# The ethics of genome editing of animals

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# Abstract

In the Western culture nowadays, a large number of animals is used for food production and because of the growing world population, the demand for animal products is increasing even more. Since the planet has its environmental boundaries, it is important that these products are produced sustainably to minimize negative environmental impacts. Modern techniques, such as genome editing (i.e. a technology that is able to add, remove or alter DNA in a way that does not occur naturally), are suggested to be able to contribute to a sustainable production of animal products.

The application of genome editing could profoundly affect a large number of animals and its outcome could shape society. Ethical reflections on the application of genome editing are therefore important. In this thesis, there was focus on four important ethical theories (utilitarianism, duty ethics, care ethics and virtue ethics) and their place in the debate on genome editing of animals. Lastly, suggestions were made to improve the debate on genome editing of animals.

Firstly, utilitarianism judges an action based on its consequences. Actions are considered right when they provide the greatest good for the greatest amount of people and when they minimize suffering for all those involved. In order to determine whether genome editing of animals is justifiable, the benefits of genome editing of animals should be balanced against the entailed costs. Besides the direct costs of genome editing on animals (e.g. the consequences for successfully genome edited animals), also the indirect costs should be taken into account (e.g. the risk of animals with an unintended disorder or risk of miscarriages at a later stage of pregnancy). However, as observed in the literature review, few authors in the literature review actually made an assessment of the consequences, which could be due to some unknown risks of genome editing. Besides, utilitarian argumentation was observed to have the tendency to miss out on other valuable arguments by solely focusing on consequences.

Duty ethics, or the animal rights theory, is a non-consequentialist theory which manifests itself in the thought that an action can be right or wrong by itself. Individuals who are able to experience life (i.e. those who satisfy the subjects-of-a-life criterion) are thought to have value in themselves, also known as inherent value. All those who have inherent value (e.g. humans and some animals such as farm animals) have it equally, and they therefore all have the right to be respected and not to be harmed. As a consequence, raising and slaughtering animals for their meat is unjustifiable because it violates their rights and genome editing for those purposes is therefore not accepted. However, as observed in the literature review, this established position on just the use of animals leaves very limited room in the discussion, which could narrow the position of duty ethics in the debate. Furthermore, since wrong-doings being part of the act are condemned, rather than the outcomes of the act, it could be difficult to reject application of genome editing of animals based duty ethics (referred to as the non-identity problem).

In care ethics, the communication between human and animal takes a central place. Communication is formed by observation of the animal (e.g. observing facial expressions or vocalizations), which leaves room for human interpretation, feelings and sentiment, resulting in an attentive, responding and caring attitude towards animals. In order to determine whether genome editing is justifiable, it is important whether the intention corresponds with a caring attitude towards animals. In the literature review, care ethics was underrepresented which could be due to the diversity of opinions within care ethics.

According to virtue ethics, we should strive to develop character traits that a morally good person would have (i.e. virtues). A virtues person is able to do what is right because the intention of the person's action is right. This could also be applied to the concept of genome editing, where the intention of genome editing of animals should be taken into account in order to determine whether genome editing is justifiable or not. Furthermore, according to virtue ethics, the essence and purpose

of a creature (i.e. telos) should be respected and the opinions are divided whether genome editing goes against this principle. In the literature review, it was observed that virtue ethical arguments are not always clearly recognizable, which could be a limitation of virtue ethics in the genome editing debate.

In conclusion, a lack of interdisciplinary reasoning was observed in the genome editing debate, which could limit the debate. To stimulate understanding and improve the debate in the future, education could play a crucial role. Furthermore, similarities between ethical theories could be used as a starting point in the debate to boost mutual understanding.

# Content

# Introduction

Animals are an important part of our daily life, fulfilling various functions like serving as a source of food, companion, status symbol etc. The use of animals differs across people, times and cultures, partly due to different results of the reflections on the human-animal relationship. In the Western culture nowadays, a large number of animals is used for food production and because of the growing world population, the demand for animal products is increasing even more. Since the planet has its environmental boundaries (Rockström et al., 2009), it is important that these products are produced sustainably to minimize negative environmental impacts. Given its substantial contribution to global emissions, a major responsibility is assigned to animal agriculture (Steinfeld et al., 2006). One way of contributing to sustainability with regard to the industry, is the development of techniques like genome editing, that are suggested to have promising possibilities for an efficient production of animal products.

However, there are various ways in which one can contribute to sustainability (e.g. the moderate consumption of meat). Personally, I decided to become a vegetarian about a year ago and, as it turned out, this decision was one of the reasons for writing my thesis on the ethics of genome editing of animals, which I will explain in the following. I became a vegetarian for a number of reasons. Firstly, I could not identify with the way the meat industry seemed to look upon animals, only as products. To me, something as alive and breathing as farm animals deserved so much more than simply going down the line. Secondly, I hated the thought that animals had to suffer for something I could so easily live without. In that time, also several slaughterhouse scandals became public in the Netherlands, revealing abhorrent stories of pigs bleeding to death while hanging on hooks and others that found an unfortunate death in boiling hot water. Thirdly, I could not ignore the impact that our Western meat consumption (or overconsumption) had on the environment. During the time I studied Animal Sciences in Wageningen, I learned that there was room for everyone to consume a little bit of animal products. However, when I looked around in my family, I quickly realized that my piece of meat (and much more) was already eaten by others. Lastly, ever since I was a child, I felt a certain reluctance to eat meat. I could not get rid of the idea that it was weird to eat a corpse, especially if it was one of our own roosters in the soup. Over the years, I got more used to the idea of eating meat although a vague feeling of unease kept lingering in the back of my mind.

Shortly after my decision to became a vegetarian, I started to question my decision to only abstain from the consumption of meat. After all, were laying hens and dairy cows also not viewed as production units? Were dairy cows not slaughtered as soon as their milk production was considered to be insufficient? And was I not still responsible for suffering once a calf was being separated from its mother? Once these questions entered my brain, they were followed by a whole lot more questions. Especially since my whole education was connected to the human-animal relationship, I started questioning our current breeding practices and the motivation to participate in them. Although the ethics of breeding practices had been discussed in some previous courses I had taken, somehow it did not appeal to me, until I started to ask the questions myself. All these questions prompted me to write a thesis on the ethics of one of the advanced, emerging techniques applied to animals, genome editing.

In the following, a background on genome editing is provided, as well as a description of the genome editing technique and its possibilities. This introduction concludes with the presentation of the research questions.

Although the genetic modification of animals is a hot topic today, the first genetically modified animal, a mouse, existed already more than 45 years ago (Jaenisch et al., 1974). A few years later, a technique called pronuclear injection was established (Gordon et al., 1980), which resulted to be a commonly used method for the genetic modification of animals in the following decades (Isola et al., 1991; West et al., 2016). This technique developed in the early 1980s and allowed the incorporation

of foreign genetic material into a host genome by injection of genetic material into the pronuclei of fertilized eggs or cells (e.g. Brinster et al., 1981; Constantini et al., 1981; Gordon et al., 1981; Wagner et al., 1981a; Wagner et al. 1981b). However, the technique had a somewhat low accuracy and if successful, the inserted genes had a tendency to be silenced over generations, resulting in a limited use of the technique, especially in larger animals (West et al., 2016). Then, in 1996, a lot of media attention was directed to the sheep Dolly, the first cloned animal that was created using somatic cell nuclear transfer (SCNT; Wilmut et al., 1997). Using SCNT, the nucleus of a somatic cell was inserted in an enucleated egg and stimulated to divide and develop as an embryo. In contrast with pronuclear injection, it was possible to check for correct integration of the foreign genetic material before the embryo was carried to term, which increased efficiency, although other difficulties remained unsolved (Su et al., 2016; West et al., 2016). Nowadays, techniques are available that can precisely target specific areas of the genome. Clustered regularly interspaced short palindromic repeats (CRISPR/CAS9) is one example of such a technique, which was inspired by the way bacteria defended themselves against viruses (Doudna et al., 2014). Recently, in 2020, the discovery of the CRISPR technique was awarded the Nobel prize. CRISPR/CAS9 uses a guide sequence of RNA, which is linked to an endonuclease called Cas9. The complex searches the genome until a sequence is found that matches the RNA. The DNA is then cut very precisely by the protein and foreign genetic material can be introduced and used to repair the breaking site. Two other examples of genome editing techniques are zinc finger nucleases (ZFN) and transcription activator like effector nucleases (TALEN) that both work in a similar way using a non-specific type II restriction enzyme called FokI. A DNA binding domain pairs with Fok1, which functions as a DNA cleavage domain when it binds to a specific sequence. Just as with CRISPR/CAS9, the DNA can be repaired by the introduction of foreign genetic material (Carroll, 2011; Gaj et al., 2013; Kim et al., 1996; Nemudryi et al., 2014).

All these advanced techniques have made it possible to make changes in the genome of an animal that would not have been feasible using traditional selection. Some possibilities of these techniques are: the modification of the pig's genome that reduces the cross-species immune barrier which holds great promise for xenotransplantation (Fischer et al., 2016; Hruhorowicz et al., 2017; Niu et al., 2017; Yang et al., 2015), the use of animals as bioreactors who are able to produce products suitable for human use such as antibodies, proteins and enzymes (Ebert et al., 1991; Houdebine, 2009; Ko et al., 2000; Kuroiwa et al., 2002; Monzani et al., 2016; Van Berkel et al., 2002; Zhang et al., 2018), the increase of disease resistance among animals (Proudfoot et al., 2019; Whitworth et al., 2015; Yao et al., 2017) thereby also contributing to an increase of animal welfare (Carlson et al., 2016; Zheng et al., 2017), animal production with a lower environmental impact (Zhang et al., 2018) and the production of animals with enhanced productivity (Cyranoski, 2015; Tait-Burkhard et al., 2018; Zheng et al., 2017).

However, in the examples stated above, there is a clear distinction between the cases. Although the terms 'genome editing' and 'genome modification' or 'genome engineering' are used interchangeably, they are targeted towards different methods. Even though traditional breeding of animals is also contributing to the genetic modification of a genome, in the following, the definition of the European Food Safety Authority (EFSA) will be used. EFSA has genetic modification defined as follows: 'Genetic modification of an animal involves altering its genetic material by adding, changing or removing certain DNA sequences in a way that does not occur naturally' (EFSA, 2020). With genome editing, on the other hand, there is no incorporation of foreign genetic material into the genome, allowing the same modification to be indistinguishable from natural mutations (Liable, 2015). Although many genetically modified and genome edited animals are created for research purposes, currently no food products derived from genome edited farm animals are on the EU market (EFSA, 2020). Although EFSA stated that the modification of DNA in plants by genome editing techniques does not pose more hazards than conventional breeding or techniques (EFSA Panel on Genetically Modified Organisms, 2020), the same statement has not been made about animals. Some

non-EU countries deviate from the strict rules set within the EU. For example, the AquAdvantage salmon, a genetically modified fish bred for efficient and fast growth, was approved by the U.S. Food and Drug Administration in 2015 (FDA, 2020). Furthermore, the UK has recently launched a consultation on using genome editing in livestock which could lead to acceptance of animal products derived from genome edited animals (Marshall, 2021).

In the following, this master thesis focuses exclusively on genome editing. The genome editing technique can be applied to different type of cells (e.g. somatic cells), but only heritable changes are performed in germline cells or zygotes. For the genome editing of zygotes, an ovum pick-up (OPU) is performed on the female donor animals. For oocyte extraction, large farm animals like cattle, goats and sheep do not require surgical oocyte retrieval methods (Baker et al., 1978; Cox et al. 2007) and only experience mild discomfort during the procedure which is mostly due to the administration of anesthesia (Petyim et al., 2007). For the oocyte collection of smaller animals like mice, who are extensively used in laboratories, euthanasia was required in the past to remove the oviducts of the animal (Nagy et al., 2003), however another technique was developed, performing oocyte collection under anesthesia which allowed the animal to maintain its reproductive capacity (Byers et al., 2009). Usually after the collection, the oocytes are placed in a maturation medium before they are in vitro fertilized (e.g. Lei et al., 2016; Proudfoot et al., 2015). Once fertilized, the zygotes are ready to be edited using techniques like CRISPR/Cas9, ZFN or TALEN. Next, the embryos are in vitro cultivated until they reach the blastocyst stage, which is when the embryos are transplanted into recipient animals who have received hormone treatment to align their reproductive cycle to the desired stage (e.g. Proudfoot et al., 2015).

Although genome editing does not necessarily have to affect the early embryo development (Hai et al., 2014; Wang et al., 2015), the mortality rate of genome edited embryos is high (Tan et al., 2016). This could be due to wrong selection of the target site in the genome thereby affecting functional genes, off-target effects, the lower viability of in vitro cultivated embryos and the low pregnancy rates of surrogate mothers that are in general observed for embryo transplantations. In pigs, for example, twenty four edited zygotes are needed to deliver one edited offspring (Tan et al., 2016). Another concern regarding genome editing is mosaicism, which is the presence of more than two alleles within an individual, which might yield negative health consequences for the individual (Henning et al., 2020; Teboul et al., 2017).

Besides concerns posed by researchers about genome editing, there are also several ethical issues raised by the public. Some of these issues are concerning consequences for humans (e.g. the safety of consumption of products from genome edited animals or the quality of those products). Other concerns are focused towards the consequences for animal welfare or animal integrity. These latter questions are requiring a reflection on the human-animal relationship.

The aim of this thesis is to answer the following research question: 'What ethical aspects are inherent in genome editing of animals?'
This main question was divided in the following sub questions:

1. What are the main ethical theories regarding the ideal human-animal relationship and what practical consequences do they yield regarding genome editing?
2. What ethical views are proposed in the literature on genome editing of animals and on what arguments are they based?
3. What are the limitations of the main ethical theories in the debate on genome editing of animals and how can this debate be improved?

To answer the first sub question, four ethical theories (utilitarianism, duty ethics, care ethics and virtue ethics) are introduced and described. These ethical theories were chosen because they contribute greatly in the ethical debate regarding animals. The second research question is answered

by a review of recent scientific literature regarding the ethics of genome editing of animals. Lastly, the results of the second research question are discussed in the light of the results from the first research question and suggestions are put forward to improve the debate on genome editing of animals.

# Research question 1

## Utilitarianism

Although utilitarian ideas were around for centuries, it was not until the eighteenth century that utilitarianism became clearly identified as a distinct, philosophical school by Jeremy Bentham (1748-1832), who is considered to be one of the founders of modern utilitarianism (Mulgan, 2014). In utilitarianism, actions are considered right when they provide the greatest good for the greatest amount of people and when they minimize suffering for all those involved (Bentham & Mill, 2004). Since actions are judged based on their outcomes, utilitarianism is considered a consequentialist theory. However, it would still take around two centuries before the consequences of utilitarian principles applied to animals, were fully taken into account. In 1975, one of the contemporary utilitarian philosophers concerned with the human-animal relationship, Peter Singer, published his ideas in the book 'Animal Liberation' (Singer, 2002). This work was considered groundbreaking and formed the foundation of the modern animal rights movement (Munro, 2012). The foundation of Singer's ethics was the principle of equality, which was introduced in analogy to sexism and racism. Singer argued that sexism and racism are unjustifiable, but his claim was not based on the similarities between people because there are also indisputable differences between humans, such as mental capacities (e.g. intelligence or pain sensitivity) or physical differences (e.g. height or skin color). However, these differences were considered to be irrelevant from a justice perspective, and could therefore not be the reason for approving sexism or racism. He concluded that equality is a moral idea and stated the following (Singer, 2002, p. 5):

> The principle of the equality of human beings is not a description of an alleged actual equality among humans: it is a prescription of how we should treat human beings.

Following this principle, all equal interests should count equally regardless of race, sex or any other factual difference such as level of intelligence. The principle could therefore be extended to animals as well, provided that they had interests. A distinction could be made between basic interests (e.g. the desire to live or the avoidance of pain) and other interests (e.g. the desire to buy a new car). According to Singer, a prerequisite to have any interests at all, is the capacity to suffer. All beings who meet this condition are called sentient beings. Farm animals, for example, are regarded as sentient because they are able to feel pain, and are therefore able to suffer. Plants and stones, on the other hand, are not regarded as sentient since they lack the capacity to feel pain, and therefore suffer. Since all interests count equally, preferring the interests of someone of one's own species, over the interests of a being of a different species is essentially as morally unjustifiable as sexism or racism, and is referred to as speciesism. From this, it follows that it is as morally unjust to inflict pain of the same intensity and duration to an animal as it is to a human.

When it comes down to whether killing is ethically permitted, the case gets more complicated. Although Singer advocates for a vegetarian lifestyle, this is merely to avoid unnecessary suffering that is associated with intensive production systems and not so much because he objects against killing per se. He firstly argued that normal, adult human beings have mental capacities that exceed those of animals, such as anticipation, hopes and dreams for the future, meaningful relationships with others and so on. From this, he follows that if one has to choose between taking a human life or an animal life, one should prefer to save the human life (Singer, 2002). This choice is not based on speciesism but on the assumption that the suffering inflicted on a human exceeds that of an animal since the human would be deprived of his goals and plans for the future etc., unlike the animal that lacks these capacities. However, this way of reasoning does not justify killing, it only serves as a guideline when an unavoidable decision has to be made between the death of different lives. There are some animals (e.g. chimpanzees, gorillas and orangutans) that appear to be rational and self-conscious and conceive themselves as distinct beings with a past and a future. Some consider the case against killing these beings therefore as strong as the case against killing intellectually disabled

human beings because they consider the mental capacities of rational, self-conscious animals and mentally disabled humans to be comparable. Singer even initiated 'The Great Ape Project' in 1993, which advocates human rights for great apes, such as the right of life, protection of individual liberty and the prohibition of torture (Scharmann, 2000). However, when it comes to animals who are not rational or self-conscious, the case against killing might appear weaker. Painless killing of the latter animals results in taking away a pleasurable life (if that is the case) and this could be replaced by the life of an animal with an equal pleasurable life. This is expressed in the so-called *replaceability argument* which states that no wrong is done if an animal is painlessly killed and replaced by an animal living an equally pleasant life, assuming that the death of the animal does not inflict suffering on other animals (Singer, 2003). The replaceability statement rests on the assumption that an animal in itself does not have intrinsic value, but only its interests. Regan, a deontological philosopher, clarified and criticized this by the cup analogy, where what goes into the cup (e.g. pleasure and pain) has value, but what not has value is the cup (i.e. the individual itself, Regan, 2003).

### Critics

Soon after the publication of 'Animal Liberation' and in the years that followed, several objections were raised of which some are highlighted in this section. Mark Rowlands challenged Singer's notion of equal consideration of interests by claiming that no such thing is feasible. According to preference utilitarianism, the decision yielding the highest fulfilling of preferences should be chosen to aggregate the greatest good. However, such a decision might negatively affect some. Therefore, Rowlands argued, there is no such thing as equal consideration of interests because treatment of an individual depends on the effect of their treatment on others and not on their own interests (Rowlands, 2009).

Another critic of Singer's work is Tatjana Višak, who challenged the replaceability argument (Višak, 2013). Singer's replaceability argument states that no wrong is done if an animal is painlessly killed and replaced by an animal living an equally pleasant life. However, Višak argued that existence or non-existence as such cannot harm or benefit an individual. Killing an animal does deprive the animal of an enjoyable future, while bringing a new animal into existence cannot harm or benefit that first animal. Therefore, if a choice should be made between not killing an animal or killing an animal and replacing it with another animal, Višak argued that not killing the animal would be the right choice from an utilitarian perspective because the net benefits would be greatest.

### Implications and view on genome editing

One of the principles of utilitarianism, and a key message in Singer's book 'Animal Liberation', is the avoidance of suffering. This was expressed in Singer's call for vegetarianism, to reduce suffering inflicted on animals in intensive production systems. Although one could argue that human preferences are satisfied by the consumption of meat, the satisfaction of the palates is not considered a basic interest outweighing the suffering experienced by animals that are used for the production of meat in intensive production systems. According to utilitarianism, induction of pain is only justifiable if outweighed by a greater amount of suffering elsewhere (Smith, 2002).

Furthermore, research that inflicts suffering on animals but does not produce any significant or relevant results is regarded as unjustifiable (Singer, 2002, p. 25-94). From this follows that the expected gains of every experiment involving animals should be balanced against the inflicted suffering imposed to animals before the experiment is executed. Since the publication of 'Animal Liberation', the EU legislation covering the use of animals for scientific purposes has been updated with the aim to strengthen legislation, improve the welfare of the animals that still needed to be used and to anchor the principle of the three Rs, to replace, reduce and refine the use of animals (Parliament, 2010).

Although in a different guise, genome editing could be compared with traditional breeding, since they both cause deliberate sequence alteration (DSA), which is, in principle and generally, not considered wrong according to utilitarianism because the action in itself does not cause suffering or frustrate interests, as opposed to its consequences (Smith, 2002). To minimize suffering accompanied with the use of the genome editing technology in animals, either germ cell donors, surrogate mothers or resulting genome edited animals, should be provided with pleasant living conditions to minimize suffering. Next, there is a risk of failures of in vitro cultivation, the process of genome editing itself or transfer of embryos leading to losses of embryos. This is not objectionable according to utilitarianism, since embryos are not regarded sentient before the third trimester of pregnancy (recital 9, Chapter 1, Article 1, Paragraph 3, European Union, 2010). However, even after a successful embryo transfer that leads to the pregnancy of a surrogate mother, there could be an increased risk of miscarriage, which could be caused by off-target events or epigenetics (Urrego et al., 2014). Miscarriages in the last trimester should be taken into account because they are affecting sentient animals. The offspring of pregnancies that are carried to term are usually checked for desired genome edits and, depending on the project, unsuccessful genome edited animals might be killed as soon as they do not add any value to the project. Once desired genome edits are found in live offspring, it can have various consequences for the animal. A consequence could be a physiological change that does not inflict suffering on the animal or even enhance its welfare (e.g. the production of polled cattle, thereby avoiding pain induced by dehorning (Carlson et al., 2016), which is regarded as acceptable (Smith, 2002). However, there is still a risk of unintentional disorders as a consequences of genome editing due to off-target events or epigenetics (Urrego et al, 2014) and suffering of these animals should be taken into account as well. Besides that, some animals might be suffering as a consequence of genome editing (e.g. the creation of animals as models for human disease (e.g. Kou et al., 2015; Liu et al., 2014), where one should ask whether the end justifies the means. Or, in other words, whether the benefits (e.g. contribution to improvement of human health) outweigh the costs (suffering of the animals and the risks thereof (Savulescu & Singer, 2019; Smith, 2002).

To briefly summarize, the alteration of the genome by genome editing per se is not objectionable according to utilitarianism. Although the use of genome editing could entail killing of unsuccessfully genome edited animals, this does not necessarily pose a problem according to Singer's replaceability statement, as long as it is performed painlessly and the life of the animal is replaced by another equally pleasant life. However, the consequences for all genome edited animals and all the other animals involved in the project (e.g. risks of miscarriages in the third trimester, animals with unintentional disorders etc.) should be taken into account and should be proportionate to the expected benefits.

## Duty ethics

A prominent, 18$^{th}$ century philosopher who formulated an influential form of duty ethics was Immanuel Kant, although deontological ideas appeared to originate much earlier in, for example, ancient Tamil literature (Punitha & Kumaran, 2014). An important characteristic of Kant's theory is that he derived it from human reason, in contrast to religious, deontological ideas (Shakil, 2013). According to Kant, animals did not have moral status because they lacked reason, which led to an absence of direct duties towards animals. Deviating from Kant's ideas was another influential work published in 1985 by Tom Regan regarding the moral status and position of animals (Regan, 1985). Both Kant and Regan based their work on deontological ideas but their exact ideas differed (Regan, 1985, p. 174-185). However, a resemblance between the work of both philosophers, which is also a core idea of duty ethics, manifests itself in the thought that an action can be right or wrong by itself and cannot be judged by its consequences. Duty ethics can therefore be described as a non-consequentialist theory, in contrast to utilitarianism. In his book 'The case for animal rights', Regan

introduces his case by making a distinction between moral agents and moral patients, thereby deviating from Kant who did not made the distinction between moral agents and moral patients. According to Regan, moral patients lack, in contrast to moral agents, the capacities that enable them to control their own behavior in such a way that they cannot be held responsible for their actions. Moral patients can therefore not do what is right or wrong, although their actions might have favorable or unfavorable effects on others. The group of moral patients contains animals and also some humans (e.g. infants, small children, the mentally disabled of a certain degree). Moral agents can, in contrast to moral patients, be held responsible for their acts and can therefore do what is right or wrong. Moral agents are mostly healthy, adult human beings. A similarity between moral agents and some moral patients is that they are subjects-of-a-life, which is defined by Regan as follows (Regan, 1985, p. 243):

> Individuals are subjects-of-a-life if they have beliefs and desires; perception, memory, and a sense of the future, including their own future; an emotional life together with feelings of pleasure and pain; preference and welfare-interests; the ability to initiate action in pursuit of their desires and goals; a psychophysical identity for others; and an individual welfare in the sense that their experiential life fares well or ill for them, logically independently of their being the object of anyone else's interest.

Those who satisfy the subjects-of-a-life criterion are by Regan thought to have value in themselves, also known as inherent value. It is important to note that, according to Regan, inherent value is categorical, one can therefore not possess inherent value in different degrees but one either has it, or does not have it. Besides this, inherent value is also not comparable with, and independent from, intrinsic value i.e. the value of experiences. This can be clarified by going back to the cup analogy that was used earlier. In contrast to utilitarianism, what has value is the cup itself (i.e. the individual itself), and not the content of the cup (i.e. experiences like pleasure and pain). Furthermore, humans and most mammals are thought to have inherent value and therefore the same moral status. Since those who have inherent value have it equally, they all have the right to be respected (a.k.a. *the respect principle*). From this follows *the harm principle* as formulated by Regan, which states that all individuals with inherent value have the right not to be harmed since they all deserve equal respect. However, rights (e.g. the right not to be harmed) are not absolute, allowing some situations to override those rights, which is accounted for in the mini-ride principle and the worst-off principle. The former provides guidance in a situation where one needs to choose between harming a few individuals versus harming many individuals, assuming that each individual is equally harmed. According to Regan's *mini-ride principle*, one ought to choose to override the rights of the few instead of the rights of the many. However, this principle does not apply in a situation where the harms are unequally distributed, for example when the individual harms of the few are greater compared to the individual harms of the many. In this case, Regan's *worse-off principle* concludes that the rights of the many with fewer harm should be overridden in favor of the rights of the few with greater harm. It is important to note that harms cannot be aggregated, the degree of the harm posed on the individual is therefore decisive. An example to which the latter principle can be applied is a situation where one should choose between the death of an animal or human. Following the worse-off principle, one should choose the death of an animal because the animal is considered less worse-off by death, compared to the human who would additionally be deprived from hopes and dreams for the future etc.

## Critics

Regan states that the subject-of-a-life criterion is a 'relevant similarity between moral agents and moral patients, one that makes the attribution of equal inherent value to them both intelligible and nonarbitrary' (Regan, 1985, p. 245). Carl Cohen, on the other hand, seems to think otherwise (Cohen, 2003). He argued that in Regan's reasoning, two definitions of inherent value are mixed up which leads to incorrect conclusions. The first, wide sense definition of inherent value states that all

subjects-of-a-life have worth in themselves resulting in the irreplaceability of lives. The second, much narrower definition, states that those beings who are morally responsible and have a moral will (i.e. moral agents) should never be treated as means and are entitled to rights. Cohen's objection is that Regan, by using the similarity between those that meet the criterion of subjects-of-a-life, assigns rights to moral patients that, although they meet the criteria of the first definition of inherent value, do not meet the criteria of the second definition of inherent value, which is a prerequisite for the allocation of rights. He concludes that rights can only be assigned to moral agents, and not to moral patients.

Another criticism, by Mary Anne Warren, refers to the difficulty of judgement relating to the subject-of-a-life criterion and animals other than mammals (Warren, 2011). Warren refers to the majority of animals of which it is unclear whether they satisfy the subjects-of-a-life criterion. Although a distinction should be made, since one either is a subject-of-a-life or one is not, this can be very complicated since some characteristics (e.g. self-awareness) come in degrees, and a wrong assessment could radically deprive an animal of its rights. A presented solution is to give unclear cases the benefit of the doubt, but she argued that it results in impossible consequences in practice, for example the inability to fight mosquitoes and cockroaches which could be regarded as necessary in some climates.

### Implications and view on genome editing

One implication of the rights view is the total rejection of breeding and slaughtering of animals for human consumption. Although suffering involved with intensive production systems is considered tragic, this is not the fundamental argument underlying this view, as opposed to utilitarianism. On the other hand, what is considered wrong is the violation of rights, in particular the right to life, since all those who are experiencing subjects-of-a-life are considered to have inherent value and are therefore possessing equal rights (e.g. the right not to be harmed for the benefit of others). Furthermore, by raising animals for slaughter, the animals are treated as renewable resources and are not viewed as having value in themselves, which is not in accordance with the respect principle that states that those with inherent value should be treated with respect. Based on these arguments, the use of animals in research is also rejected, even research that could hold real promise for humans, since animals are not considered less valuable compared to humans. From this, deontological arguments could be put forward that genome editing is rejected when used for benefitting humans, either in animal research or in animal agriculture. However, the act of genome editing in itself could possibly be tolerated since it is performed on early embryos who do not satisfy the subjects-of-a-life criterion and therefore not have inherent value. The question remains though what the intended purpose of the genome editing project is in case the embryos are brought to term (e.g. increasing efficiency of animals for meat production is not sustained), and whether the rights of the germ cell donors were violated in any way.

## Care ethics

Care ethics emanates from feminist ethical theory and offers an alternative view on the human-animal relationship compared to utilitarianism and duty ethics. Its main critique is the hyper rationalization observed in former mentioned ethical theories that exclude any kind of emotion or sentiment. It is precisely that bias towards rationalization in society that is thought to have lead towards the oppression of both women and animals (Adams, 1996; Donovan, 1990; Gilligan, 1993). Male psychology is thought to underlie the 'mathematization of the world', thereby viewing the world as a machine of which each part could be understood and explained, caused by a split between reason and emotions. Reason was considered masculine which led to the domination of men over nature. In addition, the emotional part of life was assigned to women who were therefore, together with animals, considered as subjective and irrational. This led to suppression of both, thereby interconnecting sexism and speciesism (Adams, 1996; Donovan, 1990; Gilligan, 1993).

A consequence of the tendency to rationally dissect the world into understandable parts was the Cartesian view of animals in the seventeenth century by René Descartes, which was described and criticized by Regan (Regan, 1985, p. 3-25). In short, the Cartesian view regarded animals as a composition of parts that had no souls and therefore no feelings or emotions, thereby degrading them to unconscious machines. As a result, animals were subjected to vivisection since nothing could essentially matter to them. Body language, sounds or expressions as a consequence of pain were ignored because they were meaningless according to Cartesians. However, in care ethics, the former rationalization of animal emotions is rejected because it has been argued that the simple observation of animals leads to different conclusions of their fate, namely that they do have feelings and can be hurt. Vocalizations of animals can, for example, inform us about their well-being and flight behavior shows us what an animal fears (e.g. Manteuffel et al., 2004; Marx et al., 2003). Central here is the communication with animals, which leaves room for human feelings and sentiment. By focusing on relationships between humans and animals, questions about capacities of animals (e.g. level of consciousness, rationality or moral status) are avoided. Furthermore, it is considered natural to care for others because even moral agents are dependent of care from others at some point in their lives (e.g. as a child or elderly person; Engster, 2006). This results in an attentive and responding attitude toward both humans and nonhumans that focusses on their similarities instead of differences. It could even be further extended to everything that is alive (including e.g. plants and trees), where paying respect should be a central feature. In care ethics, acceptance of diversity is supported by recognition of the aliveness and spirit of other creatures, thereby leaving room for spiritual conversation.

### Critics

Two objections against the ethics of care were raised by Robert Garner (2003). Firstly, he describes the ethics of care as vague because he considered it unable to serve as a moral guideline in situations where the interests of humans and animals clash. Secondly, Garner argues that the individual experiences, on which caring is based, are not universalizable. To clarify his argument, he sketches a picture in which some are confronted with the suffering associated with a factory farm or a slaughterhouse and, as a result, have refrained from the consumption of meat. Others, on the other hand, lack this experience and are therefore ignorant of the suffering underlying the meat producing industry. Donovan responded to this critique by stating that an individual reaction (e.g. horror by confrontation with a slaughterhouse) could actually be generalized to others in a similar situation, thereby denying the claim that individual experiences are not universalizable (Donovan, 2006).

Another difficulty of care ethics is pointed out by David DeGrazia (1998). He states that, by giving more consideration to people with whom we have emotional relationships, others might be left out (e.g. unloved people or people with whom we cannot identify). The same way of reasoning could also be applied to animals, where wild animals are given less consideration than loved, cuddly animals (e.g. pets; Regan, 1991). Donovan reacted to this by stressing that care should be applied universally and not just to those with whom one has close relationships, thereby extending the principle of care in the same way as individual experiences could be extended (Donovan, 2006).

Lastly, another critic points out that, although feminists are not united in their positions, some feminists have the tendency to bend towards subjectivity (Longino, 1989). In her critique, she emphasizes that there is nothing wrong with rationality and objectivity and that it can instead be used in science as a method to understand nature. Subjectivity, in her opinion, provides no basis for the evaluation of competing claims and is therefore unable to replace ‘masculine’ rationality in science.

### Implications and view on genome editing

Regarding vegetarianism, Donovan points out that animals can let us know how they want to be treated, for example by using emotional and spiritual conversation. From this follows that animals

should not be raised and killed to fulfill human preferences for meat, because that goes against their will (Donovan, 1990). In another article, she adds that even if animals could be raised humanely (without suffering) and slaughtered painlessly, this would still be the wrong thing to do because no animal would voluntarily go to the slaughterhouse (Donovan, 2006). Furthermore, Adams stressed the alliance between feminism and vegetarianism by pointing towards the objectification and fragmentation of animals in the meat industry and society, which has similarities with the oppression and objectification of women (Adams, 2003).

However, another feminist, Katherine Paxton-George, is in favor of a moderate consumption of meat by pointing out that the successful application of a vegetarian diet is based on the physiological norm of males, aged between twenty and fifty (George, 2000). Therefore, consequences of a vegetarian diet could entail health risks for people who cannot identify themselves with the male, psychological norm and she concludes that those people should be excused from an abstinence of meat. Yet another argument against vegetarianism is that society has no moral obligation towards animals because they are unable to enter into reciprocal relationships with humans (Noddings, 2013). While there are more feminist views on vegetarianism, the bottom line is that the opinions are divided on this topic, which also applies to the topic of animal experimentation.

Deborah Slicer expressed her antipathy towards animal research by emphasizing that a lot of research is trivial or duplicative and that animals in many cases do not serve as reliable models for human beings. However, she does not rule out that some research is justifiable, although no specifications were given (Slicer, 1991). Since political dimensions and structures could play a role in research, Donovan adds that the context of animal research should always be taken into account, thereby raising questions about who benefits economically from the research and the reliability of the published results that come from those parties (Donovan, 2006). Furthermore is animal research described as the objectification of animals which deprives them from subjectivity and being, which count as an argument against animal research (Adams, 2018). Tora Holmberg, on the other hand, sustains animal research, provided that the animals are handled with care (Holmberg, 2011). Generally, animal research is not ruled out by all care ethicists, provided that the animals are well cared for.

Lastly, when genome editing is viewed as a deliberate sequence alteration (DSA), comparable with traditional breeding practices, it is difficult to find dismissive arguments in care ethics. However, based on the former conclusions of animal use, one could conclude that the use of genome editing to enhance animal production is questionable since some feminists are opposing the consumption of meat based on the objectification of animals. On the other hand, the use of genome editing to enlarge animal welfare or to support disease resistance could be viewed as caring, because every animal would choose to live its best life and to avoid illnesses. However, when the increase in disease resistance, for example, by genome editing is solely used for the purpose of an increased efficiency of farm animals, it could possible not be viewed as a caring act. It could therefore be concluded that the rightness or wrongness of the use of genome editing depends on the context in which it is applied.

## Virtue ethics

The first version of virtue ethics dates back to long ago and was originally formulated by Aristotle. Over the years, the classical theory was developed and refined, and eventually resulted in multiple, modern versions (Annas, 2006). In the following, a version of a modern theory is described, as presented by Rosalind Hursthouse who is a contemporary advocate of virtue ethics involved with the treatment of animals (Hursthouse, 2011). In virtue ethics, as the word suggest, virtues and vices take in a central position. Hursthouse describes a virtue as ‘a morally good, admirable, or praiseworthy character trait, the sort of thing that is cited in a character reference’ and a vice as ‘a morally bad, despicable, or regrettable character trait, the sort of thing we condemn, despise or deplore people for having’ (Hursthouse, 2011, p. 125). Virtues can also be determined by identifying the character

traits that an imaginary, morally good or wise person would have (e.g. courage, kindness, loyalty, tolerance, integrity etc.), which one should also strive to develop. Conversely, vices can be determined by identifying the character traits that such a morally good person would lack (e.g. envy, fear, greed, anger, doubt etc.). It is important to note that virtues are described as excellent moral character traits, thereby being a middle ground between two extremes. For example, a deficiency of compassion would be described as 'unfeeling', but an excessive amount of compassion would be described as 'indulgent'. The virtuous trait of compassion is therefore the mean of these extremes. Another important virtue is the virtue of wisdom, which is required to make the right, ethical decisions. Besides, virtue terms can be used to describe people, but also apply to their actions. For example, a person with the virtuous character trait of honesty will also do what is honest. To assess whether an action is right or wrong, one could therefore question how a virtuous agent would act under the same circumstances (Hursthouse, 2011).

The opinions differ between modern virtue theorists regarding why a virtuous agent would perform a certain act or, in other words, what the motivation should be behind virtuous actions. According to Hursthouse, virtuous agents do the right thing, not based on an emotional impulse, but rather because they think that it is the right thing to do, or because it is worth doing it for its own sake. She emphasizes that reason should be the basis of a virtuous act, although emotions are not considered valueless since they can be shaped and formed by reason.

Furthermore, another concept made famous by Aristotle was 'telos', which can be described as the essence and purpose of a creature. The fulfillment of telos can be seen as an end goal, leading to one's well-being, happiness and a flourishing life. According to Rollin, who is a well-known veterinary ethicist, the concept of telos does apply to animals as well, and is not eternally fixed but can be shaped over time. Respect for the telos of an animal means respect for the needs flowing from that animal, that are genetically based and environmentally expressed. In the case of human-dependent animals, the fulfilment of their needs is dependent from human knowledge on it (Rollin, 2003).

## Critics

A commonly ventilated criticism of virtue ethics is that it does not provide clear guidance for the right action in a difficult situation. Therefore, it has been argued, it does not suffice as an ethical theory by itself, but should rather be used as supplementary material next to another, more robust theory (Fröding, 2013). A comparison with theories such as utilitarianism and duty ethics is easily made, where those theories provide a rather straightforward guidance for an action by each of them referring to one single principle, based on its consequences or the duties of a person. In virtue ethics however, the focus is on the development of character to ultimately be a good person who lives a good life and not so much on actions.

Although a virtuous person would also do what is right, some doubts were raised whether persons would actually be able to develop stable character traits that would give guidance for actions (Harman, 1999). Besides, practical wisdom is required for difficult decision-making, which is something that not all persons possess (e.g. persons who are self-improving but not yet virtuous). It has also been argued that a person whose character is under development but who cannot yet be classified virtuous, is able to intuitively perform right actions that an actually virtuous person would not perform, something that is not accounted for in virtue ethics (Johnson, 2003).

Furthermore, it was objected that virtue ethics is self-centered since its primary focus is on the development of character and the blossoming of one's own life, instead of being concerned about the effects of one's actions on other individuals (Swanton, 2014; Toner, 2006).

A last criticism is pointing towards the need for moral luck in virtue ethics. Since certain external factors (e.g. education, influences, natural tendencies) can influence the development of one's

character, the development of virtue is not completely under one's control and it might therefore be unjust to blame vicious persons for their vices and vicious actions (Athanassoulis, 2005).

## Implications and view on genome editing

According to Hursthouse (2006; 2011), vegetarianism could be a virtuous practice. However, it all depends on the reasons behind the decision to become a vegetarian. If one, being acquainted with the suffering of animals in intensive production systems, decides to become a vegetarian on the basis of compassion, then it is seen as a virtuous act. While those who do so based on fear of being left out by vegetarian friends for example, are not described as virtuous. In addition, people who are aware of the suffering but nevertheless decide to ignore it, are described as callous. Although there are exceptions, it could be reasoned that the majority of people in a Western society should strive towards vegetarianism because the consumption of meat is unnecessary, wasteful and causes suffering (Hursthouse 2006). Another virtue theorist, Carlo Alvaro, even opted for veganism based on the virtue of temperance or moderation. He argued that a virtuous person should strive towards a diet composed of products which are healthy and necessary. Since animal products are not essential for a healthy diet, a virtuous person would abstain from them (Alvaro, 2019). However, an example of a case where the consumption of meat could be justified is when a person needs to eat meat in order to survive because in that situation, the abstinence of meat would lead to death which could arguably not be the right decision.

Also based on her argumentation of vegetarianism, Hursthouse dismissed a lot of animal research (e.g. testing of cosmetics or duplicative research) as cruel because it posed unnecessary suffering on animals. Furthermore, it has been stressed that animals should be treated as well as possible to fulfil their needs, thereby not necessarily condemning research where benefits are actually proportionate with the suffering (Walker, 2020).

When assessing the practice of genome editing, the concept of telos leads to the division of opinions (Almond, 2000). On one side, Rollin argued that respect for telos does not preclude telos from being changed because, in his opinion, respect for telos means respect for the interests flowing from it. The implications of his view are that alteration of animals, so that they better fit their environment, thereby enabling them to better fulfill their needs (e.g. increase of disease resistance), should hence be permitted (Rollin, 2003). On the other hand, it has been argued that a change of genetics is not always accompanied with a change of telos (e.g. genome edited chickens with blunt beaks could still have the desire to engage in pecking behaviors that require a sharp beak) which could harm telos (Hauskeller 2005; Kramer & Meijboom, 2021). Furthermore, the use of genome editing to remove the desire to engage in characteristic behavior (e.g. nesting behavior) was rejected because it could prevent animals from living the good life (Kramer & Meijboom, 2021). Genome editing was viewed from another angle by Hursthouse, who argued that the creation of genome edited animals purely on the basis of fulfilling human desires goes against the virtue of respectful love and should therefore be prohibited.

# Research question 2

## Material and methods

A systematic review of recent literature on the ethics of genome editing of animals was conducted. The goal was to create an overview of arguments for and against genome editing of animals and to create a link between the arguments mentioned in literature and the four ethical theories presented in the previous part of this thesis. All reasons mentioned in the literature were included and presented in the overview, without assessing the arguments based on quality.

### Literature search strategy

For the search for articles containing arguments about genome editing of animals, the same search strategy was used as in the scientific article: 'The ethics of genome editing in non-human animals: a systematic review of reasons reported in the academic literature' by De Graeff et al. (2019). This search strategy consisted of three separate search strings namely 'Genome editing', 'Animals' and 'Ethics'. The combination of the separate search strings was used to search the databases of PubMed, Web of Science, Scopus and CAB Abstracts. The 'Advanced search' option was used for all databases. For Web of Science, the search was limited to the 'Web of Science Core Collection'. For CAB Abstracts, the search was limited to the 'CAB Abstracts' database. Only articles published between 2015 and 2019 and written in English or Dutch were selected. A recent time span of five years was chosen to provide an overview of up-to-date arguments about genome editing of animals, since the rapidly developing genome editing technique could be accompanied by a change in people's perception of the technique and its applications. The year 2020 was excluded to ensure the quality of the literature review since the processing time of new articles could differ between databases. The search resulted in 903 articles from PUBMED, 342 articles from Web of Science, 517 articles from Scopus and 5 articles from CAB Abstracts (see Fig. 1).

### Selection of articles

The filtering of articles was performed in two stages (see Fig. 1). In the first stage, 446 duplicates were removed, after which the title and abstracts of the remaining 1321 articles were screened. 1235 articles that were clearly not about the ethics of genome editing in animals were excluded. In the second stage, the remaining 86 articles were read in detail and 4 inaccessible articles, 1 article that was not written in English or Dutch, 3 articles that did not have a publication date between 2015 and 2019 and 25 articles that did not provide an ethical view on genome editing of animals or did not contain any arguments for or against genome editing of animals were excluded.

### Processing of data

The 53 articles that contained arguments for or against the genome editing of animals were included in the literature review. From the 53 selected articles, 35 articles were not included in De Graeff et al. (2019). All arguments were selected and sorted by author, whether they were for or against genome editing of animals and whether they touched upon utilitarianism, duty ethics, care ethics, virtue ethics or a remaining category.

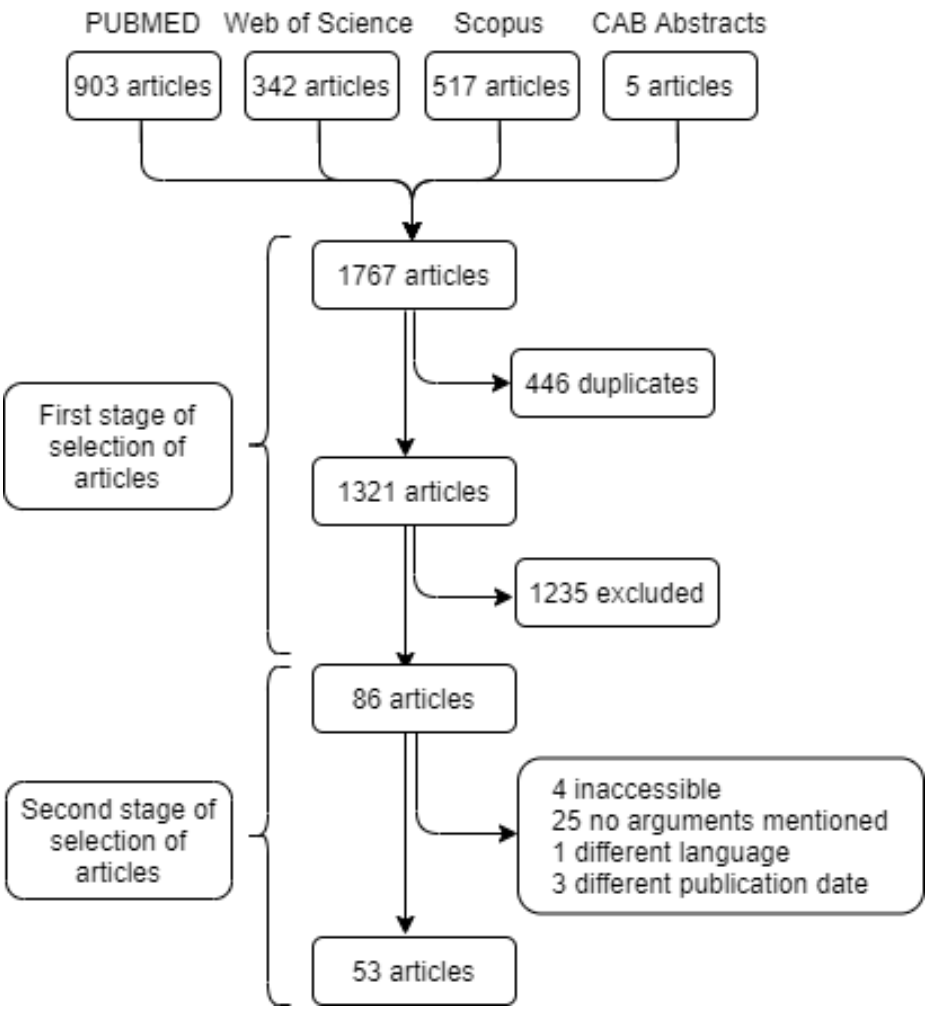


*Figure 1 The process of selection of articles. The total number of hits from PUBMED, Web of Science, Scopus and CAB Abstracts was 1767. In the first stage of the selection, 446 duplicates were removed and 1235 articles were excluded that were not about the ethics of genome editing in animals. In the second stage of selection, in total 31 articles were excluded, leaving 55 articles for the literature review.*

## Results

A total of 74 reasons concerning genome editing of animals have been mentioned in the literature, of which 30 were in favor of genome editing of animals and 44 were not in favor of genome editing of animals. Although the goal was to create a link between the ethical theories described in the first research question and the literature, many reasons were unrelated to the ethical theories. All reasons were categorized in the following 8 themes: utilitarianism, duty ethics, care ethics, virtue ethics, other beyond-welfare reasons, human-related reasons, animal welfare and environmental reasons. An overview of reasons mentioned in the literature can be found in tables below each heading.

### Utilitarianism

As long as farm animals are still used to produce animal products, the use of genome editing of farm animals was advocated because it could contribute to a significant reduction of suffering and an improved welfare. One of the applications of genome editing could be the creation of farm animals with a diminished capacity to feel pain because the reduction of suffering would outweigh chances of losing positive experiences or an increase in negative experiences (Shriver & McConnachie, 2018).

Furthermore, it was argued that the creation of research animals with a diminished capacity to experience pain was also desirable because it would contribute to a reduction of suffering (Devolder

& Eggel, 2019). On the other hand, there was a concern that animals with a diminished capacity to feel pain would be handled with less care compared to their non-genome-edited counterparts. This could lead to an increase of overall suffering, although this claim was found difficult to prove (Devolder & Eggel, 2019)

Although genome editing could be applied to reduce the suffering of wild animals, for example by changing the behaviors of animals (Johannsen, 2017), some authors objected. They stressed the complexity of ecosystems and pointed out that the impact of human intervention is hard to model. They concluded that human interference could likely cause more harm than that it would alleviate suffering (Delon & Purves, 2018; Lunshof, 2015).

*Table 1 Overview of utilitarian reasons mentioned in the literature for and against the genome editing of animals*

| **Utilitarianism** | | **Author** |
|---|---|---|
| **For** | It could contribute to a reduced suffering of farm animals. | Shriver & McConnachie, 2018 |
| | It could contribute to a reduced suffering of research animals. | Devolder & Eggel, 2019 |
| **Against** | It could increase overall suffering of research animals because of an increase of careless handling by researchers compared to their non-genome edited counterparts. | Devolder & Eggel, 2019 |
| | Its application in nature could likely cause more harm than that it would alleviate suffering. | Delon & Purves, 2018; Lunshof, 2015 |

## Duty ethics

Duty ethics was found to be unable to point out the wrongness of the creation of animals with a diminished capacity to experience pain based on two arguments (Schultz-Bergin, 2017). Firstly, animal disenhancement could create animals that fail to meet the criteria 'subjects-of-a-life', thereby disowning the created animals of any right. Secondly, even if animal disenhancement would lead to the creation of subjects-of-a-life, no existing individual would be harmed in the process. A given example is the blinding of chickens to decrease stress and aggression in crowded conditions. However, in the creation of blinded chickens, no rights of an existing, sighted chicken would be violated, which is also known as the non-identity problem (Thompson, 2008; Palmer, 2011)

The application of genome editing to increase the efficiency of food production, such as delaying maturation in salmon was rejected because it would treat animals solely as means (Iversen et al., 2016). Viewing animals merely as products without moral standing, was even suggested to hinder moral development of humans (Benz-Schwarzburg & Ferrari, 2016).

Gene drive can be useful with genome editing, where the probability of inheritance of an edit in the genome to offspring deviates from fifty percent (i.e. Mendelian inheritance pattern). Gene drives could be used as a vector to fight diseases carried by mosquitoes because a genome edit could be spread rapidly in a population. From a duty ethics perspective, no objection could be found because mosquitoes were not considered to have intrinsic value and could therefore be treated as means to an end (Collins et al., 2018). Gene drive as a tool to relieve suffering of wild animals on the other hand, could be desirable since moral status ascribed to animals would be paired with human duties towards them and it was therefore argued that humans should seek a way to relieve the suffering of wild animals without risking an ecological disaster (Johannsen, 2017). Johannson described the prominent issue of the enormous suffering of r-strategist animals who produce large numbers of offspring of which most undergo a painful death. Arising from human duties towards those animals,

genome editing is suggested as a solution to decrease the fertility of the r-strategists, thereby decreasing the numbers of offspring suffering. Furthermore, it has been suggested to provide plants that are suitable for carnivore consumption to the predators of r-strategist in order to reduce predation on r-strategists and to provide their predators with an alternative source of food.

*Table 2 Overview of deontological reasons mentioned in the literature for and against the genome editing of animals*

| **Duty ethics** | | **Author** |
|---|---|---|
| **For** | It could create animals that fail the subjects-of-a-life criterion and that therefore do not have any rights. | Schultz-Bergin, 2017 |
| | Its application to create animals with a diminished capacity to experience pain would not harm the rights of any animal (non-identity problem). | Schultz-Bergin, 2017 |
| | Its application using gene drive in mosquitoes could be accepted because mosquitoes were not considered to have intrinsic value | Collins et al., 2018 |
| | It could contribute to a reduction of suffering of wild animals which is in accordance with human duties towards animals | Johannsen, 2017 |
| **Against** | Its application to increase the efficiency of food production would treat animals solely as means. | Iversen et al., 2016 |
| | It could intensify the thought of animals as means which could hinder human moral development | Benz-Schwarzburg & Ferrari, 2016 |

## Care ethics

It was suggested that the creation of animals with a diminished capacity to experience pain could be viewed as a tool to dominate animals, thereby drawing a line between animal diminishment and sexism (Murphy & Kabesenche, 2018). The authors stated that the domination of animals could lead to abusive and exploitive patterns. Furthermore, they objected to animal diminishment because it could harm meaningful relationships between farmers and animals. These relationships were considered to be important because they could guide and direct actions of humans. Furthermore, the relationship between farmer and animal was suggested to contribute to the farmers job satisfaction, animal welfare and productivity.

*Table 3 Overview of reasons mentioned in the literature against the genome editing of animals touching upon care ethics*

| **Care ethics** | | **Author** |
|---|---|---|
| **Against** | It could contributes to the domination of animals which could lead to abusive and exploitive patterns | Murphy & Kabesenche, 2018 |
| | It could harm meaningful relationships between farmers and animals which could be harmful for both farmer and animal | Murphy & Kabesenche, 2018 |

## Virtue ethics

One objection against the diminishment of animals arose from the virtue of care. According to Murphy & Kabasenche (2018), the virtue of care manifests itself in a desire of having meaningful relationships with others which also entails care. Animal diminishment would hinder meaningful relationships and would therefore be rejected by the virtue of care.

Shriver & McConnachie (2018) argued that the use of genome editing in animals did not fail to respect an animal's telos. Instead, genome editing could be used to change telos without disrespecting it.

*Table 4 Overview of reasons mentioned in the literature for and against the genome editing of animals touching upon virtue ethics*

| **Virtue ethics** | | **Author** |
|---|---|---|
| **For** | It could change telos of animals without disrespecting telos | Shriver & McConnachie, 2018 |
| **Against** | It could be not in accordance with the virtue of care that manifests itself in a desire to have meaningful relationships with others, which also entails care | Murphy & Kabesenche, 2018 |

## Other beyond welfare arguments

Although genome editing could be used to decrease suffering by the creation of farm animals with an diminished capacity to feel pain, Murphy & Kabasenche (2018) rejected the use of genome editing in that way because they denied that experiential suffering was the root problem that needed solving. Meanwhile, they advocated an approach to change the environment of the animals instead of their genetics because they argued that the oppression of animals in the current agricultural system should rather be changed.

Another objection to genome editing of animals is based on the idea that it could harm the dignity of the animal (Greenfield, 2017). However, several authors doubt the plausibility of the argument (Bovenkerk & Nijland, 2017; Schultz-Bergin, 2017). Firstly, some authors present the non-identity problem as a counterargument by pointing out that the creation of a genome edited animal does not harm its dignity (Bovenkerk & Nijland, 2017; Schultz-Bergin, 2017). Although the species-specific capacity of animals could be harmed in the process of genome editing, it would still not harm the dignity of the animals because genome edited animals would form a new species with different species-specific capacities (Schultz-Bergin, 2017).

Animal integrity is a concept that is also put forward in literature (Bovenkerk & Nijland, 2017; Eriksson et al., 2018; Iversen et al., 2016; Saeed et al., 2015). Genome editing could possibly harm animal integrity, for example by the removal of horns from cattle (Eriksson et al., 2018). However, attaching greater value to animal integrity than to animal welfare was suggested to lead to a preference of animals with a diminished welfare over animals with a good welfare but harmed integrity, which was regarded as an ineligible result (Shriver & McConnachie, 2018)

Furthermore, various authors mentioned the unnaturalness of genome editing as an objection towards the technique (Bovenkerk & Nijland, 2017; Eriksson et al., 2018; Greenfield, 2017; Saeed et al., 2015; Shriver & McConnachie, 2018). However, naturalness is a concept that is difficult to define and frame (Eriksson et al., 2018; Shriver & McConnachie, 2018). For example, some authors pointed towards the similarities between genome editing and other breeding practices that are not necessarily frowned upon, such as domestication and selective breeding (Garas et al., 2015; Greenfield, 2017; Lanzerath, 2018; Shriver & McConnachie, 2018). Although it is difficult to obtain

moral guidance from the argument of naturalness, Bovenkerk & Nijland (2017) acknowledge the value of the argument by pointing towards other arguments that are usually behind the argument of naturalness.

The argument of unnaturalness of genome editing is related to the objection that genome editing would lead to humans playing God (Bharati et al., 2020; Bovenkerk & Nijland, 2017; Gatew & Mengistu, 2019; Saeed et al., 2015; Shriver & McConnachie, 2018. Although the argument might be presented on religious grounds (Gatew & Mengistu, 2019), it furthermore indicates that certain boundaries should not be crossed by humans (Bovenkerk & Nijland, 2017). However, it could be rather difficult to specify the boundaries (Gatew & Mengistu, 2019)

*Table 5 Overview of beyond- welfare reasons mentioned in the literature against the genome editing of animals.*

| **Other beyond welfare arguments** | | **Author** |
|---|---|---|
| **Against** | It does not solve the root problem by the creation of farm animals with a diminished capacity to feel pain | Murphy & Kabasenche, 2018 |
| | It could the harm dignity of the animal | Greenfield, 2017 |
| | It could harm the integrity of the animal | Bovenkerk & Nijland, 2017; Eriksson et al., 2018; Iversen et al., 2016; Saeed et al., 2015 |
| | It is unnatural | Bovenkerk & Nijland, 2017; Eriksson et al., 2018; Greenfield, 2017; Saeed et al., 2015; Shriver & McConnachie, 2018 |
| | It could lead to humans 'Playing God' | Bharati et al., 2020; Bovenkerk & Nijland, 2017; Gatew & Mengistu, 2019; Saeed et al., 2015; Shriver & McConnachie, 2018 |

## Human-related reasons

Several authors mentioned that the genome editing technology could be used to create improved animal models for human diseases (Bharati et al., 2020; Bhat et al., 2017; Caplan et al., 2015; Garas et al., 2015; Greenfield, 2017; Huang et al., 2018; Kiyonari & Furuta, 2019; Lanzerath, 2018; Lau & Davie, 2017; Miano et al., 2016; Shah et al., 2018; Shriver & McConnachie, 2018; Willyard, 2016; Zhang & McCarty, 2017), although some authors mentioned the limited translation from animal derived data to humans (Bailey, 2019; Dubey et al., 2019). It was also mentioned that genome edited animals could contribute to knowledge required for the development of new drugs or therapies (Greenfield, 2017). Furthermore, the creation of research animals with a diminished capacity to experience pain could facilitate the harm-benefit analysis that is required prior to the start of every experiment involving animals. Since harm is reduced when the animals experience less suffering, it is easier for scientists to meet the requirements of a positive harm-benefit analysis (Devolder & Eggel, 2019).

An advantage of genome editing of farm animals is the ability of achieving breeding goals without compromising in genetic gain, as is sometimes seen in selective breeding (Croney et al., 2018; Eriksson et al., 2018). A given example of conventional selective breeding is cross-breeding of Holsteins with Angus cattle in order to introduce the polled gene in Holsteins. This would, however, negatively affect the milk production of Holstein cattle, which can be avoided by introducing the polled gene with genome editing. Because genome editing has the potential to increase productivity

of farm animals (Bharati et al., 2020; Fears & Ter Meulen, 2017; Garas et al., 2015; Gatew & Mengistu, 2019; Greenfield, 2017; Iversen et al., 2016; Jiang & Shen, 2019; Karagyaur et al., 2019; Lanzerath, 2018; Lau & Davie, 2017; Schultz-Bergin, 2018), some authors mention genome editing as a tool to meet the increasing demand for food (Croney et al., 2018; Garas et al. 2015; Gatew & Mengistu, 2019; Saeed et al., 2015; Shriver & McConnachie, 2018; van Marle-Köster & Visser, 2018). On the other hand, it was mentioned that an increase in meat production could drive prices down, followed by increase in demand of animal product which would only put more pressure on the environment and agricultural systems, therefore having a counterproductive effect (Benz-Schwarzburg & Ferrari, 2016). Furthermore, some concerns were mentioned about the safety of food products derived from genome edited animals (Jiang & Shen, 2019; Lanzerath, 2018; Lau & Davie, 2017), such as allergic responses (Bharati et al., 2020; Gatew & Mengistu, 2019; Ishii et al., 2017; Iversen et al., 2016; Lanzerath, 2018) and antibiotic resistance caused by consumption of food containing antibiotic resistant genes (Gatew & Mengistu, 2019). One author raised the concern of a decrease of nutritional quality of products derived from genome edited animals (Gatew & Mengistu, 2019), although others mentioned that genome editing could contribute to an increase of food quality of animal products (Karagyaur et al., 2019; Lau & Davie, 2017; Saeed et al., 2015; Shriver & McConnachie, 2018; van Marle-Köster & Visser, 2018). Besides, genome editing could also contribute to the development of new food products (Iversen et al., 2016). Lastly, an objection was made that genome editing could lead to a more artificial pathway of food production, which could harm the existing food culture (Lanzerath, 2018).

Gene drive could be used in favor of human interests to eliminate diseases (Camporesi & Cavaliere, 2016; Caplan et al., 2015; Charo & Greely, 2015; Collins et al., 2018; Fears & Ter Meulen, 2017; Hammond & Galizi, 2017; Hirsch et al., 2019; Karagyaur et al., 2019; Kiyonari & Furuta, 2019; Kofler et al., 2018; Ledford, 2016; Resnik, 2018; Schultz-Bergin, 2018), to control invasive species (Kofler et al., 2018; Lau & Davie, 2017; Leitschuh et al., 2018) or to control pests, thereby benefitting human health (Leitschuh et al., 2018). Some authors noted, on the other hand, that the same technology could also assist in the spread of diseases (Camporesi & Cavaliere, 2016; Caplan et al., 2015; Shah et al., 2018).

Patenting of genome edited animals was seen as an issue (Iversen et al., 2016) that could give too much power to biotechnological companies (Sherkow, 2019), which could lead to frictions between those companies and researchers (Bharati et al., 2020). Patenting was, on the other hand, viewed as necessary to regulate the field (Sherkow, 2019).

An advantage of genome editing technology was its positive effect on the economy (Gatew & Mengistu, 2019), although another author mentioned the costs of setting up genome edited lines as a disadvantage (Garas et al., 2015)

*Table 6 Overview of human-related reasons mentioned in the literature for and against the genome editing of animals.*

| **Human-related reasons** | | **Authors** |
|---|---|---|
| **For** | It could be used to create improved models for human diseases | Bharati et al., 2020; Bhat et al., 2017; Caplan et al., 2015; Garas et al., 2015; Greenfield, 2017; Huang et al., 2018; Kiyonari & Furuta, 2019; Lanzerath, 2018; Lau & Davie, 2017; Miano et al., 2016; Shah et al., 2018; Shriver & McConnachie, 2018; Willyard, 2016; Zhang & McCarty, 2017 |

| | | |
|---|---|---|
| | It could contribute to knowledge required for the development of new drugs or therapies | Greenfield, 2017 |
| | It could decrease the suffering of research animals which would benefit researchers because the requirements of a positive harm-benefit analysis are easier to meet. | Devolder & Eggel, 2019 |
| | It could assist in reaching breeding goals without compromising as is sometimes seen in selective breeding | Croney et al., 2018; Eriksson et al, 2018 |
| | It could increase the productivity of farm animals | Bharati et al., 2020; Fears & Ter Meulen, 2017; Garas et al., 2015; Gatew & Mengistu, 2019; Greenfield, 2017; Iversen et al., 2016; Jiang & Shen, 2019; Karagyaur et al., 2019; Lanzerath, 2018; Lau & Davie, 2017; Schultz-Bergin, 2018 |
| | It could be used as a tool to meet the growing, global demand for food | Croney et al., 2018; Garas et al. 2015; Gatew & Mengistu, 2019; Saeed et al., 2015; Shriver & McConnachie, 2018; van Marle-Köster & Visser, 2018 |
| | It could contribute to an increase of quality of animal products | Karagyaur et al., 2019; Lau & Davie, 2017; Saeed et al., 2015; Shriver & McConnachie, 2018; van Marle-Köster & Visser, 2018 |
| | It could contribute to the development of new food products | Iversen et al., 2016 |
| | Using gene drive, it could be used to eliminate diseases | Camporesi & Cavaliere, 2016; Caplan et al., 2015; Charo & Greely, 2015; Collins et al., 2018; Fears & Ter Meulen, 2017; Hammond & Galizi, 2017; Hirsch et al., 2019; Karagyaur et al., 2019; Kiyonari & Furuta, 2019; Kofler et al., 2018; Ledford, 2016; Resnik, 2018; Schultz-Bergin, 2018 |
| | Using gene drive, it could be used to control invasive species | Kofler et al., 2018; Lau & Davie, 2017; Leitschuh et al., 2018 |
| | Using gene drive, it could be used to control pests, thereby benefitting human health | Leitschuh et al., 2018 |
| | It could have a positive effect on the economy | Gatew & Mengistu, 2019 |
| **Against** | It could increase the pressure on the environment and agricultural systems by increasing the demand for animal products | Benz-Schwarzburg & Ferrari, 2016 |
| | It could negatively affect the food safety of animal products | Jiang & Shen, 2019; Lanzerath, 2018; Lau & Davie, 2017 |
| | It could lead to allergic response of animal products | Bharati et al., 2020; Gatew & Mengistu, 2019; Ishii et al., 2017; Iversen et al., 2016; Lanzerath, 2018 |
| | It could cause antibiotic resistance caused by the consumption of animal products | Gatew & Mengistu, 2019 |
| | It could contribute to a decrease of nutritional quality of animal products | Gatew & Mengistu, 2019 |
| | It could harm the existing food culture by moving towards a more artificial pathway of food production | Lanzerath, 2018 |
| | Using gene drive, it could assist in the spread of diseases | Camporesi & Cavaliere, 2016; Caplan et al., 2015; Shah et al., 2018 |

| | | |
|---|---|---|
| | It could entail the issue of patenting of genome edited animals which could lead to frictions between biotechnological companies and researchers | Bharati et al., 2020 |
| | It could entail costs of setting up genome edited lines | Garas et al., 2015 |

## Animal welfare

Research on animals should nowadays conform to the principles of 3R (Reduction, Refinement and Replacement) to protect animal health and welfare. Some authors advocated the use of genome editing to create research animals with a diminished pain experience because they pointed out that it was in accordance with the principles of 3R (Devolder & Eggel, 2019; Fears & Ter Meulen, 2017)

- Reduction
  Genome editing is expected to reduce the number of animals required to establish a research strain (Greenfield, 2017), although more animals are usually generated than are actually used for research (Benz-Schwarzburg & Ferrari, 2016). Besides, the total number of animals used in research is likely going to increase with the introduction of genome editing (Greenfield, 2017; Lanzerath, 2018; Schultz-Bergin, 2018). Yet, this might be justifiable according to Greenfield (2017), because genome editing entails the opportunity to create animal models that could not have been created in the past.

- Refinement
  Genome editing does contribute to the production of better animal models, which can lead to more rapid and significant advances in scientific knowledge, thereby contributing to refinement (Greenfield, 2017)

- Replacement
  Genome editing could contribute to the replacement of complex mammals with less complex mammals. The thought behind this is that more complex animals have a higher cognitive development and therefore a higher capacity to suffer compared to less complex animals (Greenfield, 2017). It is therefore favorable to select less complex animals for research purposes (Devolder & Eggel, 2019). On the other hand, it has also been argued that genome editing could contribute to the selection of complex mammals instead of less complex animals because complex mammals could serve as improved models for human neurological diseases (Greenfield, 2017). Besides, genome editing to diminish the pain experience of animals could lead to the view that animals can be used as one pleases, thereby slowing down the development of alternative methods for animal research (Devolder & Eggel, 2019).

The use of genome editing technology was suggested to be able to contribute to a higher welfare for animals (Eriksson et al., 2018; Jiang & Shen, 2019; Schultz-Bergin, 2018; Shriver & McConnachie, 2018), by curing diseases (Bharati et al., 2020; Eriksson et al., 2018; Fears & Ter meulen, 2017; Huang et al., 2018; Jiang & Shen, 2019) and increasing disease resistance (Bhat et al., 2017; Caplan et al., 2015; Coles et al., 2015; Garas et al., 2015; Greenfield, 2017; Iversen et al., 2016; Lanzerath, 2018; Ledford, 2016; Saeed et al., 2015; Shriver & McConnachie, 2018; van Marle-Köster & Visser, 2018).

On the other hand, some authors mention welfare issues as a possible consequence of genome editing (Lanzerath, 2018; Shriver & McConnachie, 2018; Garas et al., 2015). The use of genome editing in agriculture was suggested to lead to more inhumane handling of animals and an increase in number of animals used for breeding and slaughter (Benz-Schwarzburg & Ferrari, 2016). Furthermore, the diminishment of the pain experience of farm animals was suggested to harm

animal welfare because it would be difficult for farmers to recognize the needs and interests of their animals (Murphy & Kabasenche, 2018). Although the genome editing technology could have a positive effect on the genetic diversity of a population if one selects for animals with a different genetic background, it could also negatively affect the genetic diversity if genome edited animals would be used very intensively (Eriksson et al., 2018). A decrease of the genetic diversity of a population is undesirable because it could lead to an increase in the level of inbreeding which could adversely affect the individuals. Off-target mutations are a risk of genome editing and are mentioned to be able to cause cell death and transformation (Bharati et al., 2020) and being able to inflict pain and suffering of some degree (Bailey, 2019; Benz-Schwarzburg & Ferrari, 2016; Ishii et al., 2017; Jiang & Shen, 2019; Murphy & Kabasenche, 2018; Schultz-Bergin, 2018). Furthermore, CRISPR could induce cancer in animals because it is more likely to be successful in cells where the p53 gene is deficient (Bailey, 2019). Because of a limited knowledge of the effects of every single gene and the epigenome, the welfare of animals could also be negatively affected by unforeseen pleiotropic effects (Iversen et al., 2016; Schultz-Bergin, 2018) and epigenetics (Schultz-Bergin, 2018). It was also pointed out that due to the novelty of the genome editing technique, there could be unknown consequences for genome edited animals that could impair their welfare (Benz-Schwarzburg & Ferrari, 2016; Iversen et al., 2016; Lanzerath, 2018). Furthermore, several authors mentioned the risks of artificial reproduction techniques which are used for the genome editing of animals (Bhat et al., 2017; Eriksson et al., 2018; Benz-Schwarzburg & Ferrari, 2016). Bhat et al., (2017) noticed early embryonic losses, postnatal death, and birth defects accompanied with the use of SCNT technology. There is also a possibility of suffering of an unborn animal in later stages of fetal development and suffering of deformations at birth as a consequence of SCNT (Eriksson et al., 2018). Some of the animals born with undesirable modifications, as well as surrogate animals and sperm- or egg donors, are killed because they do not yield any more value for research purposes (Benz-Schwarzburg & Ferrari, 2016).

Genome editing technology could be used to alter characteristics of sport animals (e.g. increase lung capacity or dull pain sensation), but this is more likely to benefit human interests than animal welfare (Delon, 2019; Neuhaus & Parent, 2019). Once genome editing is implemented, the number of animals that are being discarded because they do not meet the requirements of the sport could be reduced. However, on the short term, suffering is more likely to increase because non-genome edited animals that lose from genome edited counterparts are likely to be discarded or killed (Delon, 2019; Neuhaus & Parent, 2019). Although genome editing could enhance the welfare of sport animals, it is more likely that the animals are being pushed towards new limits because genome-edited animals could be regarded as a new species. Furthermore, normalizing genome editing for the human means could lead to practices such as animal labor, thereby negatively affecting other animals (Delon, 2019). Lastly, the implementation of genome editing in sports might harm the reputation and norms of the sport (Delon, 2019)

Genome editing could entail the introduction of patents, which was suggested to lead towards a business model which could harm animal welfare (Lanzerath, 2018).

*Table 7 Overview of animal welfare reasons mentioned in the literature for and against the genome editing of animals.*

| **Animal welfare** | | **Author** |
|---|---|---|
| **For** | It is in accordance with the principles of 3R | Devolder & Eggel, 2019; Fears & Ter Meulen, 2017 |
| | It is expected to reduce the number of animals required to establish a research strain | Greenfield, 2017 |
| | It does contribute to more rapid and significant advance in knowledge | Greenfield, 2017 |

| | | |
|---|---|---|
| | It could contribute to the replacement of complex animals by simpler animals in research | Greenfield, 2017 |
| | It contributes to replacement of research animals with animals that suffer less | Devolder & Eggel, 2019 |
| | It could contribute to a higher welfare for animals | Eriksson et al., 2018; Jiang & Shen, 2019; Schultz-Bergin, 2018; Shriver & McConnachie, 2018 |
| | It could contribute to the curing of animal diseases | Bharati et al., 2020; Eriksson et al., 2018; Fears & Ter meulen, 2017; Huang et al., 2018; Jiang & Shen, 2019 |
| | It could contribute to an increase of disease resistance | Bhat et al., 2017; Caplan et al., 2015; Coles et al., 2015; Garas et al., 2015; Greenfield, 2017; Iversen et al., 2016; Lanzerath, 2018; Ledford, 2016; Saeed et al., 2015; Shriver & McConnachie, 2018; van Marle-Köster & Visser, 2018 |
| | It could positively affect the genetic diversity of a population | Eriksson et al., 2018 |
| | It could reduce the number of animals that are being discarded in sports | Delon, 2019; Neuhaus & Parent, 2019 |
| **Against** | It is likely to increase the total number of animals used in research | Greenfield, 2017; Lanzerath, 2018; Schultz-Bergin, 2018 |
| | It could lead to the selection of complex individuals as research animals because they can serve as models for human diseases | Greenfield, 2017 |
| | It could slow down the development of alternative methods for research animals | Devolder & Eggel |
| | It could induce welfare issues | Lanzerath, 2018; Shriver & McConnachie, 2018; Garas et al., 2015 |
| | It could lead to more inhumane handling of animals | Benz-Schwarzburg & Ferrari, 2016 |
| | It could lead to an increase of number of animals used for breeding and slaughter | Benz-Schwarzburg & Ferrari, 2016 |
| | It could harm animal welfare if farmers are unable to recognize the needs and interests of their animals | Murphy & Kabasenche, 2018 |
| | It could negatively affect the genetic diversity of a population | Eriksson et al., 2018 |
| | It could lead to off-target mutations which could induce suffering | Bharati et al., 2020; Bailey, 2019; Benz-Schwarzburg & Ferrari, 2016; Ishii et al., 2017; Jiang & Shen, 2019; Murphy & Kabasenche, 2018; Schultz-Bergin, 2018 |
| | It could induce cancer | Bailey, 2019 |
| | It could negatively affect animal welfare because of pleiotropic effects | Iversen et al., 2016; Schultz-Bergin, 2018 |
| | It could negatively affect animal welfare because of the epigenome consequences | Schultz-Bergin, 2018 |
| | It could negatively affect animal welfare because of unknown consequences of the genome editing technique | Benz-Schwarzburg & Ferrari, 2016; Iversen et al., 2016; Lanzerath, 2018 |
| | It could cause suffering as a consequence of the use of artificial reproduction techniques | Bhat et al., 2017; Eriksson et al., 2018 |

| | | |
|---|---|---|
| | It could lead to rejection or killing of animals with undesirable modifications | Benz-Schwarzburg & Ferrari, 2016 |
| | It could lead to rejection or killing of animals in sports | Delon, 2019; Neuhaus & Parent, 2019 |
| | If applied in sport animals, it could normalize genome editing for human means which could negatively affect other animals | Delon, 2019 |
| | It could entail the introduction of patenting which could lead to a business model which might harm animal welfare | Lanzerath, 2018 |

### Environmental reasons

Genome editing of animals could have a positive effect on the environment and contribute to sustainability (Garas et al., 2015; Lanzerath, 2018; Shriver & McConnachie, 2018). On the other hand, several authors expressed concern about escapes of genome edited animals (Eriksson et al., 2018; Gatew & Mengistu, 2019; Iversen et al., 2016; Lau & Davie, 2017; Lunshof, 2015; Saeed et al., 2015) because the consequences are difficult to predict since genes might act different from individual to individual (Gatew & Mengistu, 2019).

Accompanied with the use of gene drive are consequences that could have profound effects on the ecosystem equilibrium (Bharati et al., 2020; Caplan et al., 2015; Hammond & Galizi, 2017; Kofler et al., 2018; Lau & Davie, 2017; Leitschuh et al., 2018; Lunshof, 2015; Shah et al., 2018). The diversity of natural genomes is likely to be reduced (Bharati et al., 2020; Camporesi & Cavaliere, 2016) and some valuable traits could be lost (Charo & Greely, 2015). There is also the risk of the spread of the gene drive beyond the established boundaries (Caplan et al., 2015; Collins et al., 2018; Shah et al., 2018).

*Table 8 Overview of environmental reasons mentioned in the literature for and against the genome editing of animals.*

| **Environmental reasons** | | **Author** |
|---|---|---|
| **For** | It could have a positive effect on the environment and contribute to sustainability | Garas et al., 2015; Lanzerath, 2018; Shriver & McConnachie, 2018 |
| **Against** | It could lead to the escapes of genome edited animals, which could lead to unpredictable consequences | Eriksson et al., 2018; Gatew & Mengistu, 2019; Iversen et al., 2016; Lau & Davie, 2017; Lunshof, 2015; Saeed et al., 2015; |
| | Using gene drive, it could have profound effects on the ecosystem equilibrium | Bharati et al., 2020; Caplan et al., 2015; Hammond & Galizi, 2017; Kofler et al., 2018; Lau & Davie, 2017; Leitschuh et al., 2018; Lunshof, 2015; Shah et al., 2018 |
| | Using gene drive, it could reduce the diversity of natural genomes | Bharati et al., 2020; Camporesi & Cavaliere, 2016 |
| | Using gene drive, it could lead to the loss of valuable traits | Charo & Greely, 2015 |
| | Using gene drive, it entails the risk of spread of the gene beyond the established boundaries | Caplan et al., 2015; Collins et al., 2018; Shah et al., 2018 |

### Public acceptance

A common concern regarding genome editing is animal welfare (Bovenkerk & Nijland, 2017; McConnachie et al., 2019; Ormandy, 2016). It is therefore suggested that genome editing as a tool to enhance animal welfare could possibly meet the standards set by the sense of public's ethics (Ishii,

2017; McConnachie et al., 2019). An example of this is the creation of polled cows by genome editing, thereby avoiding the suffering associated dehorning practices. The majority of people was also observed to have a positive attitude towards the consumption of the products from genome edited polled cows (McConnachie et al., 2019). Furthermore, people seemed to be more supportive of the use of genome edited animals in research to enhance human health, compared to the use of these animals for food production (Ormandy, 2016) or for enhancing animal attributes (Critchley et al., 2019). Genome editing technology as a tool to improve survival of wild populations was regarded as more acceptable than to reduce or eliminate wild populations. Risks for humans and nature accompanied with the editing of wild populations were not expected to outweigh the benefits by the public (Kohl et al., 2019)

# Research question 3

The reasons mentioned in the literature could be categorized into two types of argumentation: practical argumentation (human-related reasons, animal welfare and environmental reasons) and argumentation that went beyond practical matters (utilitarianism, duty ethics, care ethics, virtue ethics and other beyond welfare arguments). The majority of the reasons that were mentioned in the literature did not touch upon one of the ethical theories as described in the first research question, but were of a practical nature, describing benefits and risks of genome editing.

## Pattern of argumentation

Swierstra & Rip (2007) had identified different type of arguments and a pattern of moral argumentation which are emerging over time when new technologies are being introduced. One of the arguments that they identified against new technologies was that humans have a tendency to misuse the technology. The same argument was also found in this literature review when some authors objected against the use of gene drive by emphasizing that the same technology that was found to be able to eliminate diseases, also could be deployed for malicious purposes like the spread of diseases (Camporesi & Cavaliere, 2016; Caplan et al., 2015; Shah et al., 2018). Furthermore, Swierstra & Rip recognize an argumentation pattern where opponents pleaded for caution by emphasizing the novelty of the technique and in response, proponents presented the technique as nothing unusual. The same argumentation pattern could be found in this literature review where some authors objected against genome editing of animals by stressing the unknown consequences of the technique (Benz-Schwarzburg & Ferrari, 2016; Iversen et al., 2016; Lanzerath, 2018), while others denied the novelty of the technique by pointing towards the similarities between selective breeding and genome editing (Garas et al., 2015; Greenfield, 2017; Lanzerath, 2018; Shriver & McConnachie, 2018).

## Lack of interdisciplinary reasoning

Except for a few articles, striking was the lack of content written from an interdisciplinary perspective. Some articles tended to focus on the opportunities of the genome editing technique and their benefits for humans without taking the moral status of animals into account, while others solely contemplated on the consequences of genome editing with regard to the human-animal relationship.

Firstly, a missing interdisciplinary perspective could be the result of a lack of communication between scientist and ethicist, when they both move in their own circles without coming into contact with each other. Secondly, it is possible that arguments from an ethical perspective do not appeal to scientists and are therefore not taken into account. A reason for this could that ethical reflections are far from scientists' everyday reality and for that reason, ethical arguments are regarded as far-fetched and impractical. Thirdly, the desire for progress that is expressed in the development of modern technologies such as genome editing, could be a driving force for scientists to ignore ethical arguments, although ethical arguments could be considered as valid. The thought behind this could be that techniques such as genome editing will always be further developed as the opportunities are promising and tempting. In this scenario, the work of scientists that are bound by ethical concerns will be overruled by the work of scientists with less ethical concerns.

However, the development of new techniques such as genome editing should be dependent on ethical reflections on them because the application of new techniques affects and shapes society. A lack of ethical reflection has, for example, led to the birth of genome edited, human twins aimed at the creation of genetic resistance of HIV, which has led to worldwide shock and criticism (e.g. Cyranoski, 2018; Normile, 2019; Sand et al., 2019). In order to prevent such situations, interdisciplinary reflections on the ethics of genome editing in animals should be preferred in order to take into account all arguments and ethical viewpoints ventilated by different disciplines in a more central debate.

## Limits of argumentation from ethical theories

Most of the arguments concerning the ethical theories were presented from utilitarianism and deontological perspective and a minority came from a care ethics or virtue ethics perspective, which is in line with the observation that most animal ethicist are observed to argue from an utilitarian or deontological viewpoint (Bovenkerk & Nijland, 2017). Besides, Swierstra & Rip (2007) stated that people are often observed to return to consequentialist arguments because they are easier to handle than arguments coming from virtue ethics. However, the focus on utilitarian and deontological arguments could lead to missing out on other valuable arguments and aspects in the debate on genome editing. Another possible consequence could be the division between everyday-life reasoning by the public and reasoning by ethicists. An example of this is provided by Bovenkerk & Nijland (2017), where a virtue ethical approach was found to fit best everyday-life reasoning about pedigree dog genome editing and breeding instead of utilitarian or deontological approaches. The aim should be to unite everyday-life reasoning by the public and reasoning by ethicists because both types of reasoning should be able to affect the ethical debate on genome editing.

## Reasoning from utilitarianism

After the introduction of a novel technique, utilitarian arguments are mentioned to be common (Swierstra & Rip, 2007), but, although the novelty of the genome editing technique could be questioned, the presence of utilitarian arguments was limited in the reviewed literature. Many authors, however, came close to putting forward utilitarian arguments by mentioning the need to weigh benefits against risks. In reality, few authors actually made an assessment of the consequences of the use of genome editing in animals, which was also observed by De Graeff et al. (2019). A reason for this could be that it is difficult to make an assessment of the consequences of the use of genome editing in animals because some risks are still unknown. However actual benefit-risk assessment could be very valuable because they could help to identify possible weak sides of genome editing, thereby paving the way for improvement of the technique. Growing awareness of the risks and weak sides could also help to counterbalance the overestimation of possibilities of genome editing.

Although utilitarianism is able to make a valuable contribution to the debate about genome editing of animals, it also has limitations. First of all, as pointed out before, the consequences of application of genome editing of animals can be unpredictable due to unknown risks, which hinders the assessment of consequences. Secondly, utilitarian argumentation has the tendency to miss out on other, valuable arguments by solely focusing on consequences. For example, some authors objected against genome editing of animals because it could harm the integrity of animals. Others objected because genome editing of animals could exceed certain limits (Playing God argument). However, because these arguments have considerably less value amongst utilitarians, the debate with other ethicists and the public could become complicated because it is difficult to find common grounds and understanding.

## Reasoning from duty ethics

In the literature review, Johannson (2017) advocated the use of genome editing in wild animals by changing their behavior to reduce suffering, as long as there is no risk of an ecological disaster. Johannson presented this argument based on a deontological perspective where humans have duties towards animals. It is striking that the same argument based on relief of suffering could also be presented from other ethical theories, although based on different premises. For example, from an utilitarian perspective this argument could be put forward by pointing towards the possibility to provide the greatest good for the greatest amount of individuals, while minimizing the suffering for

all those involved. From the ethics of care, it could be argued that, based on the relationship and communication with animals, genome editing in wild animals to relieve suffering should be preferable as long as no ecological disaster is risked, because we care about animals and animals do not want to suffer. These similarities point out that some agreement between ethical theories is possible regardless of their differences, which could be helpful as a starting point of finding common grounds in a debate.

A limitation of reasoning from duty ethics in the debate on genome editing of animals was put forward by Schultz-Bergin (2017), who pointed towards the non-identity problem. Duty ethical views are especially vulnerable for this problem because wrong-doings to the act are condemned, rather than the outcomes of an act. As a consequence, it could be difficult to reject genome editing of animals based on a deontological perspective. In the literature review for example, Iversen et al. (2016) pointing out the wrongness of genome editing of animals to increase the food production by arguing that doing so would only treat animals as means. Firstly, the non-identity problem could also be applied to this example because no rights of existing animals are harmed by creation of genome edited animals for food production. Secondly, this argument is not specific to genome editing, since even non-genome edited animals would be treated the same way. Another limitation of duty ethical reasoning in the genome editing debate could be its established position on just the use of animals. Many applications of genome editing are involving farm animals or research animals, but the deontological view already condemns every use of these animals. This could narrow the position of duty ethics in the genome editing debate because the deontological perspective leaves very limited room for discussion.

### Reasoning from care ethics

One of the limitations of care ethics could be its underrepresentation in the genome editing debate. