The pollution caused by veterinary antibiotics within freshwater

An assessment of the pathways and the effectivity of reduction measures using VANTOM

UNIVERSITY OF TWENTE.

Master thesis
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Msc Civil Engineering and Management
March 2020

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Publicly defended on 27th of March 2020

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Preface

In front of you lies my master thesis, *“The pollution caused by veterinary antibiotics within freshwater. An assessment of the pathways and the effectivity of reduction measures with help of VANTOM.”* I have written this thesis between September 2019 and March 2020 in Enschede and forms the official end of my study Water Engineering & Management at the University of Twente.

During the process of research I have had the help of several people, whom I would like to give my gratitude. First I would like to thank in memoriam Professor Arjen Hoekstra who gave important input at the start of the thesis, which formed the basis for my research. Secondly, I would like to thank my daily supervisor Lara Wöhler who helped me a lot with help of her enthusiasm and broad knowledge on the subject. Thirdly, I want to thank Denie Augustijn, who gave me important insights to finalize my research. Finally, I would like to thank my family and friends for supporting me during my research.

I hope you enjoy reading my thesis!

Summary

The use of veterinary antibiotics is a common practice within livestock agriculture. Because of its popularity it potentially pollutes freshwater entities. Globally, high concentrations of veterinary pharmaceuticals have been detected, which can have significant ecotoxicological effects. The goal of this research is to improve the understanding of this pollution, by modelling the pathways of 8 types of antibiotics between the application on the field and inflow into freshwater. With help of the model VANTOM and the Grey Water Footprint concept, the pollution is quantified so that different scenarios and reduction measures can be compared. This is done with a case study of the Vecht catchment.

After administration to the animal, residues of antibiotics are excreted into manure, which is used for fertilizing soil. Following the application of this polluted manure, antibiotics can spread through different paths: 1) antibiotics can be transported through runoff or 2) through erosion into surface water. Other possibilities are that antibiotics 3) degrade within the soil, 4) leach through the soil into groundwater or 5) accumulate trough sorption to soil particles and persist within the soil. Leaching, erosion and runoff determine how severe antibiotics pollute freshwater.

Considering a period of one year the largest part of antibiotics degrade within the soil, namely between 90% and 100%. Between 4 and 8% accumulates within the soil. The rest is transported through erosion, runoff and leaching. Loads are sensitive to different parameters: 1) degradation and adsorption, which depend on the soil and antibiotic type, 2) the soil characteristics, such as porosity and density of the soil, 3) the slope of the field and 4) the moment of application. The largest load is caused by tetracycline, while the largest GWF is caused by chlortetracycline. The GWF of chlortetracycline within the Vecht area is around 38,000 m^3, while the GWF of tylosin is around 5,800 m^3. These numbers are significantly smaller than the average discharge of the river, which lies between 1.4 and 2.6 billion $m^3\ year^{-1}$. This means that the PNEC values are not reached by the input concentrations of the antibiotics.

Different measures can potentially reduce the pollution. These can be split into 1) reduction of input, with help of different treatment plans, composting or anaerobic digestion, and 2) mitigation measures, by applying incorporation of manure with the soil and the implementation of vegetation buffer strips. The reduction of input is the most efficient measure, because next to reducing the load within freshwater it also prevents the persistence of antibiotics within the soil matrix. Within this category, the application of a specific treatment plan has the largest potential due to the fact that no extra implementation costs are necessary. A downfall of this measure is that potentially farmers need to change their method of farming. Composting is a reliable measure, although it costs space and time. The process of anaerobic digestion needs large financial investments, but can reduce the concentration of antibiotics close to zero and has the production of biogas as an extra asset. Vegetation buffer strips and incorporation into the soil can reduce the erosion and runoff levels significantly. It, however, increases the fraction of antibiotics that accumulates within the soil, which can form a danger on the long term.

This research has sought a methodology to establish the fate of antibiotics and the effectivity of reduction measures. While this has given some new insights, the results still contain many uncertainties. It is therefore recommended to 1) do more research in the behavior of antibiotics within soil and water, 2) collect data on the total use of antibiotics which is publicly available and 3) improve the notion of legislation on antibiotic use.

Glossary

AF	Assessment factor	-
Appl	Total applied load of antibiotics applied to a field	kg or μg
α	Leaching runoff factor	-
C_{nat}	Natural background concentration	$\mu g\ L^{-1}$
C_{max}	Maximum allowed concentration	$\mu g\ L^{-1}$
GWF	Grey Water Footprint	L or m^3
k	Degradation rate	$days^{-1}$
K_d	Sorption coefficient	$mg\ L^{-1}$
L	Total Applied load	kg
$LogP$	The logarithm of the octanol water partition coefficient. Explains whether a compound is hydrophilic (low values) or hydrophobic (high values).	-
OFE	Overland Flow Element	-
$LogS$	The logarithm of solubility	-
P	Porosity of the soil	%
pKa	Explains the possible pH values of a compound in solution	-
ρ_l	Liquid density	$kg\ m^{-3}$
ρ_s	Soil density	$kg\ m^{-3}$
PNEC	Predicted no effect concentration	$\mu g\ L^{-1}$
RUSLE	Revised Universal Soil Loss equation	-
USLE	Universal Soil Loss Equation	-
VANTOM	Veterinary Antibiotic Transport Model	-
WEPP	Water Erosion Prediction Project	-

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1. Introduction

Antibiotics are a popularly used medicine to cure and prevent diseases for humans and animals. The use of antibiotics causes improvement of human and animal health (Kools et al. 2008). Due to its success, the variety of antibiotic types has grown largely since its invention at the start of the twentieth century (Mateo-Sagasta et al., 2017). Due to the fact that the world population and the demand for agricultural products have increased, the use of antibiotics has grown exponentially since the 1970s. For example, in the USA, the total antibiotic use increased from 3310 to 5580 tons between 1970 and 1978 (Kirchhelle, 2018). In Europe, the antibiotic use in agri- and aquaculture grew on average by 8% yearly between 1970 and 1980 (Culver & Castle, 2008). This growth was caused by the earlier mentioned increasing demand and the absence of clear knowledge and strict legislation on antibiotic use (Arikan et al., 2007). Moreover, if trends continue and no major policy changes are implemented, the global use will increase even more in the future. Due to growing global consumer demand, predictions are that by 2030 veterinary antibiotic use will be grown by 68% since 2015 (Van Boeckel et al. 2015).

Nowadays, antibiotics are a global issue. Aus der Beek et al. (2016) state that in countries all over the world concentrations of antibiotics are detected in different fresh water entities. These concentrations are often significantly high, which means that they potentially have dangerous ecotoxicological effects. The main source of pollution is wastewater discharge, but also hospitals and animal husbandry dispose antibiotic residues into freshwater. This has resulted in the pollution of rivers on the whole world. Some concentrations in those rivers exceed safe levels by 30 times. These high concentrations can form a danger for humans and natural life form due to toxicity and increasing chances of antibiotic resistance (University of York, 2019).

Over the years, the concern on the use of antibiotics grew, mainly due to antimicrobial resistance against antibiotics. Already in the 1940s, evidence was found that resistance could become an issue (Kirchhelle, 2018). However, it was not until the 1990s that attention to antimicrobial resistance would emerge significantly. This emersion was the result of the encounter that certain human infections could not be cured anymore by antibiotics (Podolsky, 2018).

Since this period, increasing efforts have been taken by governments to decrease the amount of antibiotic use in general and in agriculture (Geijlswijk et al., 2019). The European Commission for example has a specific strategy to reduce this amount in the environment (Commission Regulation (EU), 2009; European Commission, 2019). Next to these specific strategies, also the European Water Framework Directive seeks methods to reduce the amount of antibiotics in freshwater entities (Loos et al., 2018).

The agricultural livestock sector is a major antibiotic user. Antibiotics have become common and essential to keep animals healthy (D'Alessio et al., 2019). Since manure from animals is used on agricultural fields as fertilizer, residues of antibiotics can be transported into freshwater entities through runoff and leaching (Pikkemaat, 2016). The presence of these residues are potentially harmful for different organisms when concentrations are high (Park & Choi, 2008).

The use of antibiotics in agriculture has decreased over the last few years in the European Union and United States (Podolsky, 2018). In Europe this reduction is majorly caused by the prohibition of using antibiotics as growth promoters (Stärk, 2013). In the Netherlands, a specific strategy against microbial resistance was implemented, which more than halved the use of antibiotics in the country (Speksnijder et al. 2015). However, there is still a lack of knowledge on the levels of persistence of antibiotics in manure, soil and freshwater (Aga et al., 2016; Deo, 2014; Gothwal & Shashidhar, 2015). On top of that, a methodology is lacking that can help to measure the effectiveness of measures that potentially can reduce the pollution of antibiotics in freshwater entities (Mateo-Sagasta et al., 2017).

The Grey Water Footprint (GWF), introduced by Hoekstra et al. (2011), is one of the concepts that can help to compare the efficiency of measures. This concept can quantify the pollution of substances in different circumstances, while it can communicate the issue at hand very clearly. The input for calculating the GWF is based on the Veterinary Antibiotic Transport Model (VANTOM), an erosion and runoff driven model for determining the pollution of antibiotics on agricultural fields (Bailey, 2015). These two applications are used in combination with a case study approach to reveal the pathways of antibiotic pollution and to determine the effectivity of reduction measures.

1.1. Research objective and questions

The goal of this research is to improve the understanding of the different pathways of veterinary antibiotics after administration to animals and the effectivity of measures to the decrease pollution of freshwater by antibiotics. This is done in two steps; 1) The different pathways of pollution are revealed with help of a modelling approach; 2) the effectivity of different measures is tested with help of the model for a case study of the Vecht catchment area, on the border of the Netherlands and Germany. In this way can be tested whether antibiotics can form a risk in real life and how well they can be reduced with help of measures. Based on the research goal, the main question is defined as follows:

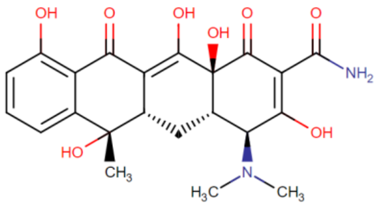
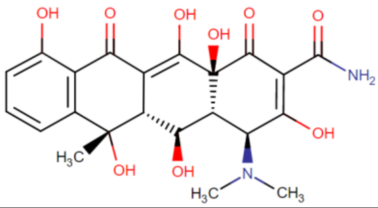
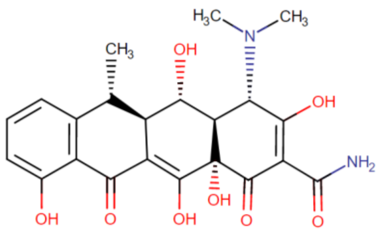
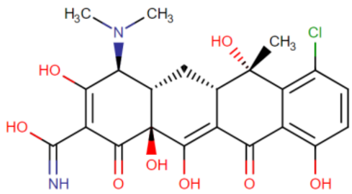
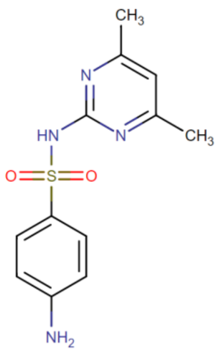
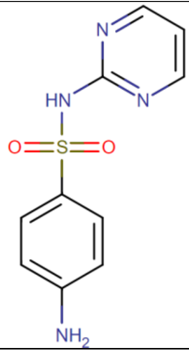
What are the different pathways of veterinary antibiotics and what is the effectivity of measures to reduce the pollution of surface water in several situations?

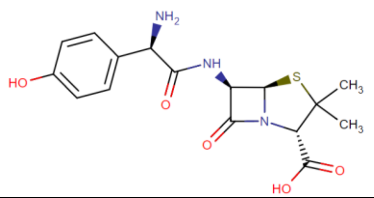
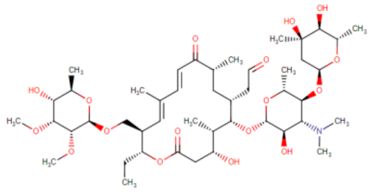
Answering the main question, it is divided into different sub-questions. These are displayed below:

1. What are the pathways and processes that determine how much antibiotics end up in soil and freshwater entities?
2. How effective are different potential measures to reduce the pollution of surface water by antibiotics?
3. What is the feasibility of the different measures for reducing surface water pollution by antibiotics?
4. What is the total antibiotic load and GWF for the Vecht catchment?

Eight antibiotics, which are frequently used in agriculture, are researched to cover a broad spectrum. The characteristics of these antibiotics are displayed in Table 1.

Table 1: Overview of the antibiotic substances considered in this study (Drugbank, 2019) .

Antibiotic	Group	Chemical Formula	Structure	Physical-chemical properties
Tetra-cycline	Tetracyclines	$C_{22}H_{24}N_2O_8$		logP = -1.30 logS = -3.12 pKa = -2.2-8.24
Oxytetra-cycline	Tetracyclines	$C_{22}H_{24}N_2O_9$		logP = -0.90 logS = -3.14 pKa = 2.84-7.41
Doxy-cycline	Tetracyclines	$C_{22}H_{24}N_2O_8$		logP = -0.72 logS = -2.8 pKa = 2.93-7.46
Chlor-tetra-cycline	Tetracyclines	$C_{22}H_{23}ClN_2O_8$		logP = 0.11 logS = -3.2 pKa = 3.58-7.97
Sulfa-methazine	Sulfonamides	$C_{12}H_{14}N_4O_2S$		logP = 0.89 logS = -3.1 pKa = 6.99-2.04
Sulfa-diazine	Sulfonamides	$C_{10}H_{10}N_4O_2S$		logP = -0.09 logS = -3.51 pKa = 6.99-2.01

Amoxi-cillin	β-lactams	$C_{19}H_{19}N_3O_5S$		logP = 0.75 logS = -2.6 pKa = 3.23-7.43
Tylosin	Macrolides	$C_{46}H_{77}NO_{17}$		logP = 1.46 logS = -3.6 pKa = 7.2 – 12.45

1.2. Outline

In the next chapter, the different process that play a role in determining the fate of antibiotics are explained. In the third chapter the methodology of the research is explained, describing how the processes are modelled and which data is used as input. In the fourth chapter, the results of the modelling are presented. The fifth chapter consists of the discussion, reflecting on the assumptions taken and comparing results with other researches. The final chapter gives the conclusion and the recommendations of the research.

2. Processes

Before veterinary antibiotics reach freshwater entities they are prone to different processes. Overland transport of antibiotics after application, the accumulation or leaching after entering the soil matrix, sorption, degradation and bioaccumulation have an influence on an antibiotic compound. These mechanisms, together with the total input of antibiotics and the excretion by animals, determine the different pathways and the fate of antibiotics. To get a better understanding, these processes are explained ahead of the modelling in the third chapter.

2.1. Application to the field

Antibiotics are applied to animals in two ways: through feed or by injection. After administration to the body of the animal, a part of the antibiotic is degraded. (Sarmah et al. 2006). Solely a certain part ends up in the manure of the animal, which means that there is a certain excretion rate, which differs per animal and antibiotic type (Spielmeyer, 2018). It is common practice that manure is stored after excretion by the animal, which ensures that there is always a certain period for the degradation of the antibiotic compounds (Ezzariai et al., 2018a). The duration of this period of storage depends on when manure needs to be applied for fertilization. After application, the manure containing antibiotic concentrations is transported through different pathways.

2.2. Overland transport of antibiotics

Two possible ways of overland transportation of are runoff and soil erosion. Runoff is driven by rain or irrigation. If the maximum infiltration capacity of the soil is reached, water cannot enter the soil anymore (Brouwer et al. 1985). The consequence is that, depending on the slope, water runs off to surface water or ends up in puddles on the field. When runoff takes place, this can cause soil erosion as well.

Runoff and soil erosion both can be responsible for overland transport of antibiotics into surface waters. In case of antibiotic transport through runoff, antibiotics are dissolved in water beforehand. If an antibiotic is transported through soil erosion, this means that an antibiotic is in solid form attached to soil particles (Cruse et al., 2006). Both processes need to be taken into account when determining the total load of antibiotics to surface water.

2.3. Accumulation and long-term leaching

The fraction of antibiotics that is not transported to surface waters via runoff and erosion, remains on or in the soil. Here they can accumulate (Hamscher et al., 2005) or they can leach through the soil into groundwater (Spielmeyer et al. 2017). Both processes are long-term processes and depend on the mobility of the compound. This means that antibiotics that are hydrophilic are easily leaching to the groundwater (Pan & Chu, 2017). Antibiotics that do not degrade quickly within the soil, can persist for years within the soil. This means that they can still leach, due to vertical water flow, into the groundwater for years after the application (Spielmeyer et al. 2017). An overview of the four possible pathways are given in Figure 1.

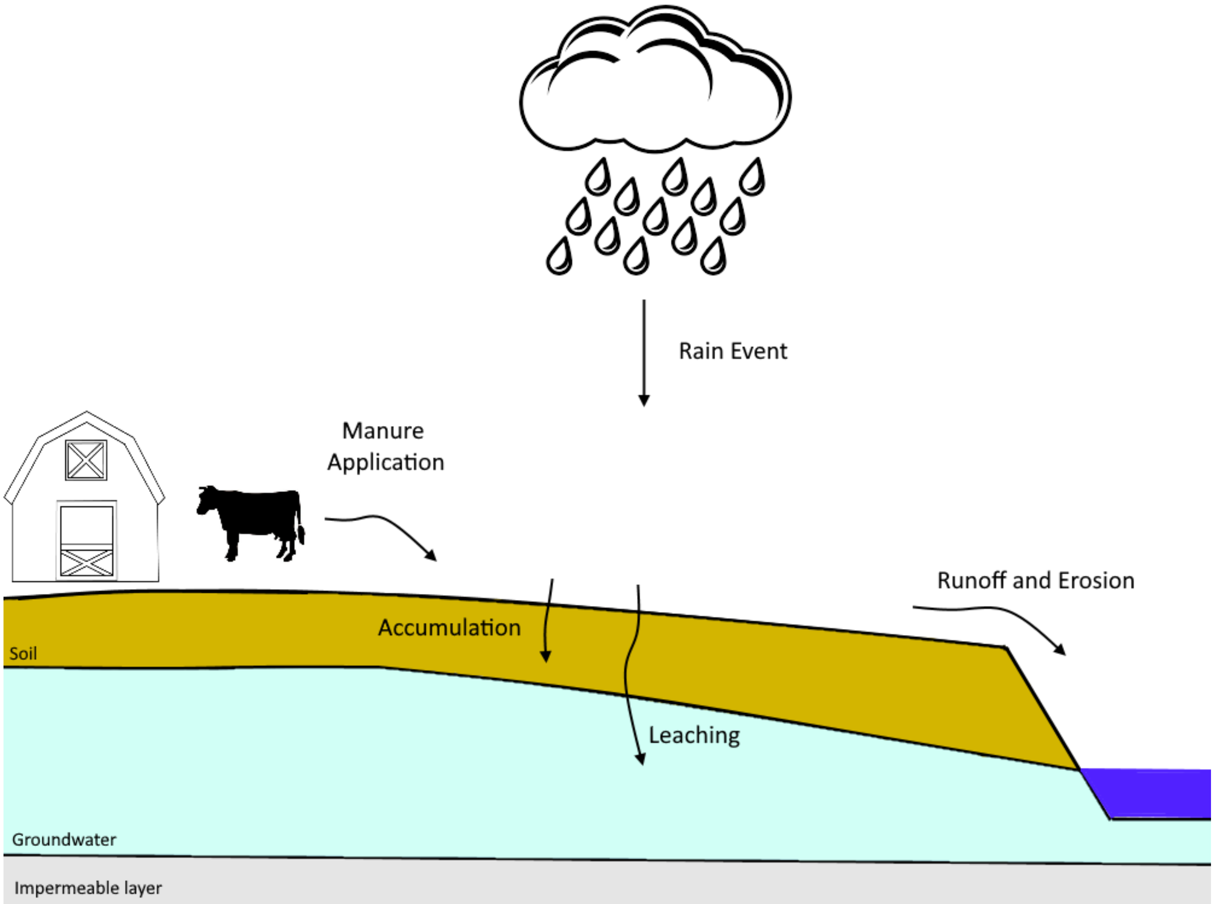


Figure 1: The possible pathways of antibiotics on field after manure application.

2.4. Sorption

The process of sorption within soil is assumed to be a time-independent process (Bailey et al., 2016). It describes three subprocesses: 1) the adhesion to soil particles, which means that an antibiotic is attached to the surface of soil particles; 2) the adsorption into soil particles, which means that an antibiotic gets merged with soil particles and 3) the desorption from soil particles, which means that antibiotics is detached from soil particles (Bailey, 2015). Many parameters have an influence on the sorption of antibiotics to soil particles. Temperature, pH, soil moisture content and the structure and type of the soil all play a role (Blackwell et al., 2009). Adsorption coefficients, or K_d values, can be used to assess how well an antibiotic sorbs to a specific soil type. For this research several K_d values of the antibiotic for different soil types are used. The values used for this research are based on literature and can be found in Appendix A.

2.5. Degradation

The degradation of antibiotics in manure or soils is a time-dependent process that reduces the total mass of the applied product. Degradation can happen in three different ways: due to exposure to 1) light (photodegradation); 2) water (hydrolysis) or 3) microbial activity (biodegradation) (Bailey, 2015; Kemper, 2008). Degradation causes that an antibiotic diminishes completely or converts into a transformation product which can be more or less harmful (Wohde et al., 2016).

The degradation rate of all these processes together can be described by a first-order degradation rate coefficient, k $(days)$. These depend on different parameters: temperature, light, pH and bio-activity (Wegst-Uhlrich et al., 2014; Wohde et al., 2016). For example, lower or more acid pH-levels cause that antibiotics are degraded more quickly (Kim & Carlson, 2007). The k values of antibiotic for different soil types are used to determine the influence of degradation on the transport of antibiotics within the soil. These values can be found in Appendix A.

2.6. Bioaccumulation

Another factor that plays a role in the fate of antibiotics in the field, is the antibiotic uptake by and bioaccumulation in plants. Manure, which contains the residue of the antibiotics used by animals, is used for growing crops in the field. These crops can accumulate antibiotics, because they collect nutrients from the soil and manure for their growth. This can potentially decrease the amount of antibiotic in the field (Li et al.2019; Pan & Chu, 2017). Due to the fact that there is a little amount of knowledge and data available, it is not possible yet to determine for a variety of crops how much antibiotics accumulate within crops. Therefore, the direct influence of crops is not taken into account in this research. Within the scenarios the focus is on degradation, sorption and runoff, erosion, leaching and accumulation within the soil.

3. Model, methods and data

The research consists of different steps, which are explained in this chapter. The first step is the collection of data, which focuses on the total application of antibiotics to animals within the livestock sector and on the processes after application, namely erosion, runoff, leaching, accumulation, degradation and adsorption. These data are used as input to model the emissions of a typical Dutch farm. For the same hypothetical farm a sensitivity analysis is carried out to evaluate the influence of different input parameters on the results. With help of data on the case study of the Vecht catchment, the effectivity of different measures is compared. At the end of the chapter, an overview of the methods are given in a conceptual model.

3.1. VANTOM modelling

VANTOM is a tool developed by Bailey (2015) with the aim to model the overland transport of antibiotics after application to the soil. Based on different input data and parameters it simulates the different pathways that cause pollution. The VANTOM model was used as a basis and further developed including the erosion data of the Water Erosion Prediction Parameter (WEPP). A schematization of the adapted version of the model is shown in Figure 2.

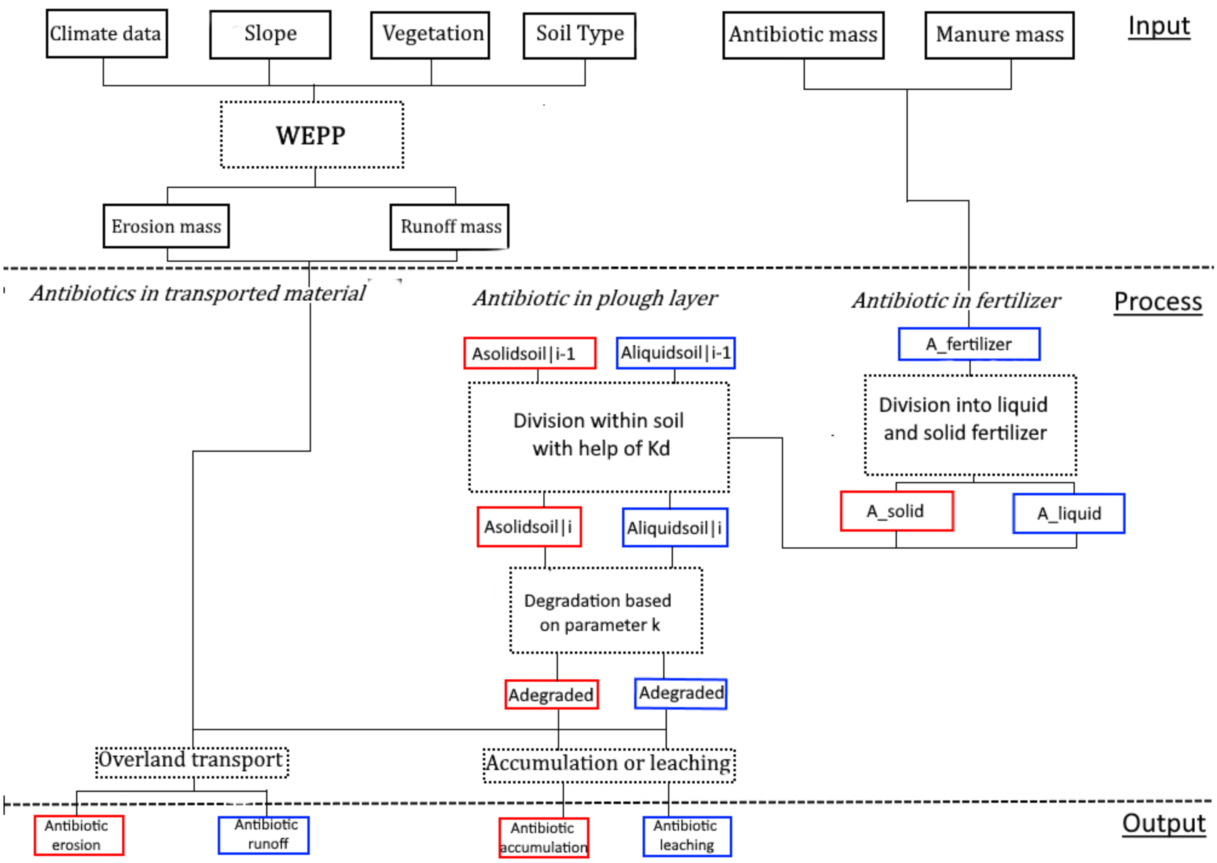


Figure 2: Schematization of model steps of VANTOM, based on Bailey (2015). *Red colors display parts in solid phase. Blue parts display compounds in liquid phase.*

VANTOM calculates transport of manure and antibiotics per timestep of a day. At the start of a timestep, a mass of manure containing antibiotics in solid and liquid phase is added to a homogeneous layer of soil. Based on this input, the masses of manure and antibiotics are divided evenly through the complete soil layer. The dynamics of these changes are explained with help of the layer concept: the soil consists of the plough layer and the sub plough layer. The plough layer has a constant depth, which means that it cannot become larger or smaller. The sub plough layer forms therefore a buffer within the model and receives the masses of antibiotics that are not diverted by runoff or erosion. The mass in the sub plough layer increases due to addition of manure, but can decrease if erosion of the plough layer takes place. This is possible, because within VANTOM the plough layer needs to be constant. Within the dynamics of these two layers, three processes determine the pathways of the applied antibiotics: the total eroded mass and runoff, sorption and degradation. The part of antibiotics that stays in the soil can be divided in two groups: a solid mass and a liquid or solved mass. Within this research it is assumed that the solid part accumulates with the soil and the liquid part leaches through soil into groundwater. Although leaching can be a very long term process, it is plausible that this liquid part will reach freshwater entities through leaching (Spielmeyer et al., 2017).

At the end of each timestep, the antibiotic load to surface water and groundwater and change in the storage of antibiotics in soil are given by the model. For this research, the timestep is one day. The end values are used for the following timestep, possibly with addition of new input defined by the user. In this way the processes within the soil can be followed over a longer period of time. A more thorough explanation can be found in Appendix B as well as in Bailey (2015).

3.2. Water Erosion Prediction Parameter

As explained in last paragraph, VANTOM is driven by runoff and erosion data generated by a different model. Bailey (2015) uses PESERA as input for erosion and runoff. This model is not suitable to use on a farm level, since it focuses on large areas. A more detailed model would make more sense for this research. Therefore, the Water Erosion Prediction Parameter (WEPP) is used. This model is developed by the United States Department of Agriculture to predict the amount of erosion and runoff in specific areas (Flanagan et al., 2001). There are three reasons for this model choice: 1) it is a continuous model with a daily time step, which makes it compatible with the VANTOM model; 2) it is suitable for small areas, so on farm and catchment level it can predict erosion and runoff levels; 3) it focuses on both runoff and soil erosion, instead of only soil erosion which is the case for the commonly used models USLE or RUSLE (Kinnell, 2017).

Modelling erosion and runoff within WEPP is carried out within one particular area, for example a field, a hillslope or a river catchment. Such a particular area is described as an OFE, an Overland Flow Element Within this element, the model keeps track of different factors, such as plant growth, water balance, infiltration and erosion. Based on user inputs of rainfall, climate, soil type and slope, the model generates values per day for soil erosion and runoff (Han et al., 2016). Further, the model considers levels of evapotranspiration, partly through vegetation and the infiltration levels of specific soil types. Based on the output of this model, a runoff and erosion values can be created for VANTOM.

3.3. Grey Water Footprint

The GWF is the "volume of freshwater that is required to assimilate the load of pollutants given by natural background concentrations and existing ambient water quality standards" (Hoekstra, 2013). The main advantage of the GWF is that different types of pollution are explained with one central denominator, which is in this case the total volume of water that is assimilated by the polluter. In this way it is very easy to compare different pollutants, or in this thesis, different antibiotic types and usage.

The calculation of the GWF is done in the following way:

$$GWF = \frac{L}{C_{max} - C_{nat}} \text{ (Eq. 1.)}$$

Where GWF is the grey water footprint (in L), L the load (in μg), C_{max}, the maximum allowable concentration (in $\mu g\ L^{-1}$) of the pollutant and C_{nat} the natural background concentration (in $\mu g\ L^{-1}$) of the pollutant.

For diffuse sources, such as agricultural fields, a different formula is used:

$$GWF = \frac{\alpha\ x\ Appl}{C_{max} - C_{nat}} \text{ (Eq. 2.)}$$

Where α is the leaching run-off fraction, which means the fraction of the chemical or the pollutant that flows into a freshwater body. This is a dimensionless factor. $Appl$ is the total mass of the pollutant over time applied into the soil (in kg).

Since C_{nat} is 0 in natural conditions for pharmaceutical effluents, C_{nat} can be neglected. Therefore the formula becomes:

$$GWF = \frac{\alpha\ x\ Appl}{C_{max}} \text{ (Eq. 3.)}$$

C_{max} is based on values for the Predicted No Effect Concentration (PNEC) because there is not a clear legislation yet on maximum allowed concentrations for antibiotics (European Parliament & the Council of the European Union, 2018). The total load is given by the output load of VANTOM. The formula then becomes:

$$GWF = \frac{Load_{VANTOM}}{PNEC} \text{ (Eq. 4.)}$$

3.3.1. PNEC

The PNEC is defined by European Chemicals Bureau (2003) as the *"concentration of a chemical that is not expected to give any adverse effects to ecosystems at any time".* If C_{max} is replaced by the PNEC, a precautionary principle is followed: it does not create a negative effect for the environment in its common nature.

A PNEC value can be developed by doing a risk assessment of ecotoxicological effects of a compound on specific organisms. This is done with help of the equation below:

$$PNEC = \frac{NOEC}{AF} \text{ (Eq. 5.)}$$

In this formula NOEC stands for No Observed Effect Concentration. This value is determined by ecotoxicological tests of substances on specific organisms. AF stands for the Assessment Factor, which is advised by the technical report of the European Union to be 100 when using NOEC, because it protects even the most vulnerable organisms in water, for example algae (European Chemicals Bureau, 2003; Hommen et al., 2010).

Many of these PNEC values have been determined for different potential toxic compounds. Also for antibiotics there is data available. The PNEC values that are used for this research are presented in Table 2. To assure consistency, solely the PNEC values of Bergmann et al. (2011) are used.

Table 2: Different PNEC values of antibiotic used for animals based on Bergmann et al. (2011).

Antibiotic	PNEC ($\mu g\ L^{-1}$)
Tetracycline	0.251
Oxytetracycline	1.1
Doxycycline	0.054
Chlortetracycline	0.03
Sulfamethazine	1
Sulfadiazine	1.35
Amoxicillin	0.0156
Tylosin	0.34

3.4. Input data

MARAN is a database that provides data on the total sold antibiotics by veterinarians in the Netherlands (Geijlswijk et al., 2019). The data is solely explained per antibiotic compound group, such as tetracyclines, sulfonamides or macrolides. To get a more detailed assessment of total sales per antibiotic type in the Netherlands a factor is developed based on the sales data within Germany (Wallmann et al., 2018). In the analysis, the total administration for cows, chicken and pigs is used. Unfortunately, the excretion rates of animals is an under researched subject (Zhao et al. 2010), which means there is not enough data available for this matter. The total excretion rate of the antibiotic is assumed to be equal to the human excretion rate, although this might not reflect reality. The rates are based on Hirsch et al. (1999) and Moffat et al. (2011). These rates are given in Appendix A.

The effect of pollution due to antibiotics depends on the moment of time manure is deposited on land. For example, if manure is applied in a wet and cold season, the runoff and infiltration is high and the degradation low. In the Netherlands it is allowed to deposit manure between February and September (RVO, 2019). For this study, it is assumed that the total amount of manure is deposited two times per year: at the start of spring (11-03-2019) and at the end of the summer (01-08-2019). Between these days lies a gap of 143 days. During this time, manure of animals is stored for a total of 143 days. To assess the degradation of antibiotics within this manure, the model of Wöhler et al. (2020) is used.

