is why the underestimation remains within acceptable limits. The partial ban on hormonal substances in livestock animals on the one hand and the extensive use of hormones as contraceptives in humans on the other hand can explain the immense difference in the quantities used.

Following the markedly different applications of pharmaceuticals in animals and humans, there are differences and similarities in contamination through pharmaceutical residues found in the environment. Those refer to the remnants, byproducts, and fragments of pharmaceutical substances. Unlike intact pharmaceuticals, residues encompass metabolized or unchanged forms of these substances and persist in the environment after initial use. According to Fick et al. (2009), surface, ground, and drinking water can be contaminated during the production process. Subsequently, pharmaceutical residues are typically excreted and introduced into surface water through sewage systems. While sewage treatment plants can remove some substances, others such as ethinylestradiol, diclofenac, propranolol, macrolide antibiotics, fluoxetine, tamoxifen, and carbamazepine are poorly removed and are thus partially discharged into water bodies (Comber et al., 2018). Additionally, wastewater is sometimes used for irrigation, and roughly 15% of sewage sludge is utilized as fertilizer. In agriculture, residues enter fields and aquatic systems through manure and dung (Hamscher & Mohring, 2012). Consequently, residues are particularly detected in soil (Monteiro & Boxall, 2009) and water samples (Hirsch et al., 1999; Kolpin et al., 2002). Improper disposal of medications also contributes to increased environmental contamination (Barnes et al., 2004; Comeau et al., 2008; Götz et al., 2015; Ruhoy & Daughton, 2007).

As the volume of consumption and the diversity of active substances in human medicine are generally much higher than in veterinary medicine, we expect to find more environmental occurrences originating from human medicine. Furthermore, given the significantly higher use of hormones and anti-inflammatory drugs in human medicine, it is likely that most of these detected preparations primarily originate from the human medical sector. However, many substances cannot be clearly attributed to just one sector. Approximately half of the veterinary medicinal substances found in the environment are used as human pharmaceuticals as well. This is not surprising, as drug development is costly, leading to only few medications being developed exclusively for the smaller veterinary market, with many being used additionally for animal treatment alongside humans. Additionally, residues of substances have been found in the environment that were not used in 2020 in human medicine according to IQVIA or in veterinary medicine according to our findings. These could be substances used for the treatment of companion or other animals, which we did not survey, or substances that were used prior to 2020 (Spielmeyer et al., 2020). Additionally, the list of substances found in the environment includes metabolites and transformation products, which naturally are not found among the active substances used.

In environmental findings, various antibacterial and anti-inflammatory substances are most commonly encountered. Among individual active substances, diclofenac, ibuprofen, clotrimazole, sulfamethoxazole and carbamazepine, were most frequently detected in Germany. Globally, the pattern is similar, with diclofenac being the most commonly detected, followed by ibuprofen, carbamazepine, sulfamethoxazole, and naproxen (aus der Beek et al., 2016; German Environment Agency, 2022; Graumnitz & Jungmann, 2021). The environmental findings database is based on scientific publications. Given the longstanding public focus on antibiotic residues and diclofenac, there is a bias in the number of substance detections due to a higher number of research projects in these areas. Further comprehensive investigations are needed for an accurate description of residual quantities of all active substances that are relevant for measurements in the environment.

After pharmaceutical substances are found in the environment, a simple environmental risk assessment is conducted. The impact of pharmaceutical residues on both ecosystems and human health has been extensively documented, particularly concerning specific active substances or substance groups. Some substances, such as penicillins or cephalosporins, degrade rapidly in the environment, while substances like tetracyclines or fluoroquinolones tend to accumulate (Kumar et al., 2019). For example, tetracyclines accumulate in the upper soil layers over years but are scarcely leached into groundwater. In contrast, sulfonamides penetrate deeper soil layers and enter water bodies (Blackwell et al., 2007; Spielmeyer et al., 2020). The individual concentrations of pharmaceutical substances or their metabolites found in the environment are often too low to exert a direct toxic effect (Straub, 2016). However, there is evidence suggesting that chronic effects may occur and that mixtures of pharmaceuticals can have much stronger effects than individual substances (Geiger et al., 2016). Furthermore, knowledge about the effects of transformation products of pharmaceuticals is still very limited (Maculewicz et al., 2022). The public is well aware that the use of antibiotics in both human and veterinary medicine contributes to the emergence of antibiotic resistance (Bártíková et al., 2016; Wellington et al., 2013). In addition to direct and indirect environmental impacts, antibiotic resistance genes released into the environment can affect human health as well (Larsson & Flach, 2022). Additionally, the use of antiparasitic agents fosters resistance development as well, limiting their effectiveness (Charlier et al., 2022). Moreover, aquatic invertebrates face lethal poisoning upon exposure to antiparasitic agents like moxidectin during the application of manure and dung (Mesa et al., 2018). Parolini (2020) demonstrates that freshwater invertebrates are exposed to a mixture of various anti-inflammatory agents, which are toxic to them as well. Another example of the ecological impact of anti-inflammatory agents is the near-extinction of vulture populations in Pakistan due to the treatment of cows with diclofenac (Oaks et al., 2004). Even in Europe, scavenging vultures continue to succumb to residues in cattle meat (Herrero-Villar et al., 2021). When hormones enter the environment, estrogen, for instance, significantly influences fish reproduction in Canada, posing a threat to their existence (Kidd et al., 2007). Residues of oxazepam, an anxiolytic used in human medicine, demonstrably alter the behavior of perch, carrying ecological and evolutionary consequences (Brodin et al., 2013). Even banned substances like methamphetamine, whose residues reach water bodies, induce addiction and alter habitat preferences in brown trout (Horký et al., 2021). All these examples demonstrate that pharmaceuticals not only affect the target organism, but they pose a risk to the environment and the ecosystem as well.

The risk analysis indicates that not only the quantity of active substances used, as measured by the PEC value, is relevant for potential environmental hazards.

While active substances such as ibuprofen and diclofenac, which are used in large quantities, are associated with a high calculated risk, substances like altrenogest, ivermectin, or ethinylestradiol, which are deployed in significantly smaller amounts, also exhibit some of the highest values in the risk analysis. This is due to the low PNEC values of these substances. Conversely, trimethoprim, despite being used in large quantities, poses no environmental risk due to its significantly higher PNEC values. The examination of antibiotics also reveals that it is not a substance group per se that poses a danger to the environment, but that rather the active substances must be considered individually or within a subgroup. Thus, antibiotics are found across all three risk categories.

Comparing our results with those from other studies proves to be challenging. Gunnarsson et al. (2019) calculated the risk quotient for pharmaceuticals in human medicine, noting that hormones often display high risk quotient values due to their low PNEC levels. Direct comparisons between their data and ours are not feasible, since our data additionally incorporate information from veterinary medicine.

Our calculation of the risk quotient assumes a worst-case scenario. It presupposes that 100% of active substances used is released into the environment, and that 100% of the residues deposited on soils are transported into the groundwater. For example, in the case of ivermectin, substances such as monosaccharide-, aglycone derivatives, and 24-hydroxymethyl metabolites are additionally excreted (Fink & Porra, 1994), each possibly having different environmental impacts than the original active substance. Moreover, the behavior of the active substance in the environment and its ability to degrade are not considered. Penicillins such as amoxicillin are rapidly degraded in the environment, whereas tetracyclines tend to accumulate in soil (Kumar et al., 2019). Additionally, neither the potential for emerging resistances nor the enhanced efficacy of active substance mixtures (Geiger et al., 2016) are incorporated into risk assessments. Overall, PNEC values could be calculated for only a fraction of the substances used in Germany. Pharmaceutical companies are required to provide detailed information for an environmental impact assessment only under certain conditions during the authorization process (European Medicines Agency, 2006, 2016, 2024). Consequently, only few values are available for calculation (Giunchi et al., 2023). Nevertheless, this risk analysis provides an initial overall impression of environmentally relevant substances from veterinary and human medicine.

In our study, we quantified the use of pharmaceuticals in Germany and compared the utilized groups of active substances between human and veterinary medicine. Substantial differences were observed in both the substances administered and the treatment strategies. These differences exist not only among different animal categories but between animals and humans as well. We demonstrate that there are several pathways for pharmaceuticals to enter the environment and many substances already being found in the environment. However, the risk posed by individual substances in the environment can only be assessed to a limited extent, while its complexity has not yet been conclusively clarified and requires further research efforts.

As demonstrated, there are no reliable official data on pharmaceutical consumption in veterinary medicine in Germany. It is therefore necessary to discuss the obligation of pharmaceutical industry to disclose production numbers and the central digital recording of consumption data. In addition, more research is needed to assess which entries occur and to comprehensively evaluate the direct and indirect risks of individual substances and combinations of pharmaceuticals to the environment and, consequently, to humans.

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6.S Supplemental Material

Table 6.S.1: Summary statistics of farm characteristics categorized by animal category. Means are given in the lower part of the table.

Variable	Description	Dairy cow	Cattle fattening	Piglet production	Pig fattening	Laying hens	Broiler
n	Farms	50	15	16	33	10	5
nAni	Animals	13,565	5,765	31.615,5	30,127	105,750	206,800
nPre	Prescriptions	10,221	1,054	3,163	882	36	168
nLU	Livestock Units	11,681	3,585	3,249	9,038	1,480	14,47
nLUGER	Livestock Units in Germany	6,504,650	1,697,848	1,121,802	4,779,071	844,438	775,862
mAni	Animals	271	384	1,976	913	10,575	41,360
mAir	Exhaust air filtration	0	0	5	12	0	4
mAge	Farm manager's year of birth	1974	1970	1973	1968	1981	1977
mArea	Farmed area (in ha)	150.81	189.60	92.11	35.03	38.5	55
mBiogas	Biogas Plant	17	4	3	11	0	4
mCY	Construction year of barn	1996	2004	2008	2004	2014	2013
mGraz	Farms with grazing	18	6	1	1	7	0
mLManu	Liquid manure	19	2	10	23	0	0
mPre	Prescriptions	204.4	70.3	197.7	26.7	3.6	33.6
mSManu	Solid manure on external areas	9	5	0	0	5	5
mStaff	Workers	3.96	2.89	2.18	1.03	1.88	3.4

Note: Values above the demarcation line are aggregated numbers, below the line represent mean values per farm.

Table 6.S.2: Conversion factors for livestock units.

Animal	livestock unit (LU)
1 dairy cow	1
1 cattle	0.8
1 calf	0.4
1 piglet	0.027
1 sow	0.5
1 fattening pig	0.3
1 laying hen	0.014
1 broiler	0.007

Source: Eurostat (2021)

Table 6.S.3: PEC values categorized by human and veterinary medicine; within veterinary medicine, further divided according to the calculation parameters for soil and groundwater.

	Veterinary			Human	Total
Substance	PEC soil $\mu g/kg$	PEC groundwater $\mu g/1$	PEC surfacewater $\mu g/1$	PEC surfacewater $\mu g/1$	PEC surfacewater $\mu g/1$
Acetylsalicylic acid	0.465	0.198	0.066	7.557	7.623
Altrenogest	0.006	0.003	0.001	-	0.001
Amoxicillin	17.730	7.535	2.512	2.327	4.839
Azithromycin	-	-	-	0.058	0.058
Beclometasone	-	-	-	0.002	0.002
Budesonide	-	-	-	0.005	0.005
Carbamazepin	-	-	-	0.556	0.556
Citalopram	-	-	-	0.109	0.109
Clarithromycin	-	-	-	0.104	0.104
Clarithromycin	-	-	-	0.104	0.104
Cypermethrin	0.002	0.001	0.0003	-	0.0003
Dexamethasone	0.016	0.007	0.002	0.005	0.007
Diclofenac	-	-	-	1.288	1.288
Dinogest	-	-	-	0.013	0.013
Doramectin	$1.65\ 10^{-06}$	$7.03\ 10^{-07}$	$2.34\ 10^{-07}$	-	$2.34 * 10^{-07}$
Doxycycline	4.662	1.981	0.660	0.076	0.736
Drospirenone	-	-	-	0.002	0.002
Enrofloxacin	0.032	0.013	0.004	0.000	0.004
Eprinomectin	0.007	0.003	0.001	0.000	0.001
Erythromycin	-	-	-	0.031	0.031
Estriol	-	-	-	0.001	0.001
Ethinylestradiol	-	-	-	0.001	0.001
Fenbendazole	0.795	0.338	0.113	0.000	0.113
Florfenicol	0.132	0.056	0.019	0.000	0.019
Flubendazole	0.392	0.167	0.056	0.000	0.056
Fluoxetin	-	-	-	0.027	0.027
Fluticasone Furoate	-	-	-	0.0002	0.0002
Ibuprofen	-	-	-	21.143	21.143
Ivermectin	0.028	0.012	0.004	0.003	0.007
Ketoprofen	0.114	0.049	0.016	0.004	0.020
Lidocaine	$2.89\ 10^{-06}$	$1.23\ 10^{-06}$	$4.10\ 10^{-07}$	0.268	0.268
Naproxen	-	-	-	0.558	0.558
Naproxen	-	-	-	0.558	0.558
Oxytetracycline	0.231	0.098	0.033	0.000	0.033
Paracetamol	0.084	0.036	0.012	7.674	7.686
Permethrin	0.005	0.002	0.001	0.038	0.038
Sulfadiazine	0.861	0.366	0.122	0.002	0.124
Sulfadimethoxine	0.014	0.006	0.002	0.000	0.002
Sulfamethoxazole	0.354	0.151	0.050	0.351	0.401
Tetracycline	0.256	0.109	0.036	0.028	0.064
Trimethoprim	0.284	0.121	0.040	0.081	0.121

Table 6.S.4: Values for calculating PNEC values.

Substance	PNEC	EC50/ LC50 $\mu g/1$	EC10 $\mu g/1$	NOEC $\mu g/1$	Source
Acetylsalicylic acid	2.83			283	Janusinfo.se (2021)
Altrenogest	0.000004			0.0004	European Medicines Agency (2016)
Amoxicillin	0.0078			0.78	Andreozzi et al. (2004)
Azithromycin	0.0019			0.19	Ecotox Center (2016)
Beclometasone	0.0013			0.13	European Medicines Agency (2021c)
Budesonide	0.00032			0.032	European Medicines Agency (2021b)
Carbamazepin	0.025			2.50	Ferrari et al. (2004)
Citalopram	3.2			320	North Rhine-Westphalia State Agency for Nature, Environment and Consumer Protection (2016)
Clarithromycin	0.006		0.6		Baumann et al. (2015)
Closantel	0.02559	25.59			Veterinary Medicines Directorate (2016)
Cypermethrin	0.00025			0.03	Veterinary Medicines Directorate (2015)
Dexamethasone	0.105			10.50	Teigeler et al. (2024)
Diclofenac	0.0004			0.04	German Enviroment Agency (2021b)
Dinogest	0.000035			0.0035	Teigeler et al. (2024)
Doramectin	0.036	0.04			Boxall et al. (2003)
Doxycycline	0.225			22.50	College ter Beoordeling van Geneesmiddelen (2020)
Drospirenone	0.0023			0.23	European Medicines Agency (2021a)
Enrofloxacin	0.11	0.11			Ebert et al. (2011)
Eprinomectin	50			5000	French Agency for Veterinary Medicinal Products (2018)
Erythromycin	0.05		5		German Enviroment Agency (2021c)
Estriol	0.000002			0.00018	German Enviroment Agency (2021a)
Ethinylestradiol	0.000000016			0.000016	German Enviroment Agency (2021a)
Fenbendazole	0.0165	0.02			Oh et al. (2006)
Florfenicol	0.25	0.25			Richter et al. (2016)
Flubendazole	0.066	0.07			Oh et al. (2006)
Fluoxetin	0.006			0.60	Oakes et al. (2010)
Fluticasone Furoate	0.0029			0.29	European Medicines Agency (2018)
Ibuprofen	0.0014			0.14	European Commission (2022)
Ivermectin	0.00001	0.01			Liebig et al. (2010)
Ketoprofen	0.178			17.80	Janusinfo (2022a)
Lidocaine	0.7429				Janusinfo (2022b)
Naproxen	0.32			32	Janusinfo (2021a)
Oxazepam	0.18			18	Brodin et al. (2013)
Oxytetracycline	0.261	261.00			Health Products Regulatory Authority (2020)
Paracetamol	1			100	Janusinfo (2021b)
Permethrin	0.000135			0.0135	Ecotox Center (2022)
Sulfadiazine	25			2500	Veterinary Medicines Directorate (2018)
Sulfadimethoxine	248	248			Kim et al. (2007)
Sulfamethoxazole	0.59			59	Ferrari et al. (2004)
Tetracycline	33			3300	González-Pleiter et al. (2013)
Trimethoprim	16.7	16700			Veterinary Medicines Directorate (2018)

Table 6.S.5: Surveyed consumption quantity of substance groups in kg, partitioned by animal category for the year 2020 in sample.

Substance group	Dairy Cow (A)	Cattle fattening (B)	Piglet production (C)	Pig fattening (D)	Laying hens (E)	Broiler (F)	Total
Antibiotics	89.71	313.08	255.69	471.48	0	96.64	1226.61
Electrolytes	426.52	0.50	42.82	0	0	177.40	647.24
Anti-inflammatories	64.84	72.32	78.51	170.23	0	0	385.90
Carbohydrates	336.59	0.78	0	0	0	0	337.36
Antiparasitics	4.46	0.58	10.81	26.60	4.13	0	46.57
Vitamins	0.96	0.58	0.50	0	0.08	22.61	24.73
Bismuth compounds	22.25	0.00	0	0	0	0	22.25
Dermatologicals	6.40	0.75	1.25	0	0	0	8.40
Anesthetics/Narcotics	1.76	0.28	3.02	0.0005	0	0	5.06
Boric acid compound	1.99	0	0.05	0	0	0	2.04
Expectorants	0.07	0.75	0.01	0	0	0	0.83
Disinfectants	0.42	0.001	0.23	0	0	0	0.65
Hormones	0.08	0.000	0.55	0	0	0	0.63
Roborants	0.37	0.002	0.12	0	0	0	0.49
Other	0.41	0	0	0	0	0	0.41
Sedatives	0.09	0.095	0.09	0.0002	0	0	0.28
Tocolytics	0.00	0	0.13	0	0	0	0.13
Muscle relaxants	0.11	0.002	0.003	0	0	0	0.12
Antimycotics	0.10	0.010	0	0	0	0	0.11
Parasympatholytics	0.04	0.009	0.002	0	0	0	0.05
Diuretics	0.03	0.002	0.002	0	0	0	0.04
Antithrombotics	0.01	0	0	0.01	0	0	0.03
Antitympanics	0.01	0	0	0	0	0	0.01
Hyperemic agents	0.00	0	0	0.002	0	0	0.003
Proton pump inhibitor	0.00	0	0	0	0	0	0.001
Analeptics	0.0007	0	0	0	0	0	0.0007
Parasympathomimetics	0.0006	0	0	0	0	0	0.0006
Sympatholytics	0	0	0.00005	0	0	0	0.0001
Sympathomimetics	0.00003	0.000001	0.0000002	0	0	0	0.00003

Table 6.S.6: Extrapolated consumption quantity of substance groups in t, partitioned by animal category for the year 2020 for Germany.

Substance group	Dairy Cow (A)	Cattle fattering (B)	Piglet production (C)	Pig fattering (D)	Laying hens (E)	Broiler (F)	Total
Antibiotics	49.96	148.25	88.28	249.30	0	51.79	587.58
Electrolytes	237.51	0.24	14.78	0	0	95.08	347.61
Anti-inflammatories	36.10	34.25	27.11	90.01	0	0	187.47
Carbohydrates	187.43	0.37	0	0	0	0	187.80
Antiparasitics	2.48	0.27	3.73	14.06	2.36	0	22.91
Vitamins	0.54	0.27	0.17	0	0.05	12.12	13.15
Bismuth compounds	12.39	0	0	0	0	0	12.39
Dermatologicals	3.56	0.36	0.43	0	0	0	4.35
Anesthetics/Narcotics	0.98	0.13	1.04	0.0002	0	0	2.15
Boric acid compound	1.11	0	0.02	0	0	0	1.13
Expectorants	0.04	0.36	0.003	0	0	0	0.40
Disinfectants	0.23	0.000	0.08	0	0	0	0.31
Hormones	0.04	0.0001	0.19	0	0	0	0.23
Roborants	0.21	0.001	0.04	0	0	0	0.25
Other	0.23	0	0	0	0	0	0.23
Sedatives	0.05	0.04	0.03	0.0001	0	0	0.13
Tocolytics	0	0	0.04	0	0	0	0.04
Muscle relaxants	0.06	0.001	0.001	0	0	0	0.06
Antimycotics	0.06	0.005	0	0	0	0	0.06
Parasympatholytics	0.02	0.004	0.001	0	0	0	0.03
Diuretics	0.02	0.001	0.001	0	0	0	0.02
Antithrombotics	0.01	0	0	0.01	0	0	0.01
Antitympanics	0.01	0	0	0	0	0	0.01
Hyperemic agents	0.001	0	0	0.001	0	0	0.002
Proton pump inhibitor	0.001	0	0	0	0	0	0.001
Analeptics	0.0004	0	0	0	0	0	0.0004
Parasympathomimetics	0.0003	0	0	0	0	0	0.0003
Sympatholytics	0	0	0.00002	0	0	0	0.00002
Sympathomimetics	0.00001	0.0000004	0.0000001	0	0	0	0.00002

Note: Extrapolation is based on livestock units.

Table 6.S.7: Comparison of extrapolated consumption volumes with reported sales volume in Germany in 2020.

Substance group	Extra-polation in t	Sales volume* in t	Extra-polation in %	Sales volume* in %
Beta-Lactames	268.36	281.3	45.67	40.13
Tetracyclines	146.47	148	24.93	21.11
Makrolides	51.15	61	8.71	8.70
Sulfonamides	45.00	73.9	7.66	10.54
Polypeptid antibiotics	30.73	60	5.23	8.56
Aminoglycosides	26.42	36	4.50	5.14
Lincosamides	13.17	13	2.24	1.85
Fenicoles	2.95	6.3	0.50	0.90
Fluorchinolones	1.56	6.4	0.27	0.91
Pleuromutilines	1.77	11	0.30	1.57
Other	0.00	4.1	0.00	0.58
Total	587.58	701	100	100

*Source: Federal Office of Consumer Protection and Food Safety (2021)

Table 6.S.8: PCU of substance groups in 2020.

Substance group	mg/PCU Survey	mg/PCU Extrapolation	mg/PCU DE*
Antibiotics	83.10	83.26	83.80
Electrolytes	43.85	49.26	-
Anti-inflammatory drugs	26.14	26.56	-
Carbohydrates	22.86	26.61	-
Antiparasitics	3.16	3.28	-
Vitamins	1.68	1.86	-
Bismuth compounds	1.51	1.76	-
Dermatologicals	0.57	0.62	-
Anesthetics/Narcotics	0.34	0.31	-
Boric acid compound	0.14	0.16	-
Expectorants	0.06	0.06	-
Disinfectants	0.04	0.04	-
Hormones	0.04	0.03	-
Roborants	0.03	0.04	-
Other	0.03	0.03	-
Sedatives	0.02	0.02	-
Tocolytics	0.01	0.01	-
Muscle relaxants	0.01	0.01	-
Antimycotics	0.01	0.01	-
Parasympatholytics	0.004	0.004	-
Diuretics	0.002	0.003	-
Antithrombotics	0.002	0.002	-
Antitympanics	0.001	0.001	-
Hyperemic agents	0.0002	0.0002	-
Proton pump inhibitor	0.0001	0.0001	-
Analeptics	0.00005	0.0001	-
Parasympathomimetics	0.00004	0.00004	-
Sympatholytics	0.000003	0.000002	-
Sympathomimetics	0.000002	0.000002	-

*Source: European Medicines Agency (2021d)

Chapter 7

Concluding Remarks

This dissertation has ventured across diverse landscapes of data analysis, encompassing a wide range of topics pivotal to current public discourse: from the societal impacts of statistical literacy to the global challenge posed by the COVID-19 pandemic, the realm of health economics, the nuances of human and veterinary medicine, and the environmental repercussions of pharmaceutical usage. Each research project has not only deepened our understanding of these subjects but has also highlighted common methodologies and the path for future interdisciplinary research.

The exploration began with a critical look at statistical literacy and its influence on the portrayal of survey results in media, underscoring the need for improved understanding and reporting standards. This examination of data's role in shaping public perception extended into analyzing the COVID-19 pandemic. Through cross-sectional datasets and panel data analysis, I uncovered factors affecting mortality rates and assessed the impact of policy measures and individual behaviors on the pandemic's trajectory in Germany. Venturing into veterinary medicine, my analysis based on survey data and descriptive statistics revealed insights into drug use on dairy farms, opening discussions on the environmental impact of pharmaceuticals. Collectively, these projects underscore the versatility of data analysis across disciplines, showcasing both the power and the challenges of leveraging data to inform societal discourse and policy.

My cumulative work marks a significant contribution to the field of data analysis by showcasing its applicability and crucial role across different domains. From public policy implications to understanding environmental impacts, the methodologies and insights presented here highlight the importance of data analysis in unraveling complex societal issues. Moreover, by fostering an interdisciplinary approach, my dissertation underscores the value of integrating diverse analytical perspectives to uncover nuanced insights and advance comprehensive solutions to global challenges.

Despite these contributions, the journey is marked by limitations. The variation in analytical standards across disciplines, particularly the reliance on descriptive statistics in some fields, emphasizes the challenge in reaching a methodological consensus. This highlights the need for a move towards more robust, causal inference methodologies to enhance the impact and quality of interdisciplinary research.

Building on the recommendations within each chapter, the overarching directive for future research is clear: embrace interdisciplinarity. The richness of perspectives gained from collaborating across domains cannot be overstated. As evidenced in this dissertation, merging data analysis techniques across various data structures and environments offers a fertile landscape for discovery and innovation. Future endeavors should continue to break down silos, encouraging researchers to learn from and with their colleagues in the same or other disciplines.

Reflecting on the end of this doctoral journey, a blend of melancholy and gratitude fills me. The journey through interdisciplinary data analysis has not only contributed to the academic community but has also profoundly influenced my professional and personal growth. The lessons learned, the challenges overcome, and the insights gained will inevitably shape my future endeavors.

I am ready to turn the page and embrace new adventures – onwards to new horizons!

Affidavit

I hereby declare that I completed the papers submitted and listed hereafter independently and with only those forms of support mentioned in the relevant paper. When working with the authors listed, I contributed no less than a proportionate share of the work. In the analyses that I have conducted and to which I refer in the papers, I have followed the principles of good academic practice, as stated in the statute of Justus Liebig University Giessen for ensuring good scientific practice.

Gießen, June 26, 2024, Jenny Bethäuser

Submitted Papers

I Bethäuser, J., Menold, N. & Winker, P. (2024). The Impact of Statistical Literacy and Economic Incentives on the (Mis-)Use of Survey Based Statistics in Media Reporting – A Framework. will be submitted to *Public Opinion Quarterly.*

II Bethäuser, J. & Muschol, J. (2020). The Die is Cast – Factors Influencing Mortality during the COVID-19 Pandemic. *MAGKS Discussion Paper*, 20-2020.

III Bethäuser, J. (2024). Causal Impact of Policy Measures and Behavior on the COVID Pandemic in Germany. *MAGKS Discussion Paper*, 11-2024.

IV Abdallah, M., Bethäuser, J., Tettenborn, F., Hein, A. & Hamann, M. (2024a). Survey of Drug Use and its Association with Herd-level and Farm-level Characteristics on German Dairy Farms. *Journal of Dairy Science*, 107(5), 2954-2967.

V Abdallah, M., Bethäuser, J., Tettenborn, F., Hein, A. & Hamann, M. (2024b). Pharmaceutical Consumption in Human and Veterinary Medicine: Potential Environmental Challenges. under review in *Frontiers in Environmental Science.*