The parameters that determine the fate of antibiotics within different soils, respectively K_d and k, are based on different scientific literature. It should be noted that there are differences in circumstances among the literature that potentially can decrease the consistency of the data (Sukul et al., 2008). These differences are neglected. The values for these parameters are given in Appendix A.

The main driver of the VANTOM model, which is rainfall and the subsequent infiltration, erosion and runoff, is based on the levels of rainfall per day at the rain station of Twenthe airport in the Netherlands (KNMI, 2019). This rain station is chosen because of the central position within the Vecht catchment. The weather data of this station is used within WEPP to determine runoff and erosion levels.

Within VANTOM, there are four soil properties of importance: porosity of the soil P, density of the soil ρ_s, water density ρ_l and the initial saturation within the pore volume of the soil. The values of these parameters are given in Table 3.

Table 3: Parameter values of different soil types (Terzaghi et al. 1996).

	Clay	Loamy Sand	Sand
$P\ (-)$	0.66	0.30	0.34
$\rho_{s\ (kg\ m^{-3})}$	1580	1860	1750
$\rho_{l\ (kg\ m^{-3})}$	997	997	997
Initial saturation of the pore volume	70 %	16 %	19 %

3.5. Sensitivity Analysis

Based on the methods and data presented in the sections above, a sensitivity analysis is executed to understand the influence of different processes. This is done based on a reference case: a typical Dutch farm with 100 cows. The factors or parameters that are used within the analysis can be non-influential by humans, such as degradation, adsorption, soil type and the slope of the field, but also on factors that can be influenced through farming practices, e.g. the type of animals on the farm and the moment of application. They are described in the following sections.

3.5.1. Differences in degradation and sorption

The level of pollution in freshwater of antibiotics depends on two factors: the total amount of antibiotics applied on the field and the persistence of the compound in the soil. The persistence within the soil mainly depends on adsorption and degradation processes (Pikkemaat et al., 2016). The total GWF of the reference case is compared with the largest and smallest degradation and adsorption rates found in literature, independent from soil and antibiotic type. These values can be found in Appendix A. The influence of these parameters is shown by the changes in GWF assessed in the sensitivity analysis.

3.5.2. Different soil types

The texture and type of soil also determine the fate of antibiotics, because every compound reacts differently within different types of soils (Cycoń et al., 2019). Sorption and degradation rates are here as well the most influential parameter. Besides that, erosion and runoff levels can differ between soil types, due to varying infiltration rates. Due to the fact that clay soils have smaller pores than sandy and loamy soils, they have a lower infiltration rate. This causes different levels of runoff and erosion (Berhanu et al. 2012). Degradation rates and sorption coefficients differ as well per soil, but are already assessed with help of the former paragraph. Therefore, these are not assessed during this part of the sensitivity analysis.

3.5.3. Moment of application

In the Netherlands it is not allowed between 1 September and 31 January to apply manure just before or during a rainfall event (RVO, 2019). This has as a goal to reduce leaching of phosphorus and nitrate in surface water. The effect of this measure on the fate of antibiotics is not clear yet. For the reference case, the antibiotics are applied before a rainfall event. These values are compared with the total GWF of a situation where antibiotics are applied after a rainfall event.

3.5.4. Slope

The slope of the field plays a role because for steeper slopes of agricultural land, precipitation gets less time to infiltrate into the soil and flows over the field quicker, which causes more erosion and runoff (Kim et al. 2010; Lin et al. 2019; Wang et al. 2018). The influence of slope is tested by changing the input parameters in WEPP. This means that the erosion and runoff levels are found for the slope of 1% and 5%. Since in the Netherlands there are barely any steep slopes, these values are considered sufficient for the scope of this research.

3.6. Mitigating Measures

In this section different measures that can potentially reduce antibiotic loads are explained. Figure 3 shows the pathways of antibiotics from animal to freshwater (surface- and groundwater). The green boxes indicate the different measures. Within this study, the effectiveness of these measures reducing antibiotic loads to freshwaters is assessed.

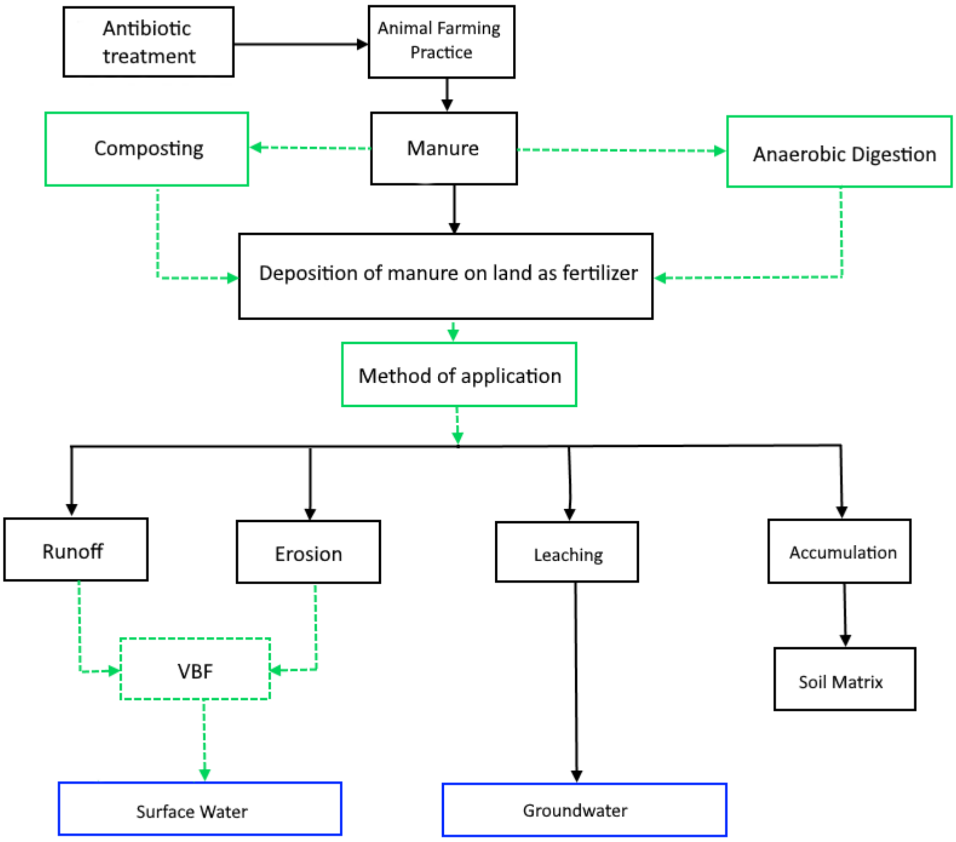


Figure 3: Schematization of the pathways and measures to reduce effects of antibiotic use. Blocks in green are measures that have a mitigating effect within the location of that pathway.

3.6.1. Input reduction

A solution that directly decreases the pollution by antibiotics is the implementation of a certain treatment plan that reduces the total input of antibiotics within the herd of animals. Regulations are for that matter of essence, so that farmers are motivated to reduce their antibiotic use (Van Boeckel et al. 2017). An example could be the Dutch model which set up a collaboration between different stakeholders such as the pharmaceutical industry, farmers and the government to reduce the use of antibiotics. This strategy has reduced the use of antibiotics within agriculture with 56% between 2007 and 2012. The goal is to reduce the use even more in the coming years (Speksnijder et al. 2015).

Because of the successful reduction of usage, it is of interest to see what the effect is on the pollution of freshwater. Therefore, two different reduction scenarios are implemented within VANTOM to compare with the normal situation: 20% and 1% of the normal usage.

3.6.2. Composting

Composting is a conventional measure to reduce the amount of pollutants within manure, while the nutrient content of the manure is retained. During the process of composting manure is collected in a depot where it can decompose into a nutrient-rich humus, which is very useful as a fertilizer (Youngquist et al. 2016). During this process, unwanted pollutants can be removed by degradation. Antibiotics are removed through the same process (Spielmeyer, 2018).

Three different methods of composting exist, which are described by the United States Environmental Protection Agency (2019); 1) Windrow composting, meaning that large parts of manure are deposited in piles and are aerated by turning them. This can be done in a manual or mechanical way. 2) Aerated static piles, has the same principal, but does not need mechanical or manual turning. This is because it is put on wooden shelves to assure the addition of oxygen. 3) In-vessel systems can process large amounts of manure, because it is collected within, for example, a silo. The advantage of these systems is that the circumstances for composting can be regulated precisely and extra volumes of air can be pressed into the system to increase the speed of composting.

Dolliver et al. (2008) found a significant increase in degradation of oxytetracycline and tylosin if an in-vessel system is used instead of a managed composting method, such as windrows. For this comparison, the same composting period is used. This period is based on the average composting time of Mackay, Mason, & Di Guardo (2005), which is 143 days. Within Table 4 the removal rates for this period are given, which are calculated with help of the equation below.

$$C = C_0 e^{-kt} \quad \text{(Eq. 6)}$$

where C is the concentration after composting, C_0 is the initial concentration of antibiotics within manure, k is the first order degradation rate (in $days$) and t is the time (Augustijn, 2018).

Table 4: The part of antibiotics that is degraded during a composting period of 143 days,

Antibiotic compound	Reference treatment	Windrows	Aerated static piles	In-vessel systems	Source
Tetracycline	82.0%	57.6%	-	~100%	Ezzariai et al. (2018)
Oxytetracycline	68.1%	~100%	~100%	~100%	Dolliver et al. (2008)
Doxycycline	53.8%	~0%	~0%	~0%	Ezzariai et al. (2018)
Chlortetracycline	-	68.1%	-	~100%	Ezzariai et al. (2018)
Sulfamethazine	~100%	~100%	-	~100%	Ezzariai et al. (2018)
Sulfadiazine		70.8%	-	89.9%	Ezzariai et al. (2018)
Amoxicillin	~100%	-	-	-	
Tylosin		98.4%	99.8%	99.5%	Dolliver et al. (2008)

3.6.3. Anaerobic Digestion

Anaerobic digestion can be described as a microbial process of decomposition, which happens under anaerobic circumstances (Youngquist et al., 2016) Often a combination of maize and liquid manure is disposed in a fermentation tank or area, that is fixed at a specific temperature (Holm-Nielsen et al. 2009).

Two temperature conditions are used: mesophilic, which is at a maximum of 41 ℃ and thermopilic temperature conditions with a maximum of 55 ℃ (Youngquist et al. 2016). The process produces two useful products: biogas, which can be used as fuel and a digested substrate, which can be used as a concentrated fertilizer (Holm-Nielsen et al., 2009). It is necessary to continuously add manure to the tank. Inside, temperature and pH-levels are kept constant (Youngquist et al. 2016).

In many cases, antibiotics are degraded during this process (Feng et al. 2017; Mitchell et al. 2013). Different removal rates for mesophilic and thermophilic conditions of Youngquist et al. (2016) are used to determine the effectiveness of anaerobic digestion at mesophilic of thermophilic circumstances. These values are displayed in Table 5.

Table 5: Removal rates of antibiotic compounds for anaerobic digestion is used (Youngquist et al.,2016).

Antibiotic compound	Mesophilic	Thermophilic
Tetracycline	-	-
Oxytetracycline	59%	68%
Doxycycline	-	-
Chlortetracycline	75%	98%
Sulfamethazine	0%	0%
Sulfadiazine	-	-
Sulfathiazole	0%	-
Amoxicillin	-	-
Tylosin	-	100%

3.6.4. Method of application

Three manure application methods are compared; 1) slurry of manure can be poured on top of the soil, which is called broadcasting (Joy et al., 2013); 2) manure can be applied within the upper layer by injection (Tullo et al. 2019). 3) mixing, which means that manure is mixed with the top layer of the soil with the manure (Joy et al., 2013). Injection and mixing are meant to decrease the chances of runoff and erosion of antibiotics during a rainfall event. Le et al. (2018) found in their experiments that on average 2% less antibiotic residue ended within the runoff, when manure was injected into the soil 3 days before a rainfall event. Caused by the different levels of persistence, the percentage that ends up in runoff differs per antibiotic compound.

The different application methods are tested with help of VANTOM by varying the value of the depth of manure application. The depth variations are based on the experiments of (Joy et al., 2013). For broadcasting this is 1 cm, for mixing this is 8 cm and for injection the depth is 13 cm.

3.6.5. Vegetation buffer strips

Vegetation buffer strips reduce the amount of erosion and runoff. In this way it prevents antibiotics attached to soil or solved in water from ending up in surface water. The reduction in erosion and runoff caused by the application of VBF is tested with help of changing parameters within the erosion model WEPP. In this way it can be checked whether the total runoff and erosion reduces when a VBF is implemented and what the effect would be of the load of antibiotics in different compartments.

3.7. Feasibility

In the previous sections, different quantitative results have been described that mean to explain how well different measures can mitigate the use of antibiotics. The measures are different in their ease of implementation and are therefore not evenly feasible. There are several aspects along which the feasibility of measures can be tested. This depends on three different aspects: costs, space, and time frame. When these aspects are increasingly high, it becomes much less attractive for farmers or governments to implement these measures (Speksnijder et al. 2015; Wezel et al. 2017).

A measure should also be robust so that the user can rely on it. This means that if the measure is in place or used, it is working properly and does not need constant maintenance or repairs. If a measure is working for the future period for a significant amount of time, it is more attractive to implement such a measure (Speksnijder et al. 2015).

The negative and positive side effects that can potentially be caused by the measures also play a role. For example, the decrease in odor by using the method of in-vessel composting or the production of biogas in anaerobic digestion installations are effects that can help the farmers themselves (Sara et al., 2013).

3.8. Conceptual Model

In the paragraphs above, the different steps from input data to results of these thesis have been explained. Since it is hard to get an overview from the beginning, the steps are summarized in Figure 4. In the next chapter the results are presented, which are collected with help of this conceptual model.

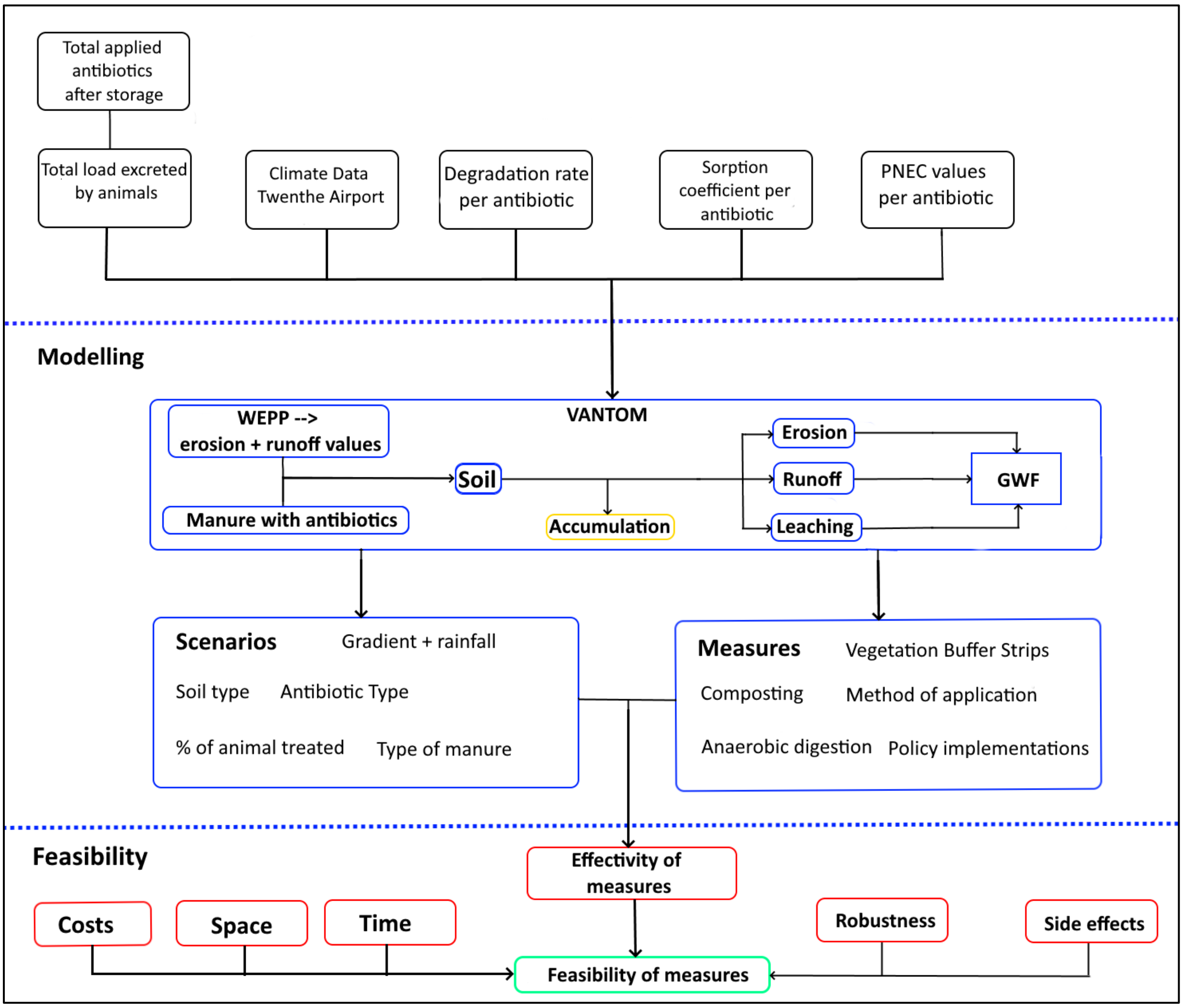


Figure 4: The conceptual model of the research.

4. Results

This chapter presents the results of the research. First, a reference case was constructed for which the results are outlined. For the reference case, antibiotic emissions and related GWFs of a hypothetical farm are presented. Input parameters chosen for this reference case are based on typical numbers for the Netherlands. To increase understanding of the robustness of the generated results, the sensitivity of the results to the change of model inputs is analyzed for the reference case. To demonstrate a realistic case, the antibiotic emissions and according GWFs are modelled for the transboundary Vecht catchment that is shared by Germany and the Netherlands. By comparing GWFs to the available (average annual) discharge in the catchment, the pollution level within the catchment is estimated. This gives an indication of the severity of pharmaceutical pollution from agricultural activities in the catchment. Further, different measures that potentially decrease antibiotic emissions to water are modelled for the Vecht case, and evaluated. These measures cover load reduction approaches, manure application techniques and VBF.

4.1. Reference case

To form a basis for comparing the influence of different processes and parameters, a reference case is introduced. The characteristics of the reference case found on the attributes of a typical Dutch farm. These are presented in Table 6. Based on these, the total antibiotic application and loads to freshwater are determined as well.

Table 6: The reference case used for comparison. A slope of 1% is chosen for the functionality of the model and because it is close to slopes found in the Netherlands.

Typical Dutch farm		Source	
Amount of animals	100 cows	CBS (2019a)	
Surface	40 hectares	CBS (2019b)	
Main soil type	Clay	-	
Slope	1%	-	
Antibiotics	Total application (in mg)	Total Load into surface water (in mg)	Remaining part after degradation and accumulation
Tetracycline	42804	464	1.1%
Oxytetracycline	6991	77	1.1%
Doxycycline	57812	297	~0%
Chlortetracycline	40770	205	~0%
Sulfamethazine	3508	4	~0%
Sulfadiazine	1449	14	~0%
Amoxicillin	4496	34	0.1%
Tylosin	65108	454	~0%

The major part of the applied antibiotics does not reach surface water entities after application: for all antibiotics this is less than 1%. This means that degradation and accumulation have an important influence on the load reduction

Due to the fact that tylosin is the most applied antibiotic, but does not cause the largest load. The degradation of tetracycline is less rapid, which makes it more persistent than tylosin within the soil.. Sulfamethazine is the least persistent antibiotic within the soil because it degrades rapidly. This can be seen in Table 7.

Table 7: Percentages of loads through different pathways in one year. The leaching and runoff loads have an insignificant impact and are therefore not added.

	Accumulation	Erosion	Degradation
Tetracycline	8.1%	0.9%	91.1%
Oxytetracycline	8.5%	0.9%	90.5%
Doxycycline	4.0%	0.4%	95.6%
Chlortetracycline	3.9%	0.4%	95.7%
Sulfamethazine	0.4%	0.0%	99.5%
Sulfadiazine	7.5%	0.8%	91.7%
Amoxicillin	6.7%	0.7%	92.5%
Tylosin	6.0%	0.6%	93.4%

Although the erosion, runoff and leaching fractions of antibiotics are relatively low, some still cause a significant GWF (see Figure 5). While chlortetracycline does not have the highest load into surface water, it causes the highest GWF because it has the lowest PNEC value. Tetracycline has the highest load, but has a significantly lower GWF. Due to the lower loads of oxytetracycline, sulfamethazine and sulfadiazine, their GWF is very low compared to the others. This is primarily caused by the lower use of these antibiotics in livestock.

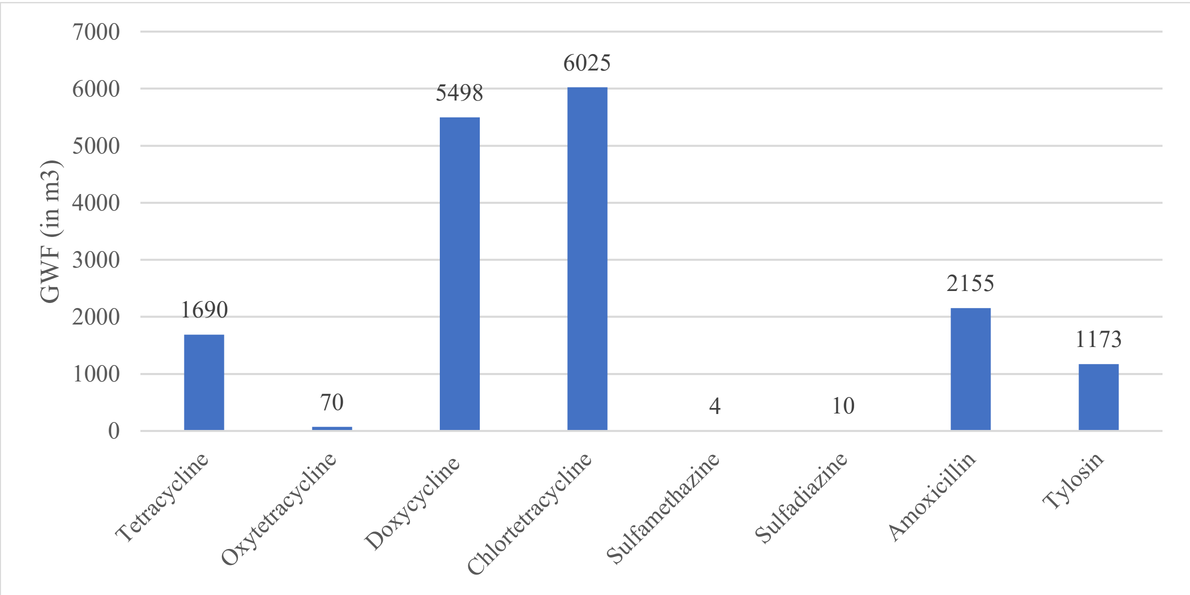


Figure 5:The annual GWF of eight antibiotics based on the reference case.

4.2. Sensitivity Analysis

The reference case presented above is used to understand how changing model input parameters influence results. This is done for the antibiotic which is the most administered (tylosin) and the one that has the largest GWF (chlortetracycline).

4.2.1. Degradation

Based on the results from Table 7 can be stated that degradation plays an important role in the fate of antibiotics. The degradation rate depends on the circumstances, for example Cycoń et al. (2019) have found more than 8 different degradation rates within literature for chlortetracycline in the same but also different soil types. Therefore, different rates of from literature and soil types are used here to find their influence. These rates are displayed in Table 8 together with the resulting GWFs.

Table 8: Degradation rates of different antibiotics and the resulting GWF.

Antibiotic	k of reference case $(days)$	High k $(days)$		Small k $(days)$	
Chlortetracycline	0.025	0.175		0.000147	
Tylosin	0.099	0.175		0.000147	
	GWF of reference case (in m^3)	GWF high degradation	% change	GWF with low degradation	% change
Chlortetracycline	6,025	5,905	-2%	6,146	2%
Tylosin	1,173	1,103	-6%	1,279	9%

Although a major part of antibiotics degrade after application to the soil (see Table 7), there are not many differences if the rates are fluctuated. For example, if chlortetracycline the rate is increased with 14%, the GWF of chlortetracycline is only decreased by 2%. The same counts if the rate is decreased. For example, a decrease for tylosin of 99%, means an increase of GWF of 9%. A plausible cause for these results is the time span of one year, which means that antibiotics always get sufficient time to degrade within the soil, even if the compound does not degrade fast.

4.2.2. Adsorption

Changing sorption parameters barely results in changes of GWFs. These are displayed in Table 9. The GWF of chlortetracycline increases with $2 * 10^{-6}\ m^3$, which can be assumed as negligible. This is remarkable, because other literature state that sorption plays an important role in whether antibiotics persist within soil or are transported by erosion or runoff (Conde-Cid et al., 2019; Hamscher et al., 2005).

Table 9: Different K_d values and the resulting GWF.

Antibiotic	K_d reference case ($L\ kg^{-1}$)	High K_d ($L\ kg^{-1}$)		Small K_d ($L\ kg^{-1}$)	
Chlortetracycline	423	90758		22	
Tylosin	5520	6520		8.3 (Sandy Loam)	
	GWF reference case (in m^3)	GWF high sorption (in m^3)	% change	GWF low sorption (in m^3	%change
Chlortetracycline	6,025	6,025	0%	6,025	0%
Tylosin	1,173	1,173	0%	1,173	0%

4.2.3. Soil type

Between soil types there are differences in the behavior of antibiotics (Aust et al., 2010). This caused by the different characteristics of soils, such as porosity and soil density. The results caused by these differences are displayed in Table 10. For tylosin and chlortetracycline the lowest GWF was found for loamy sand. This is because runoff and erosion values are much smaller for loamy sand than for clay. On top of that, less antibiotics are transported through leaching than within sand. A negative aspect of this is that a higher percentage of antibiotics accumulates within the soil. Therefore, farming on loamy sand can be beneficial for reducing pollution in freshwater, but not within soil.

Table 10: The annual GWF for different soil types.

Antibiotic	GWF (in m^3)			Change (in %)	
	Clay (reference case)	Loamy sand	Sand	Loamy Sand	Sand
Chlortetracycline	6,025	3,953	6,230	-34%	+3%
Tylosin	1,173	821	1,352	-30%	+15%

4.2.4. Rainfall and timing of application

Within the Netherlands it is not allowed to apply manure before a rainfall event. This with the goal to reduce the chance of erosion and runoff of phosphorus and nitrate into surface water (RVO, 2019). In Table 11, the differences of applying manure that contains VAs between before and after a rainfall event are displayed. The reference case uses applied manure just before rainfall events, to demonstrate a potential worst case. The results show that applying manure on a later moment after a rainfall peak is very beneficial for reducing the GWF. An application shift by four days after a rainfall, results into a 12% reduction of pollution. This is primarily caused by the longer period of degradation within the soil and by the less intense rainfall events after the 12th of March.

Table 11: The GWF of a late application (on 19-03-2018 and 02-08-2018) compared with the reference application (on 13-03-2018 and 01-08-2018).

Antibiotic	GWF (in m^3)		
	Reference application	Late application	Percentage reduction
Chlortetacycline	6,025	5,302	-12.0%
Tylosin	1,173	1,031	-12.1%

4.2.5. Slope

The slope of the agricultural field has a major influence on the pollution level of antibiotics. This is displayed in Table 12. For example, if a slope is increased from 1% to 5%, the total GWF of tylosin increases nearly twenty times. This very large increase is caused by the larger runoff and erosion that transports more antibiotics directly into surface water after rainfall. If the slope is increased to larger numbers, GWF levels become unrealistically stable.

Table 12: The annual GWF for a slope of 1% and 5%. The results for a slope of 10% are unrealistically large and are therefore not shown.

Antibiotic	GWF (in m^3)		
	1% slope (reference case)	5% slope	Change (%)
Chlortetracycline	6,025	111,802	+>100%
Tylosin	1,173	21,798	+>100%

4.2.6. Conclusion sensitivity analysis

In the paragraphs above an overview has been presented of the sensitivity of the model. Within this analysis it was clear that the degradation parameter k plays an important role in determining the total load. Lowering the parameter with a factor 2 gives a GWF increase of 2%. Varying sorption parameters causes no changes within the results. Differences in soil type are also very sensitive for changes. This is caused by the differences in degradation rates and the erosion likeliness of these soils. The moment of application can also have a significant role in the total GWF. Applying antibiotics a few days after a rainfall instead of the day beforehand gives a decrease of 12%. The most sensitive parameter is the slope of the field. If a slope is steeper, erosion and runoff values become increasingly higher and GWFs very large. An overview of all the effects are given in Figure 6.

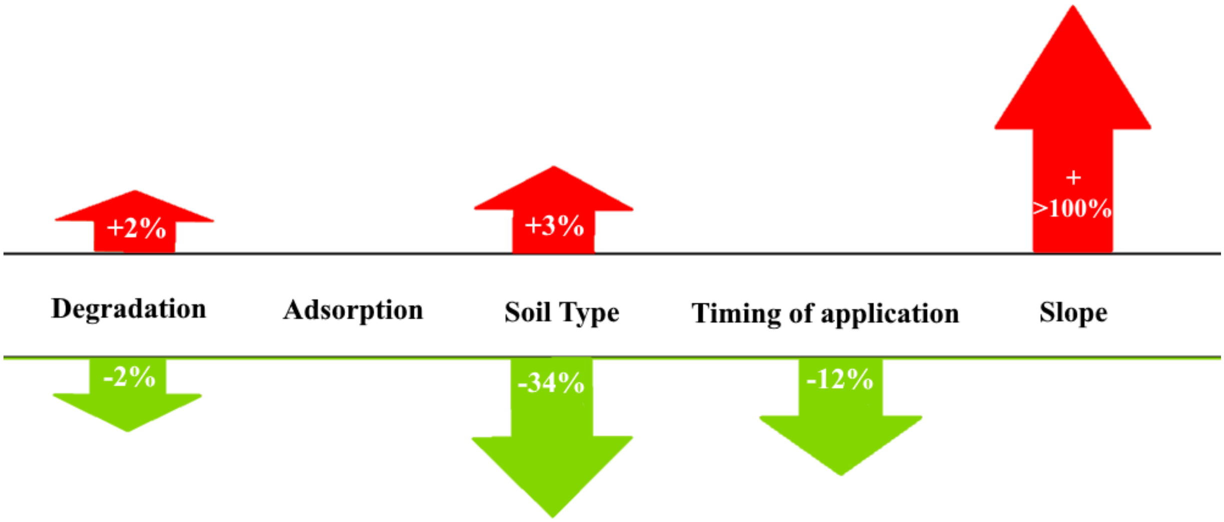


Figure 6: Reduction or increase levels within the sensitivity analysis. Here the maximum levels for chlortetracycline are shown. Red arrows explain an increase in GWF. Green arrows display a decrease in GWF.

4.3. The Vecht catchment area

The sensitivity analysis above has explained the influence of different parameters on the pollution by antibiotics. This has given a few insights on different circumstances which are important when manure is applied. With specific reduction measures, the pollution of antibiotics can be reduced even more. In this section the effectivity of these measures are compared with help of a case study of the Vecht catchment. An overview of the area is given in Figure 7.

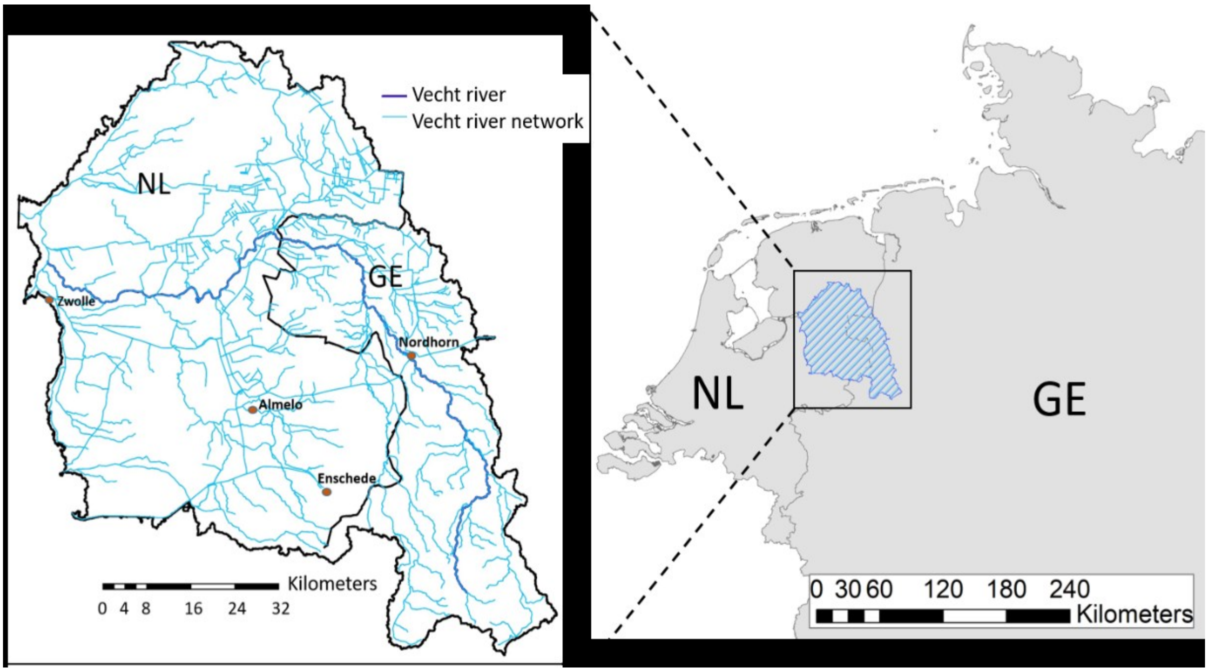


Figure 7: The Vecht catchment area in the Netherlands and Germany (Wöhler et al. 2020).

The Vecht river is 167 km long and contains an area of 6000 km^2 (Verdonschot & Verdonschot, 2017). The average discharge of the river is between 45 and 83 $m^3\ s^{-1}$ (Wojciechowska et al. 2002), which is between 1.4 and 2.6 billion $m^3\ year^{-1}$. Within the catchment, large areas are used for farming: 3600

km^2 (Copernicus, 2019). The area has relatively high activity of animal farming: per hectare there is at least 1.6 animal unit. The main animal farming types are cows, pigs and chicken (CBS, 2019b; Statistisches Bundesamt, 2020). For example in 2016, 97% of the livestock population in both the Netherlands and Germany was based on these animal types (Eurostat, 2020). On top of that, 99% of the veterinary antibiotics in the Netherlands were given to cow, pig or chicken populations in 2018 (Geijlswijk et al., 2019). This case study focuses therefore on these type of animals and antibiotic use by other animal species is neglected. The data used is displayed in

. The major soil type in the area is sand. Although other types are present, it is assumed that the whole area has a sandy soil (Brouwer 2006). On top of that, it is assumed that the input of antibiotics per animal type are the same for both Germany and the Netherlands. This is based on the researches of Geijlswijk et al. (2019) and Wallmann et al. (2018).

Table 13:Data on animals within the Vecht catchment area in the year 2018.

Region	Data on animals and surface				
	Cows	Pigs	Chicken	Total	Source
Germany	304,000	2,115,000	14,325,000	16,744,000	Statistisches Bundesamt (2020)
The Netherlands	923,000	2,130,000	19,210,000	22,263,000	CBS (2019)
Total Vecht area (in hectare)	1,225,000	4,240,000	33,530,000	38,995,000	Statistisches Bundesamt (2020)
Average bodyweight Animal type (in kg)	550	200	2	-	CBS (2019b)
Total bodyweight in Vecht area (in kg)	674,000,000	848,000,000	67,000,000	1,589,000,000	
% of total bodyweight in area	43%	53%	4%	100%	

Within the Vecht catchment, the Dutch part has the larger animal population, with 5 million more chicken and 600,000 more cows than Germany. Its assumed that the administration rate of both countries is the same, which would mean that the Dutch catchment part has a larger potential to cause pollution of antibiotics. The largest group of animals in numbers are chicken, followed by pigs and cows. Since the applied dose depends on the bodyweight of an animal (Geijlswijk et al., 2019), it is better to look at the total bodyweight of animal types in the region. From this perspective chicken are the smallest population, while pigs are the largest. With help of this data and the total input of antibiotics, the total GWF is calculated and presented in Table 14.

Table 14: The total annual GWF of chlortetracycline and tylosin in the Vecht catchment area.

Chlortetracycline	Annual GWF data per animal type			
	Cow	Pig	Chicken	Total
Total GWF per animal type (in m^3)	20,360	10,360	7,470	38,190
Total GWF per unit of weight (in $m^3\ kg^{-1}$)	$3.0 * 10^{-6}$	$1.2 * 10^{-6}$	$1.1 * 10^{-5}$	-
Percentage of total GWF	53%	27%	20%	-
Tylosin	**GWF data per animal type**			
	Cow	Pig	Chicken	Total
Total GWF per animal type (in m^3)	3,750	1,090	950	5,790
Total GWF per unit of weight (in $m^3\ kg^{-1}$)	$5.6 * 10^{-7}$	$1.3 * 10^{-7}$	$1.4 * 10^{-6}$	-
Percentage of total GWF	65%	19%	16%	

The total annual GWF of production tylosin, the substance with the highest application rate in the reference case, was estimated with 5790 m^3 for the Vecht area if no measures are applied. The load of chlortetracycline is half the load of tylosin, but causes a GWF more than 6 times larger. Within the Vecht, these GWFs are a really small fraction compared to the average discharge of the Vecht of 1.4 to 2.6 billion m^3 annually (Wojciechowska et al. 2002). The PNEC value is therefore not nearly reached by the concentration of the two antibiotics within the river.

The largest GWF of chlortetracycline and tylosin within the Vecht catchment area is caused by the output of cow manure. Chicken manure causes the smallest GWF. The difference is caused by the total animal weight present in the area. There is a larger bulk of cow weight within the Vecht area, compared to chicken. Although the total GWF of chicken manure is lower, it has the largest GWF per kilogram bodyweight for both tylosin and chlortetracycline. This means that the manure of chicken contains the largest concentration of antibiotics. Since the administration rate per kg bodyweight for chicken for most antibiotics is the highest of the three types (Geijlswijk et al., 2019), this is a logical consequence. Pig manure is the least polluting fertilizer and most attractive for fertilization. Because of the differences in quantities of animals between the countries in the region, there are differences in GWF between the regions as well. These are presented in Figure 8.

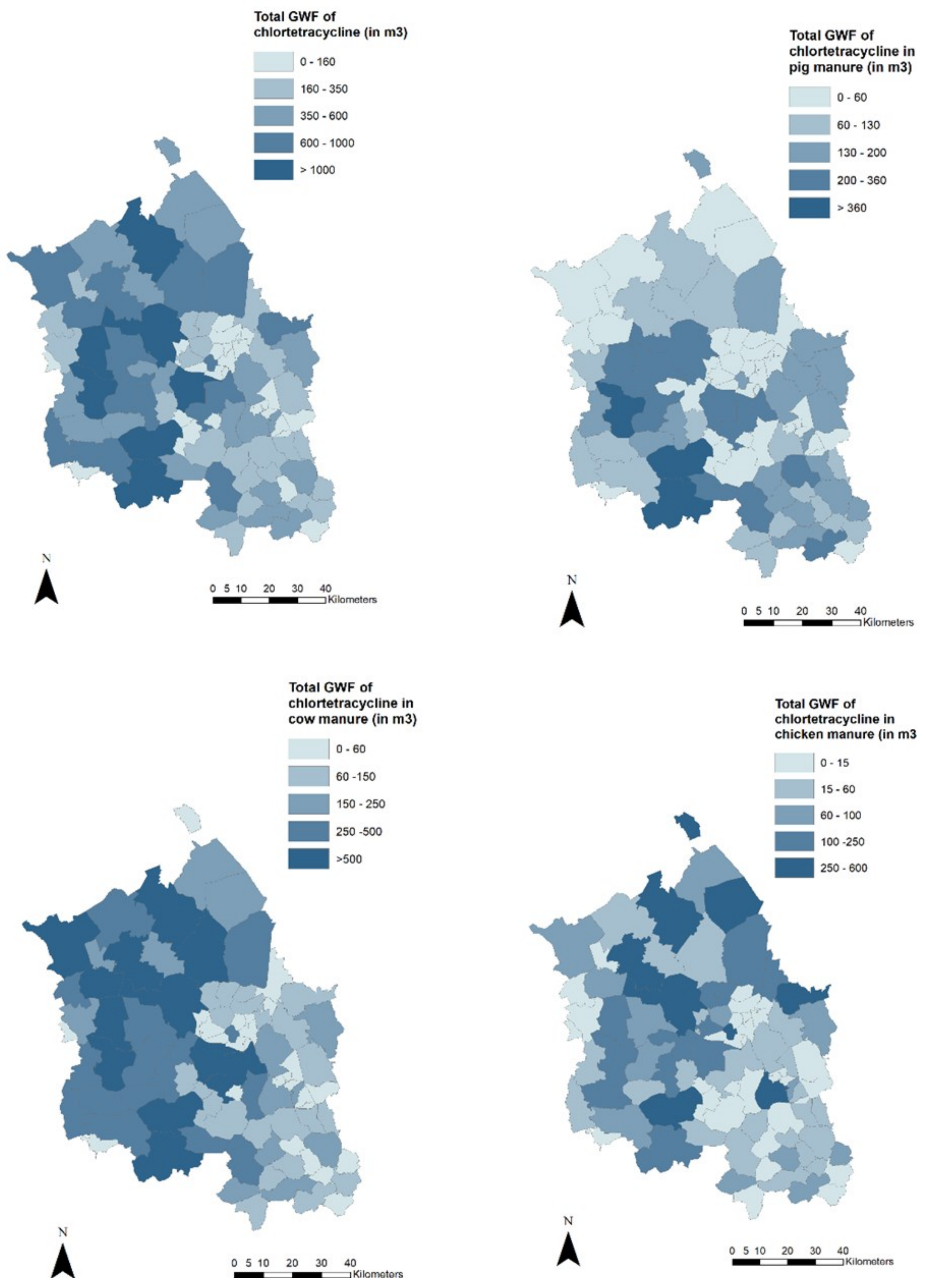


Figure 8: The total annual GWF of the Vecht catchment per municipality in total (top left), for chicken (top right), for cows (bottom left) and pigs (bottom right)

The largest GWFs are caused by the agricultural activity in the Netherlands. This is caused by the larger quantities of cows within the Dutch part. causes a clear division in total GWF between the Dutch and the German part: in the Netherlands a larger pollution is the issue. The GWF of pigs is mostly caused in the southern part of the region, where large farms of this animal type are located (CBS, 2019b). Chicken cause pollution in different municipalities in both countries.

4.4. Effectivity of measures

Several measures are tested in their effectivity in reducing the pollution of antibiotics. This is done in context of the Vecht catchment.

4.4.1. Input Reduction

Reducing environmental inputs of veterinary antibiotics has two main benefits: it reduces the pollution of antibiotics within surface water, but also prevents antibiotics from entering the soil matrix. Both risk in soil and water are reduced. The easiest method for this would be to reduce the total administration to the animal herd. If only animals are treated when they are ill, the administration can be reduced to nearly 1% of the current one. Because the model gives an approximately linear result, this reduces the annual GWF as well until 1%. A smaller reduction to 20% of the herd also causes that the GWF is reduced to 20%. The effects are displayed in Figure 9.

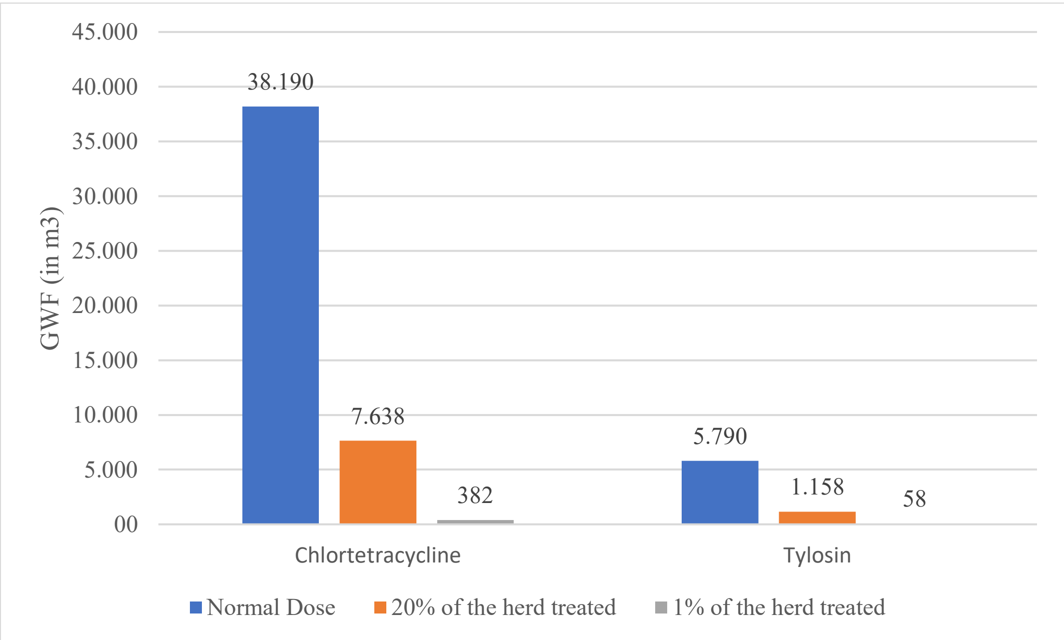


Figure 9: Effect of the input reduction on the total GWF within the Vecht catchment.

Treating manure before application to the field is also possible. There are two other methods for reducing the input of antibiotics on the field. Anaerobic digestion reduces the amount of tylosin for nearly 100% and chlortetracycline for 98%. Therefore, for specific antibiotics, the method of anaerobic digestion is very efficient. Composting is the second treatment method. The reduction caused by in-vessel composting is shown in

Table 15.

Table 15: The annual GWF of chlortetracycline and tylosin for normal application and reduction of input by composting.

Chlortetracycline	Total GWF (in m^3)		
	Normal Application	Composting	Change(%)
Cows	20,360	2,700	87%
Pig	10,360	670	94%
Chicken	7,470	30	100%
Total	38,190	3,400	91%
Tylosin	Total GWF (in m^3)		
	Normal Application	Composting	Change (%)
Cows	3,750	1,000	73%
Pig	1,090	120	89%
Chicken	950	20	98%
Total	5,790	1,100	80%

Composting can be effective to reduce input of antibiotics by treating manure before application. There is a difference in effectivity though between antibiotics. For example, the composting of chlortetracycline has a higher effectiveness (91%) compared to tylosin (80%). Next to that, if a larger amount of manure is present, composting becomes less efficient. This can be seen in the difference in effectivity between chicken and cow GWFs. The composting method needs to process a larger amount of antibiotics in cow manure than in chicken manure, which causes a relative difference of 13% between the two for the composting of chlortetracycline.

4.4.2. Method of application

Besides reducing the input, it is also possible to reduce the GWF by mitigating the effects of antibiotics. Injection or mixing of manure with or into the soil is one of those methods. The effectivity of injection is displayed in Table 16.

Table 16: The total annual GWF with and without the injection of manure.

Antibiotic	Total GWF (in m^3)		
	Normal Application	Injection	Change (%)
Chlortetracycline	38,190	1,200	97%
Tylosin	5,790	200	97%

The injection of manure has a major effect on reducing the GWF. Because manure, contaminated with antibiotics, is deposited deeper within the soil, less antibiotics are transported through erosion and runoff. This gives a decrease of 97% in GWF. The smaller fraction that pollutes surface water is a positive effect, but injection also increases the fraction of antibiotics that accumulate within the soil. This load increases by around 6000 mg in the Vechte area, which is an increase of 17% compared to normal application.

4.4.3. VBF

The second mitigative measure is the implementation of VBFs between the field and surface water. In Table 17 the effectivity of this measures is displayed.

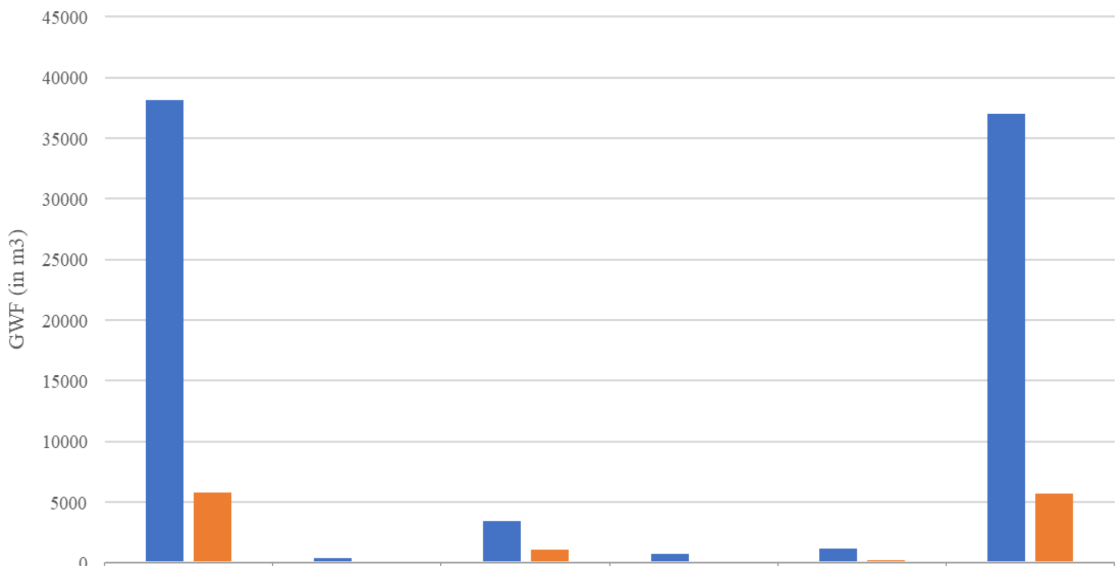
Table 17: The total annual GWF with and without the implementation of VBFs

Antibiotic	Total GWF (in m^3)		
	Normal Application	VBF	Change (%)
Chlortetracycline	38,190	37,000	-2%
Tylosin	5,790	5,700	-2%

VBFs reduce the runoff and erosion of soil, but reduces the GWF only for a small fraction. The major reason for this is that it is modelled for a slope of 1%, which means that not a lot of erosion or runoff takes place. On steeper slopes VBFs are more effective. The GWF of tylosin for example is reduced by 12% on a slope of 5%. Because more runoff and erosion occur on these slopes, the VBFs can be used better to their potential. Within the Vecht area, which consists majorly of a flat surface, VBFs are not an efficient measure.

4.4.4. Conclusions

In this section the effectivity of several measures have been presented for the Vecht catchment. Within this case, several results can be pointed out: 1) chicken manure is the most polluting fertilizer, because it has the largest GWF per unit of bodyweight. Therefore, it is more attractive to use pig manure for fertilization of soil. 2) reducing input by composting, anaerobic digestion or less intensive farming is the most beneficial measure. Next to assuring a reduction in pollution of surface water, accumulation of antibiotics within the soil is prevented as well. 3) Injection of manure reduces the GWF by decreasing the erosion and runoff load. A negative side effect is the larger fraction that accumulates within the soil. 4) VBFs can be an efficient measure on steeper slopes. The Vecht catchment is fairly flat, which causes that VBFs are an measure without significant effect in this area. A complete overview of the effectiveness of measures is given in Figure 10.



	Normal Application	Input Reduction	Composting	Anaerobic Digestion	Application Method	VBF
Chlortetracycline	38190	382 (-99%)	3400 (-91%)	764 (-98%)	1200 (-97%)	37000 (-3%)
Tylosin	5790	58 (-99%)	1100 (-81%)	6 (-99%)	200 (-97%)	5700 (-2%)

Figure 10: The annual GWF of chlortetracycline and tylosin for different situations within the Vecht catchment area.

4.5. Feasibility of measures

Beside the effectivity of the measures, the implementation of the different measures is not evenly straightforward. Based on costs, space, time, the quality of the measure and other side effects, measures become more or less attractive. The assessment of these factors is shown in Table 18 and explained below.

Table 18: The feasibility of the different measures. ++ = Very feasible; + = feasible; +/- = average feasibility; - = unfeasible; -- = Very unfeasible.

	Input Reduction	Composting	Anaerobic Digestion	VBFs	Application method
Costs	+/-	+	--	+	+/-
Space	+/-	-	-	-	++
Timeframe	+	-	-	++	+/-
Robustness	++	++	+/-	-	+
Positive Side Effects	-	-	++	+	+

The reduction of input has proven to be an effective measure, since it directly reduces the input into soil and freshwater. It is as well a robust measure, since the pollution is reduced without having the antibiotics within the soil matrix. This does not mean that other issues are at stake. Farmers potentially need to change their method of farming to reduce chances of illness within the animal herd, instead of using antibiotics (Kahn et al., 2019). Strategies that can be implemented are improved hygiene, larger sheds for animals and increased levels of monitoring (Tullo et al. 2019). Since there are no positive side effects that increase the motivation for farmers, governments should increase their efforts by subsidies or legislation (Kahn et al., 2019).

For the different composting methods, it is essential to have sufficient space for depositing manure. Windrows and aerated static piles can be put outside, which makes them easy to implement (Ezzariai et al., 2018a). In-vessel composting is executed within a silo which takes a lot of space (Dolliver et al. 2008). Costs for in-vessel composting are therefore high as well. Windrows and aerated static piles do not need this, which means that costs are negligible (Cessna et al., 2011). While VBFs and manure incorporation work directly, composting takes time to be effective. This is because it takes time to let antibiotics degrade within the manure (Spielmeyer, 2018; Wohde et al., 2016). Although the method is slow, composting is a reliable measure: the reduction of antibiotics is a certainty and often very thorough (Aga et al., 2016).

Anaerobic digestion comes with the important issue that it is not yet sufficiently researched how reliable the method is in reducing antibiotics in manure (Spielmeyer et al. 2014). This is also because it actually has two main goals with a different focus: the production of biogas and nutrient-rich digestate (Sara et al., 2013). The possible depletion of antibiotics is the positive side-effect for this matter. The implementation of an anaerobic digester is cost- and space-intensive. A digester for common farm practice costs around 1.2 million dollars (E3A4U 2019). For Dutch farms, with an average yearly revenue of 340,000 euro it is a large investment (CBS, 2019a).

For changing the application method from broadcasting to mixing or injection, specific equipment is necessary. A farmer practicing conventional farming, therefore needs to invest, which gives extra costs. Applying the manure within the soil also takes more time (Joy et al., 2013). This gives an increasing level of costs and loss of time. In terms of space for farming, there is no loss at all, which makes the measure attractive for farmers. While manure incorporation lessens the GWF of antibiotic substances, it also reduces the emission of nitrates and phosphates and odor (Atiyeh et al., 2015). Plus, it places nutrients closer to the crop, which boosts their ability to grow (Rasmussen, 2002). Due to the fact that large machines execute the injection a few times per year (RVO 2019; Tansakul et al. 2007), the measure is robust.

A VBF is a relatively easy measure to implement on a farm. A simple vegetation strip of grass or weed is not an expensive matter, so costs are low (Qi & Altinakar, 2011). Due to the fact that after implementation the VBF stays in place and works directly (Krutz et al., 2005), it is not a time-intensive intervention. Plus, it reduces the pollution caused by nitrates, phosphates and herbicides (Lin et al. 2011). Negative points of VBFs are that the field loses effective surface for farming practice and that maintaining is necessary to keep their functioning effective (Qi & Altinakar, 2011).

4.6. Monitoring and policy changes

To motivate different stakeholders to reduce the freshwater pollution, regulative measures in farming practice should be implemented as well. As stated by Speksnijder et al. (2015), regulative measures are of essence to divert farming practice from antibiotics. Here three potential regulative measures are presented.

The first method is decreasing the lack of knowledge by improving monitoring and data collection of antibiotic use. For example, the research of Menz et al. (2019) states that antibiotics are potentially more harmful to the environment than the regulations of the European Union prescribe, because they do not dare to give a conclusive answer on this due to incomplete data knowledge. Although there has been an improvement in the monitoring of use of antibiotic in some countries in Europe and the United States, there are still large steps to be taken in data collection (O'Neill, 2015). If these steps are taken, a more conclusive view can be created on the levels of antibiotics in the environment. Next to an improvement of the monitoring of use of antibiotics, it is of essence that more research becomes available on the behavior of antibiotics in soil and water, the excretion rates from animal manure and how antibiotics end up in water resources.

With help of this increased monitoring, legislation on the use of antibiotics would get more backup (O'Neill, 2015). There are some examples of legislation that help to reduce the antibiotic use. In the Netherlands, farmers are obliged to develop treatment and health plans for their animals. This plan is created with help of their personal veterinarian, who also monitors the total antibiotic use of the farm. A farmer is solely allowed to treat when an animal in the herd gets ill (FAO, 2018). On top of that, a farmer is obliged to improve the quality of life standards of the animals, so that chances of illness become low (European Commission, 2015). The implementation of these measures have caused in the Netherlands a significant reduction of 56% in antibiotic use between 2007 and 2012 (Speksnijder et al. 2015).

Momentarily, this legislation is not implemented in every region of the world. Therefore Van Boeckel et al. (2017) have proposed different scenarios that could reduce the amount of antibiotic use all over the world, by reducing the input or by reducing the meat consumption: 1) In Europe the total consumption of antibiotic does not exceed 50 mg per kg animal per year (Van Boeckel et al. 2017). If this maximum cap is applied over the whole world, the antibiotic use would reduce with 64%. 2) Decreasing the meat consumption to a maximum of 40 gram per person per day would reduce the global consumption of antibiotics by 66%. Since this target is a not very realistic one (meat consumption in the USA is on average 260 grams per person per day (OECD, 2020), the European target of 235 grams (Van Boeckel et al. 2017) per day is a more realistic one. This would give a global reduction of 22%. 3) Imposing a fee for antibiotic users of 50% of the price, so that antibiotic use is reduced and other measures become more attractive. On top of that, this would give extra revenues that could be used to implement those measures. This would give a reduction of around 30% in antibiotic use. A negative effect of this measure could be the increase in prices for the farms and therefore the increase of prices of meat. However, this would also imply a reduction in popularity of meat under the population (Van Boeckel et al. 2017).

These measures are not easy to implement, because they need to fit in the legislation of different countries. However, the prospect of such legislations makes that they are attractive to solve the risks of antibiotic use in agriculture. Together with the mitigating measures explained in this thesis, they are essential to reduce the total use of antibiotics all over the world significantly.

5. Discussion

In chapter 4, the total GWF and loads of veterinary antibiotics through different pathways have been revealed with help of the VANTOM model. This has been applied to the Vecht catchment case, to see how patterns of antibiotic pollution evolve within a real life case. Next to that, the effectivity of different measures has been evaluated. This section discusses the results and the choices made during the research. This is done by analyzing the functioning of the model and the assumptions made for the different parameters. Next to that, the results are set into context by comparing with literature, illustrating the scientific addition of this study to the field.

5.1. Evaluation of the model

The combination of modelling with VANTOM and WEPP as the main input for erosion and runoff is a suitable method to compare the different pathways of antibiotics. With help of the input of parameters it gives an assessment on how antibiotics are transported through erosion and runoff, are accumulated within the soil, or leach to the groundwater (Bailey, 2015). On the other hand, because the drivers of VANTOM are solely the erosion and runoff values from WEPP, it is an unspecific assessment. For example, if the slope of an agricultural field is close to zero and erosion and runoff is negligible, VANTOM does not explain any transportation. This means that the amount of leaching cannot be assessed, while this value is potentially larger if no erosion and runoff takes place (Spielmeyer et al. 2017). On top of that, leaching can be accelerated by holes and cracks within the soil. Residues of pesticides are known to be transported through these cracks and consequentially increase their concentration in groundwater (Scorza & Boesten, 2005). The same can happen with antibiotics (Kay et al. 2005), which means that the drainage system of the soil is of importance within the modelling. VANTOM neglects drainage, while it is a fundamental addition for determining the load caused by leaching. Therefore, it is possible that results found for leached loads in this study are underestimated.

Degradation of antibiotics within VANTOM is assumed to be homogeneous within the whole volume of soil. However, degradation depends on temperature and bioactivity within the soil, which both potentially decrease with depth in the soil. Spielmeyer et al. (2017) have found for example the leaching of antibiotics four years after application. A low amount of data is available on the behavior of antibiotics within the deeper parts of the soil (Bailey et al., 2016). It would therefore also be possible that injecting antibiotics can be negative due to a lower level of photodegradation. No research has been done on this subject, so a clear opinion on this is impossible yet. The development of rest products from the degradation of antibiotics have not been researched. They can also form a danger within freshwater (Wohde et al., 2016), which means a more thorough research is necessary.

Next to degradation, antibiotics can sorb as well to soil particles. Residues of antibiotics can attach to soil, which change their potential to be transported through erosion, runoff and leaching. It depends on the characteristics of the soil and antibiotics how well they attract each other (Conde-Cid et al., 2019; Gao & Pedersen, 2005; Spielmeyer et al., 2015). However, the sensitivity analysis revealed that changing the sorption parameter within VANTOM barely influences the GWF of antibiotics. For example, the GWF of chlortetracycline does not change if the sorption parameter K_d is increased by 10%. This change is negligible. Relating this with the literature mentioned above, means that the results should be interpreted with care. Further analysis of the model has found that sorption definitely plays a role within VANTOM, which could not be implemented within this research due to restricted time issues. With help of a preliminary sensitivity analysis could be revealed that GWF levels are possibly significantly higher. Further development of the model is therefore necessary for finding better substantiated results.

The applied manure in VANTOM is assumed to be homogeneously mixed with soil in the field. This means that it does not matter where manure is applied, the load of antibiotics is equally distributed on top of the surface. Since manure in real life is applied evenly spread over the field as well (RVO, 2019), this is a realistic assumption. However, it is not possible to assess whether a buffer between the applied antibiotics and surface water can help to reduce the erosion and runoff load. A potential solution is to divide the field in different cells, wherein some cells receive more manure containing antibiotics than others. This would create the possibility to assess clearly on the direction of antibiotic transportation.

Agricultural fields are covered with plants or crops a the major part of the year (Pikkemaat et al., 2016). These plants take up nutrients from the soil. During this process, the residues of antibiotics are collected as well. Due to uptake, the concentration of antibiotics is reduced within soil (Azanu et al., 2016; Du & Liu, 2012; Li et al., 2019). VANTOM falls short in determining the influence of uptake, because it is neglected within the model. The VBF measure can therefore potentially be more efficient, if not only the reduction of runoff is taken into account. For example, Sauvêtre & Schröder (2015) found that the reed *Phragmatis Australis* can remove 90% of the pharmaceutical carbamazepine after nine days. Also, other antibiotics can be collected in large quantities by these type of plants and by grass. The research of Liu et al. (2019), which found that at least 90% of oxytetracycline had been found in a wetland construction with reed. Hijosa-Valsero et al. (2011) point out a reduction of 39% of doxycycline within the sludge of wastewater, in which *Phragmatis Australis.* Chu et al. 2010 found that oxytetracycline particles sorb well to grass and agroforestry buffers, especially when clay is the main soil type. To understand the effect of plants on the load of antibiotics within soil and freshwater, VANTOM is not suitable.

5.2. Assumptions and limitations of study

The PNEC value was used as a maximum concentration within the GWF equation. This value causes large differences in GWFs between antibiotics. For example, the load of tetracycline within the reference case is 200 mg larger than chlortetracycline, while the GWF of chlortetracycline is approximately 4300 m^3 higher than tetracycline. This gives a good method to compare different antibiotics, because they have different levels of ecotoxicity. The downfall of PNEC values is that they can differ between regions, since they are determined with help of assessment factors and the NOEC. The NOEC is based on tests with different organisms, while the assessment factor is determined by researchers themselves (European Chemicals Bureau, 2003). Often there is a lack of data on how antibiotics or other pollutants develop within nature (Amiard & Amiard-Triquet, 2015). This can potentially cause that assessment factors are determined with large uncertainties can differ between regions (Janssen et al., 2004). This results in two possible risks for PNEC values: uncertainty on whether the value is correct or is too strict value caused by too large assessment factors. Since the PNEC values in this thesis are from a one research (Bergmann et al. 2011), this downfall is partly bypassed. However, because the collected values are based on different input data and circumstances, there are still a lot of uncertainties.

The administration of antibiotics to animals is assumed to be the same as well as the total sold antibiotics in the Netherlands and Germany (Veldman & Mevius, 2018). Since antibiotics in the Netherlands can only be bought with help of a specific treatment plan for farming (Speksnijder et al., 2015), it is admissible to assume that the sold antibiotics are used for treatment. Since the total use of specific antibiotics can differ between regions, the results become uncertain. A more detailed dataset of the total used antibiotics distinguishing between appliance to different animal types is therefore necessary.

Antibiotics have different behavior per compound, but also react differently after administration to the animal. Caused by the processes within the body of an animal, the concentration of antibiotics within manure is decreased. This depends on the specie, the antibiotic type, but also on the circumstances such as healthiness of the animal and temperature (Haller et al., 2002). Since there is not sufficient data available on the excretion of antibiotics by animals, the human excretion rates have been used. The data from this research would become more reliable if animal excretion rates are available.

Two important parameters that co-determine the fate of antibiotics have been simplified as static: pH and temperature. These parameters can play an important role within processes such as adsorption and degradation. A higher temperature within the soil for example can increase the degradation of an antibiotic (Pan & Chu, 2016). Sorption and degradation vary as well if pH changes (Franco et al., 2009). This results into variations of their parameters, k and K_d. Within this research the choice has been made to choose fixed values for k and K_d to make data suitable for comparison. However, the results are therefore circumstantial and can change if other levels of pH or temperatures occur (Sassman et al. 2007).

One of the assets of the measure of anaerobic digestion is that it produces biogas which potentially can be used for commercial purposes (Pan & Chu, 2016). During the process of anaerobic digestion several rest or transformation products can be produced (Spielmeyer, 2018). It is not clear for what level these isotopes are a threat for the environment as well. On top of that, the production of gas is often reported reduced by the addition of antibiotics within the manure (Álvarez et al., 2010).

A final issue of this research is the limited time frame that has been used. First, the period of analysis that has been used is solely one year. Since veterinary antibiotics have been used for decades (Kirchhelle, 2018) and antibiotic residues have been found in age-dated groundwater (Kivits et al., 2018), it is of interest to check the development of antibiotics in soil and freshwater over longer periods of times. In this way can be found what the total pollution is on a specific location, caused over a longer period. Degradation and leaching processes get in this way also more time, which can give a better understanding of their influence. Secondly, the total manure application is executed in just two separate days. It is more realistic that manure is spread in several days, since it depends on when crops need fertilization (Li et al., 2019).

5.3. Results in context

The total annual GWF estimated within the Vecht catchment is only a small fraction of the average discharge of the river. This means that the concentration of antibiotic within the Vecht does not reach PNEC levels and pollution levels are expected to be on the safe side. Large amounts of antibiotics degrade within the pathways, however still a remarkable 4 to 8% can accumulate with the soil. On the long term this can have three consequences: damage to vital organisms with soil, the leaching of antibiotics into surface water and the increase of resistance by bacteria (Jechalke et al., 2014). Measures such as VBFs and injection reduce the direct GWF by decreasing the chance of transport through erosion and runoff but increase the accumulation. The chances of damage on the longterm is therefore increased. Measures that focus on reducing the total input of antibiotics prevent that antibiotics enter either freshwater or the soil matrix are therefore more beneficial. Composting and anaerobic digestion are therefore more useful measures.

Composting is a method that has a large effectivity for reduction. This effectiveness differs per antibiotic type, but is overall high: between 70% and 99%. Although the results are in line with other researches, it is difficult to compare them. Dolliver et al. (2008) for example found a 99% decrease of chlortetracycline within 23 days caused by composting of swine manure. For tylosin they found a 74% reduction. Other literature also name reduction efficiencies in this order of magnitude (Ezzariai et al. 2018a; Mitchell et al. 2015; Youngquist, Mitchell & Cogger 2016). The comparison with these results should be taken with care, because these researches use input data collected in different circumstances.

Anaerobic digestion can potentially reduce the concentration of antibiotics while it produces biogas at the same time (Spielmeyer, 2018). Chlortetracycline is reduced by 98% while tylosin is completely diminished. However, it is unclear whether the measure works for every type of antibiotic and how toxic transformation products of antibiotics can be for the environment that still persist in the manure. (Schoumans et al., 2010; Yin et al., 2016). More research is needed whether and for which antibiotics anaerobic digestion is useful.

The injection of antibiotics has also been tested by Joy et al. (2014), who found that injection and mixing manure into soil can reduce the runoff and erosion load of antibiotics by 95% for chlortetracycline. For tylosin this is less, but still causes a reduction of 55-75%. These numbers are closely related to the values found in this study.

VBFs reduce the load by a just a fraction of 2%, caused by the fact that they are less effective on shallow slopes. On steeper slopes, reduction levels can be larger, because then strips have more potential to reduce the runoff and erosion. The total reduction by uptake has not been incorporated within this analysis, while it would actually be very effective when erosion and runoff do not play a crucial role. For example, a strip of *P. Australis* can collect 90% of antibiotics within the soil by uptake (Carvalho et al., 2012), which would make the VBF measure more beneficial.

The average GWF of the most polluting antibiotic chlortetracycline within the Vecht case is estimated 38,190 m^3 per year. When specified on cows, the total annual GWF of oxytetracycline is 0.0056 $L\ kg^{-1}$ for the catchment area. Wöhler et al. (2020) found a much larger level for the most polluting antibiotic and per kg meat of cows. Amoxicillin causes a GWF of 93 billion m^3 per year. This is 3000 times larger than the GWFs determined with help of VANTOM. The GWF of beef meat and amoxicillin in Germany is estimated 654 $m^3\ kg^{-1}$year in the research of Wöhler et al. (2020). This more than a million times larger than the GWF levels found with help of VANTOM. A logical explanation of for the difference in results are the method of determining the total load applied in freshwater. Wöhler et al. (2020) assume a worst case scenario, which means that the complete application load of antibiotics finds its way to fresh water. This research uses VANTOM to divide the applied load into different pathways and adds the processes of degradation and adsorption. This does not mean that the worst-case scenario approach is wrong. Since antibiotics can persist within deeper soil layers due to low degradation rates and long term leaching over several years can take place (Spielmeyer et al. 2017). It therefore is also possible that VANTOM underestimates the GWFs. Due to a low amount of data, it is unclear whether this is really the case.

6. Conclusion and recommendations

The goal of this research is to improve the understanding of the different pathways of antibiotics after administration to animals and the effectivity of measures to decrease their pollution. To reach this goal, several questions have been stated in section 1.1, which are answered within this chapter. To finalize this thesis, several recommendation for further research are stated at the end.

6.1. Conclusion

What are the pathways and processes that determine how much veterinary antibiotics end up in soil and surface water entities?

Antibiotics are applied on the field through manure. Through input of rainfall or irrigation, the antibiotics are transported into different directions. One the one hand, if the slope and amount of rainfall are sufficiently high, antibiotics can be transported through runoff and erosion. On the other hand, if slope and rainfall levels are too low, than antibiotics are not transported. Three processes are influential: 1) antibiotics accumulate and persist within the soil; 2) antibiotics degrade and are diminished; 3) antibiotics are transported to groundwater through leaching. The major part of antibiotics are degraded within the soil, although the accumulated fraction is still significant. The pathway that is most important for the pollution of freshwater is through erosion. The loads of runoff and leaching are close to zero and therefore negligible.

The influence of model input parameters on results differs largely. The degradation which depends on the soil type determines for the major part whether an antibiotic persists or not. The effect of sorption is negligible. If manure is applied after a rainfall event instead of before, the pollution of antibiotics is reduced to a minimum. The slope has as well a large influence. The GWF is 18 times larger if the slope of the field is changed from 1% to 5%.

How effective are different potential measures to reduce the pollution of veterinary antibiotics?

Reducing the input is the most effective method. Next to a reduction of pollution in freshwater, accumulation within the soil is prevented as well. Reduction of input can be done in three ways: 1) by applying a treatment plan, in which solely ill animals are treated. 2) composting means that manure is deposited in a specific way, so that antibiotics gets time to degrade 3) anaerobic digestion means that manure is treated within a digestion tank. These measures are all very effective in reducing the GWF, although the effectivity can differ between different types of antibiotic. VBF and incorporation of manure within soil by mixing or injection are mitigating measures. VBF are an ineffective measures to reduce runoff and erosion on a soil with a low gradient. Different plants can however help to reduce concentrations through uptake which improves the effectivity of VBFs. Injection or mixing is a very effective measure to reduce antibiotic pollution through erosion and runoff. The disadvantage of this measure is the increase of the accumulated fraction of antibiotics.

What is the feasibility of the different measures for reducing the GWF of veterinary antibiotics?

Reducing the input is a very robust measure to have a smaller GWF. Although it is necessary to adapt the farming method, it is the most effective way to reduce the pollution of freshwater and to reduce the chances of antimicrobial resistance. Composting is already a conventional method to reduce the amount of pollutants within manure. Although it uses space and time, it is estimated to be easily implementable within the current methods of farming. The application of anaerobic digestion is more complicated: the construction of a silo is necessary, which is an expensive matter. The high costs can however be compensated with help of the production of biogas. The incorporation of manure within soil needs more specific material for spreading than broadcasting. On top of that, it is more time-intensive. However, it has many advantages: no extra space is necessary, odor is reduced and the emission of nitrate and phosphate decreases. VBFs are an easy implemented measure with a low amount of costs. Negative points are the loss of effective farmland and the necessity of maintenance.

What is the total pollution caused by veterinary antibiotics within the Vecht catchment area?

Within the Vecht area large farms with cows, chicken and pigs are located. The most polluting antibiotic chlortetracycline causes an annual GWF of 38,190 m^3. Compared to the annual discharge of the Vecht, approximately 6 billion m^3 per year, this is a very small fraction. The PNEC value of chlortetracycline is therefore not nearly reached. In the Dutch part of the Vecht catchment, the total GWF is larger, due to the higher quantity of cows within this area. The GWF caused by chicken is centered in the German part, while pigs are spread all over the country. Due to the fact that the inflow of veterinary antibiotics is not hindered, there is still a constant inflow of these antibiotics. With help of measures before application or by mitigation on the field, these inflows can be reduced.

6.2. Recommendations

Based on the conclusions described above, several recommendations for further research can be made. The main issue of this subject of research are the many unknowns caused by a lack of data. More data needs to be collected on the mobility of antibiotics within soil and water. On top of that, within this research it is assumed that the total sold antibiotics within a country is used to treat animals. To get better results, data on administration of administration should be made more public. If those data gaps are filled, then the pollution caused by veterinary antibiotics can be quantified more precisely.

VANTOM is a tentative model with the goal find the pollutive pathways of veterinary antibiotics. Although it gives important insights of these pathways, it has some important issues within this research that need to be solved, so that the model can be developed further. These issues are the non-influence of sorption changes, the large input and output files that need to be made more automatic and assumption that no vertical water flows exist. If these steps are taken, than the VANTOM model could become a useful tool for researchers.

The legislation on the maximum allowed concentration of antibiotics within freshwater needs more research. The PNEC value varies a lot, because of its contextual nature and there is no maximum allowed concentration determined by governments such as the European Union. Therefore, it is necessary to do more research in the toxicity of different types of antibiotics in freshwater. In this way the maximum allowed concentration of antibiotics can be determined. With help of these maxima, rules can be more strict and measures mandatory to reduce pollution of antibiotics in a structured way.

While European governments increase their efforts to decrease the total antibiotic use, this is not always the case for other countries. Since growing economies such as India and China will increase their meat production, their use of antibiotics will increase significantly as well. The risk of the growth of antimicrobial resistance will therefore be increasingly high from a global perspective. Therefore it is of essence to have a global approach through possibly a partnership, that will stop the growth of antibiotic use over the whole world.

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Appendix A: Input Parameters

Table 19: The degradation rate of antibiotics within clay.

Antibiotic	Group	Abbreviation	Degradation k $(days^{-1})$	Source
Tetracycline	Tetracyclines	TC	0.012	Pan and Chu (2016)
Oxytetracycline	Tetracyclines	OTC	0.038	Boxall et al. (2006)
Doxycycline	Tetracyclines	DC	0.0000147	Cycoń et al. (2019)
Chlortetracycline	Tetracyclines	CTC	0.025	Cycoń et al. (2019)
Sulfamethazine	Sulfonamides	SMZ	0.014	Pan and Chu (2016)
Sulfadiazine	Sulfonamides	SDZ	0.0026	Engelhardt et al. (2015)
Amoxicillin	Penicillines	AMX	0.035	Braschi et al. (2013)
Tylosin	Macrolides	TYL	0.175	Cycoń et al. (2019)

Table 20: The degradation rate of antibiotics within loamy sand

Antibiotic	Group	Abbreviation	Degradation k $(days^{-1})$	Source
Tetracycline	Tetracyclines	TC	0.000018166	Cycoń et al. (2019)
Oxytetracycline	Tetracyclines	OTC	0.032	Cycoń et al. (2019)
Doxycycline	Tetracyclines	DC	0.0000147	Cycoń et al. (2019)
Chlortetracycline	Tetracyclines	CTC	0.0006	Cycoń et al. (2019)
Sulfamethazine	Sulfonamides	SMZ	0.097	Bailey (2015)
Sulfadiazine	Sulfonamides	SDZ	0.0508	Yang et al. (2009)
Amoxicillin	Penicillines	AMX	0.175	Braschi et al. (2013)
Tylosin	Macrolides	TYL	0.013	Cycoń et al. (2019)

Table 21: The degradation rate of antibiotics within sand.

Antibiotic	Group	Abbreviation	Degradation k $(days^{-1})$	Source
Tetracycline	Tetracyclines	TC	0.07	Bailey (2016)
Oxytetracycline	Tetracyclines	OTC	0.043	Boxall et al. (2006)
Doxycycline	Tetracyclines	DC	0.0104	Szatmári et al (2012)
Chlortetracycline	Tetracyclines	CTC	0.04	Thiele-Bruhn et al. (2004)
Sulfamethazine	Sulfonamides	SMZ	0.08	Bailey (2016)
Sulfadiazine	Sulfonamides	SDZ	0.0179	Shen et al. (2018)
Amoxicillin	Penicillines	AMX	0.035	Braschi et al. (2013)
Tylosin	Macrolides	TYL	0.0071	Cycoń et al. (2019)

Table 22: The sorption coefficient of antibiotics in clay.

Antibiotic	Group	Abbreviation	Adsorption rate K_d (L/kg)	Source
Tetracycline	Tetracyclines	TC	1290	Bailey (2016)
Oxytetracycline	Tetracyclines	OTC	2694	Bailey (2016)
Doxycycline	Tetracyclines	DC	1329	Teixidó et al. (2012)
Chlortetracycline	Tetracyclines	CTC	423	Sassman and Lee (2005)
Sulfamethazine	Sulfonamides	SMZ	0.6	Tolls (2001)
Sulfadiazine	Sulfonamides	SDZ	4.1	Sukul and Spiteller (2006)
Amoxicillin	Penicillines	AMX	-	-
Tylosin	Macrolides	TYL	5520	Sassman and Lee (2005)

Table 23: The sorption coefficient of antibiotics in loamy sand

Antibiotic	Group	Abbreviation	Adsorption rate K_d (L/kg)	Source
Tetracycline	Tetracyclines	TC	680	Tolls (2001)
Oxytetracycline	Tetracyclines	OTC	420	Wang & Wang (2015)
Doxycycline	Tetracyclines	DC	3.09	Teixido et al (2012)
Chlortetracycline	Tetracyclines	CTC	3102	Sassman & Lee (2005)
Sulfamethazine	Sulfonamides	SMZ	2.1	Tolls (2001)
Sulfadiazine	Sulfonamides	SDZ	1.5	Sukul et al. (2008)
Amoxicillin	Penicillines	AMX	10.9	YoungKeun Kim
Tylosin	Macrolides	TYL	128	Halling & Sorensen

Table 24: The sorption coefficient of antibiotics in sand.

Antibiotic	Group	Abbreviation	Adsorption rate K_d (L/kg)	Source
Tetracycline	Tetracyclines	TC	174	Bailey (2015)
Oxytetracycline	Tetracyclines	OTC	417	Bailey (2015)
Doxycycline	Tetracyclines	DC	6.05	Teixido et al. (2012)
Chlortetracycline	Tetracyclines	CTC	22	Sassman & Lee (2005)
Sulfamethazine	Sulfonamides	SMZ	1.3	Bailey (2015)
Sulfadiazine	Sulfonamides	SDZ	2.4	Sukul et al. (2008)
Amoxicillin	Penicillines	AMX	-	-
Tylosin	Macrolides	TYL	20	Halling-Sørensen et al. (2005)

Table 25: The PNEC values of the different antibiotics.

Antibiotic	Group	Abbreviation	PNEC $(\mu g/L)$	Source
Tetracycline	Tetracyclines	TC	0.251	Bergmann et al. (2011)
Oxytetracycline	Tetracyclines	OTC	1.1	Bergmann et al. (2011)
Doxycycline	Tetracyclines	DC	0.054	Bergmann et al. (2011)
Chlortetracycline	Tetracyclines	CTC	0.03	Bergmann et al. (2011)
Sulfamethazine	Sulfonamides	SMZ	1	Bergmann et al. (2011)
Sulfadiazine	Sulfonamides	SDZ	1.35	Bergmann et al. (2011)
Amoxicillin	Penicillines	AMX	0.0156	Bergmann et al. (2011)
Tylosin	Macrolides	TYL	0.34	Bergmann et al. (2011)

Table 26: Human excretion rates of the different antibiotics

Antibiotic	Group	Abbreviation	Excretion rate (%)	Source
Tetracycline	Tetracyclines	TC	85%	Hirsch et al. (1999)
Oxytetracycline	Tetracyclines	OTC	81%	Hirsch et al. (1999)
Doxycycline	Tetracyclines	DC	40%	Moffat et al. (2011)
Chlortetracycline	Tetracyclines	CTC	40%	Moffat et al. (2011)
Sulfamethazine	Sulfonamides	SMZ	8%	Moffat et al. (2011)
Sulfadiazine	Sulfonamides	SDZ	50%	Moffat et al. (2011)
Amoxicillin	Penicillines	AMX	60%	Moffat et al. (2011)
Tylosin	Macrolides	TYL	60%	Moffat et al. (2011)

Table 27: The degradation coefficients for different composting methods.

Antibiotic compound	Reference treatment	Windrows	Aerated static piles	In-vessel systems	Source
Tetracycline	0.012	0.0066	-	0.154	Ezzariai et al. (2018)
Oxytetracycline	0.0080	0.665	0.727	0.868	Dolliver et al. (2008)
Doxycycline	0.0054	~0	~0	~0	Ezzariai et al. (2018)
Chlortetracycline		0.00798	-	0.63	Ezzariai et al. (2018)
Sulfamethazine	0.069	0.32	-	0.34	Ezzariai et al. (2018)
Sulfadiazine		0.0086	-	0.016	Ezzariai et al. (2018)
Amoxicillin	0.139	-	-	-	
Tylosin		0.029	0.042	0.037	Dolliver et al. (2008)

Appendix B: Mathematical steps VANTOM

In this research the fate of antibiotics is modelled with help of VANTOM, a timestep based model developed by Bailey (2015). In this appendix, an explanation is given in on the functioning of the model.

VANTOM models six different processes after the application of manure to the soil: the application of fertilizer contaminated by antibiotics to the field itself, the sorption and degradation of antibiotics, runoff, erosion of the soil, transportation of antibiotics due to erosion and runoff and the accumulation of antibiotics within the soil itself.

Processes

The development of antibiotics is explained over time with help of different steps: $i = 1,2,3 \dots i_{max}$. The first time step or the initialization is at step $t = t_{i-1}$ and the step ends at $t = t_i[s]$. The duration of the timestep is Δt_i $[s]$. Space is explained in one large cell, in which antibiotics, soil and manure masses enter or leave. A fertilizer event becomes input at the start of a certain timestep. The total mass of fertilizer and the total mass of antibiotic contained in the fertilizer is user defined.

The behavior of antibiotics after application is based on degradation and sorption parameters. Sorption is assumed to be static and given based on the linear sorption equation and a corresponding K_d value. Degradation is continuous and given based on an exponential first-order decay equation. Metabolites, that potentially could of the antibiotic into consideration.

VANTOM model makes a calculation of a budget between the masses of antibiotics in solid state $a_{solid|i}$ and in liquid state $a_{liquid|i}$ at the end of each time step. This is based on the initial value of the time step, given as $a_{solid|i-1}$ and $a_{liquid|i-1}$ and the events that increase or decrease those values. For fertilizer events and sorption, this is an addition: $a_{solid,fertilizer|i}$ and $a_{liquid,fertilizer|i}$. For degradation, $a_{soliddegraded|i}$ and $a_{liquiddegraded|i}$,runoff, $a_{soliderosion|i}$ and $a_{liquidrunoff|i}$, this is a subtraction. The equations are given below and all values are in kg.

$a_{solid|i} = a_{solid|i-1} + a_{solid,fertilizer|i} - a_{solid\text{degraded}\ |i} - a_{soliderosion|i}$ (Eq. 7)

$a_{liquid|i} = a_{liquid|i-1} + a_{liquid,fertilizer|i} - a_{liquiddegraded\ |i} - a_{liquidrunoff|i}$ (Eq. 8)

The total masses of antibiotics in the soil depend on the total mass of soil at the end of each time step. These are given in both solid ($M_{solid|i}$) and liquid form ($M_{liquid|i}$). Mass is added due to a fertilizer event and subtracted due to a runoff event, which is explained in equations 9 and 10. All masses are in kg.

$M_{solid|i} = M_{solid|i-1} + M_{solidfertilizer|i} - M_{soliderosion|i}$ (Eq. 9)

$M_{liquid} = M_{liquid} + M_{liquidfertilizer|i} - M_{liquidrunoff|i}$ (Eq. 10)

Depth concept

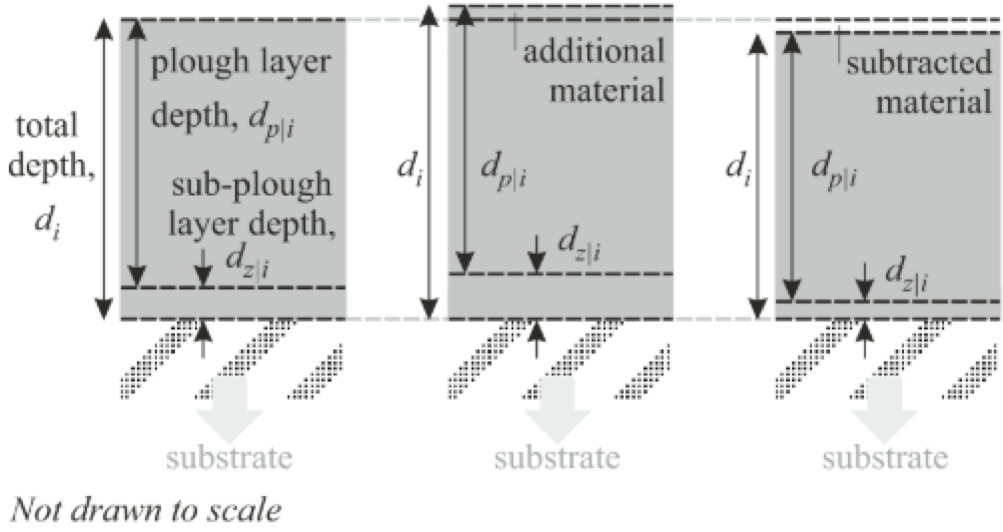

Figure 11: Schematization of the plough layer concept (Bailey, 2015)

The VANTOM model makes use of two different layers to address the pathways of antibiotics. The upper layer is the plough layer, measured in its total depth: d_p. This is defined as the area where fertilizer and antibiotics are homogenously mixed across the whole cell area during a fertilizer event. This plough layer depth stays constant over time, but is not fixed at a specific height. For this method is chosen, so that the plough layer can be prone to runoff and soil erosion and the addition of fertilizer. Every single event can differ this specific height, which is displayed in Figure 11.

To address the fluctuations in height of the plough layer d_p, a buffer zone is added called the sub-plough layer d_z. This layer is added to account for the material, antibiotics and soil, that is pushed downwards due to the addition of material. Within d_z antibiotics are homogeneously mixed. When a timestep is finalized, the total amount of antibiotics and in both layers are added in one term for both the liquid part and the solid part. The equations for these paths are explained in the following sections.

The division between the plough and sub-plough layer is not a realistic schematization of reality. The plough layer concept is introduced so that only antibiotics that are added on top of the field can be transported due to runoff. The part that ends up in the schematized sub-plough layer, is collected within the soil and cannot be transported due to erosion and runoff. This assures that a division exists between parts of antibiotics that can be transported and the part that can accumulate during the timesteps.

Initialization

The masses of soil and antibiotic within the plough and sub-plough layer need to be determined at the start of every time step. At time step $i = 1$ the initial masses are determined. The initial antibiotic solid and liquid masses are defined by the user ($a_{ploughliquid|0}$ and $a_{ploughsolid|0}[kg]$). The liquid and solid masses of the soil are based on the depth of the plough layer ($d_p[m]$) and the sub-plough layer (d_z) the initial soil water content $\phi_o [m^3\ m^{-3}]$, the soil porosity $P\ (-)$, the soil solid density $\rho_s\ [kg\ m^{-3}]$ and the soil liquid water density $\rho_l\ [kg\ m^{-3}]$.

$M_{ploughsolid|0} = d_{ploughlayer} * A * (1 - P) * \rho_s$ (Eq. 11)

$M_{ploughliquid|0} = d_{ploughlayer} * A * P * \phi_0 * \rho_l$ (Eq. 12)

$M_{subploughsolid|0} = d_{subploughlayer|0} * A * (1 - P) * \rho_s$ (Eq. 13)

$M_{subploughliquid|0} = d_{subploughlayer|0} * A * P * \phi_0 * \rho_l$ (Eq. 14)

Where $M_{ploughsolid|0}$ is the initial solid mass of the plough layer, $M_{ploughliquid|0}$ is the initial liquid mass of the plough layer, $M_{subploughsolid|0}$ is the initial solid mass of the sub-plough layer and $M_{subploughliquid|0}$ is the initial liquid mass of the sub-plough layer. These values are all in kg.

Input of events

A fertilizer event takes place at the start of a time step which adds an amount of fertilizer determined by the user $M_{fertilizer|i}$. This contains a defined mass of antibiotic ($a_{fertilizer|i}$). The fertilizer solid and liquid mass are calculated with help of the fertilizer liquid content $\phi_{fertilizer|i}$, which is as well defined by the user. The loads of antibiotics are also divided through this equation.

$M_{solidfertilizer|i} = M_{fertilizer|i} * (1 - \phi_{fertilizer|i})$ (Eq. 15)

$M_{liquidfertilizer|i} = M_{fertilizer|i} * \phi_{fertilizer|i}$ (Eq. 16)

By adding the depth of fertilizer ($d_{f|i}$), which explains how deep the fertilizer is placed, the plough layer can be changed in height and can make changes to the sub-plough layer ($d_{z,|i}$). This is explained with help of equations 17 and 18.

$d_{f|i} = \frac{1}{A} * \left(\frac{M_{solidfertilizer|i}}{\rho_s} + \frac{M_{liquidfertilizer|i}}{\rho_l}\right)$ (Eq. 17)

$d_{z,i} = d_{z,i-1} + d_{f|i}$ (Eq. 18)

In these equations A is the surface (in m^2), ρ_s is the density of the soil ($kg\ m^{-3}$), ρ_l is the density of water ($kg\ m^{-3}$). These values can be used to create factor $x_{fertilizer|i}$, which is the relationship between the depth of fertilizer during an event and the depth of the plough layer.

$x_{fertilizer|i} = \frac{d_{fertilizer|i}}{d_{ploughlayer|i}}$ (Eq. 19)

With help of this factor, $M_{ploughsolid|i}$ and $M_{ploughliquid|i}$can be calculated, which are the masses of solid soil and liquid soil in the plough layer.

$M_{ploughsolid|i} = M_{ploughsolid|i-1} * \left(1 - x_{fertilizer|i}\right) + M_{solidfertilizer|i}$ (Eq. 20)

$M_{ploughliquid|i} = M_{ploughliquid|i-1} * (1 - x_{fertilizer|i}) + M_{liquidfertilizer|i}$ (Eq. 21)

Together with determining the masses of the soil, the new mass of antibiotic in the plough layer ($a_{ploughsolid|i}[kg]$ and $a_{ploughliquid|i}$ $[kg]$) should also be determined. A large amount of the fertilizer which is in liquid form, sorbs to the soil solid mass of the plough layer during the mixing process. This mass is called $a_{sorb|i}$ $[kg]$. This is explained in equations 22 and 23:

$a_{ploughsolid|i} = a_{ploughsolid|i-1} * (1 - x_{fertilizer|i}) + a_{solidfertilizer|i} + a_{sorb|i}$ (Eq. 22)

$a_{ploughliquid|i} = a_{ploughliquid|i-1} * (1 - x_{fertilizer|i}) + a_{liquidfertilizer|i} - a_{sorb|i}$ (Eq. 23)

The partitioning of antibiotics between the solid and liquid state is explained with help of the sorption coefficient, K_d $[kg\ kg^{-1}]$.

$\frac{a_{ploughsolid|i}}{M_{ploughsolid|i}} = K_d * \frac{a_{ploughliquid|i}}{M_{ploughliquid|i}}$ (Eq. 24)

The masses of the antibiotic and the soil for both the liquid and solid state within the sub-plough layer are also determined with help of the factor $x_{fertilizer|i}$, as explained with help of equations 25-28:

$M_{subploughsolid|i} = M_{subploughsolid|i-1} + x_{fertilizer|i} * M_{ploughsolid|i-1}$ (Eq. 25)

$M_{subploughliquid|i} = M_{subploughliquid|i-1} + x_{fertilizer|i} * M_{ploughliquid|i-1}$ (Eq. 26)

$a_{subploughsolid|i} = a_{subploughsolid|i-1} + x_{fertilizer|i} * a_{ploughsolid|i-1}$ (Eq. 27)

$a_{subploughliquid|i} = a_{subploughliquid|i-1} + x_{fertilizer|i} * a_{ploughliquid|i-1}$ (Eq. 28)

Based on equations 25-28 the effects of a fertilizer event have been accounted for. The next step is to incorporate degradation within the model.

Degradation

Degradation is a factor that constantly takes place between a fertilizer event and a runoff event. Within this timestep, the mass of soil solid and liquid stays constant. Based on the exponential first-order decay formula, the masses of the antibiotic that stay in the plough layer, $a_{ploughsoliddegraded|\mathrm{i}}$ and $a_{\mathrm{ploughliquiddegraded|i}}$ or in the sub-plough layer, $a_{subploughsoliddegraded|\mathrm{i}}$ and $a_{subploughliquiddegrade|\mathrm{i}}$, can be determined. The degradation factor k $(days)$.

$a_{ploughsoliddegraded|\mathrm{i}} = a_{ploughsolid} * e^{-k_s * \Delta t_i}$ (Eq. 29)

$a_{ploughliquiddegraded} = a_{ploughliquid} * e^{-k_l * \Delta t_i}$ (Eq. 30)

$a_{subploughsoliddegraded} = a_{subploughsolid} * e^{-k_s * \Delta t_i}$ (Eq. 31)

$a_{subploughliquiddegraded} = a_{subploughliquid} * e^{-k_l * \Delta t_i}$ (Eq. 32)

This gives the solution for the influence of degradation within the soil. After these events have taken place, the antibiotics can potentially be transported due to irrigation or rainfall as explained in the next paragraph.

Transportation

Transportation of antibiotics within soil is caused by the addition of water. The amount of water is defined as M_{runoff} $[kg]$ which causes that a mass of soil solid $M_{soliderosion|i}$ $[kg]$ and soil liquid $M_{liquidrunoff|i}$ $[kg]$ is transported to a neighboring cell or eventually a neighboring surface water entity. The total amount of M_{runoff} $[kg]$ is determined with the soil erosion and water runoff model, which is in this case WEPP (Flanagan et al. 2001). The antibiotics and soil particles are assumed to be transported from a fixed depth, which differs between soil and liquid states. $d_{erosion|i}$ $[m]$, which is the removal depth of soil solid depends on the transported soil solid mass $M_{solidrunoff|i}$ $[kg]$, the soil solid density $\rho_s[kg\ m^{-3}]$, and the cell surface area A $[m^2]$.

$d_{erosion|i} = \frac{M_{soliderosion|i}}{\rho_{s*A}}$ (Eq. 33)

For liquid masses VANTOM assumes that within the maximum depth, the whole mass is removed out of the cell. This depth is not the same as the removal depth for solid particles, because this would mean that liquid particles are only transported when soil erosion takes place. The removal depth $d_{l,r}$ is therefore determined based on the erosion model WEPP (Flanagan et al., 2001). VANTOM assumes that antibiotics within this depth are removed from the plough layer. This means that the equation becomes:

$M_{liquidrunoff|i} = \frac{d_{runoff|i}}{d_{p|i}} * M_{ploughliquid|i}$ (Eq. 34)

After that, the masses of the antibiotic that are removed due to soil erosion ($a_{soliderosioni}$ $[kg]$)and runoff ($a_{liquidrunoff|i}$ $[kg]$) can be determined based on these depths. This is explained with help of equations 35 and 36. Due to the assumed homogeneity in the soil layers, the use of depths is sufficient to determine the erosion and runoff of antibiotics.

$a_{soliderosion|i} = \frac{d_{erosion|i}}{d_{p|i}} * a_{ploughsoliddegraded|\mathrm{i}}$ (Eq. 35)

$a_{liquidrunoff|i} = \frac{d_{runoff|i}}{d_{p|i}} * a_{ploughliquiddegraded|\mathrm{i}}$ (Eq. 36)

The runoff causes a subtraction of the surface and therefore lowers the plough layer. In this way a final depth of the sub-plough layer is created $d_{z|i}$ $[m]$. With help of the factor $x_{r|i}$ the relationship between the removed solid soil depth $d_{erosion|i}$ and the sub-plough layer $d_{subplough|i}$ can be explained. This is displayed in equations 37 and 38.

$d_{subplough|i+1} = d_{z|i} - d_{erosion|i}$ (Eq. 37)

$x_{r|i} = \frac{d_{erosion|i}}{d_{z|i+1}}$ (Eq. 38)

For determining the final masses, this factor is used. This can be done for soil solid, $M_{ploughsolid|i}$ $[kg]$ and soil liquid $M_{ploughliquid|i}$ $[kg]$ and the antibiotic mass in solid state $a_{ploughsolid|i}$ $[kg]$ and in liquid state $a_{ploughliquid|i}$ $[kg]$ within the plough layer. On top of that, these masses can be determined within the sub-plough layer, so for: $M_{subploughsolid|i}$, $M_{subploughliquid|i}$, $a_{subploughsolid|i}$ and $a_{subploughliquid|i}$ $[kg]$. This is explained with help of equations 39-46.

$M_{ploughsolid|i+1} = M_{ploughsolid|i} - M_{soliderosion|i} + x_{r|i} * M_{subploughsolid|i}$ (Eq. 39)

$M_{ploughliquid|i+1} = M_{ploughliquid|i} - M_{liquidrunoff} + x_{r|i} * M_{subploughliquid|i}$ (Eq. 40)

$a_{ploughsolid|i+1} = a_{ploughsoliddegraded|i} - a_{soliderosion|i} + x_{r|i} * a_{subploughsoliddegraded|i}$ (Eq. 41)

$a_{leaching|i+1} = a_{ploughliquiddegraded|i} - a_{liquidrunoff|i} + x_{r|i} * a_{subploughliquiddegraded|i}$ (Eq. 42)

$M_{subploughsolid|i+1} = M_{subploughsolid|i} * (1 - x_{r|i})$ (Eq. 43)

$M_{subploughliquid|i+1} = M_{subploughliquid|i} * (1 - x_{r|i})$ (Eq. 44)

$a_{subploughliquid|i+1} = a_{subploughliquiddegraded|i} * (1 - x_{r|i})$ (Eq. 45)

$a_{subploughliquid|i+1} = a_{subploughliquiddegraded|i} * (1 - x_{r|i})$ (Eq. 46)

Based on these formulas the mass balances are complete. Fertilizer events, sorption, degradation and runoff events have been taken into account. The final step is to find the total concentration of antibiotic that flows into the surface water and the total concentration that stays within the soil.

Concentration

Based on the values found in the sections above, the concentrations of antibiotic in different compartments can be determined. The concentration of antibiotic in the fertilizer, namely $C_{fertilizer|i}$ $[kg\ kg^{-1}]$ is assessed based on the total mass of the fertilizer and the total mass of antibiotic within the fertilizer. In this way, the total input concentration can be determined. Other values that are of importance, are the concentration values that are transported to surface water systems, namely $C_{soliderosion|i}$ and $C_{liquidrunoff|i}$ $[kg\ kg^{-1}]$. The final concentration that can be determined is the concentration of antibiotics that accumulate within the plough layer, in solid and liquid state: $C_{ploughlayersolid|i}$ and $C_{ploughlayerliquid|i}$ $[kg\ kg^{-1}]$.

$C_{fertilizer|i} = \frac{a_{fertilizer|i}}{M_{fertilizer|i}}$ (Eq. 47)

$C_{soliderosion|i} = \frac{a_{soliderosion|i}}{M_{soliderosion|i}}$ (Eq. 48)

$C_{liquidrunoff|i} = \frac{a_{liquidrunoff|i}}{M_{liquidrunoff|i}}$ (Eq. 49)

$C_{solidsoil|i} = \frac{a_{ploughsolid|i}}{M_{ploughsolid|i}}$ (Eq. 50)

$C_{leaching|i} = \frac{a_{ploughliquid|i}}{M_{runoff|i}}$ (Eq. 51)

All the different parameters that can be assessed with help of VANTOM have been explained above. The most essential values for this research are on the one hand $a_{fertilizer|i}$, because it explains the total load of antibiotic on a certain field and on the other hand $a_{soliderosion|i}$, $a_{liquidrunoff|i}$ and $a_{ploughliquid}$, because together they explain the load of antibiotics from the farming field into the surface water system. With help of a maximum allowed concentration, c_{max}, the grey water footprint can then be assessed.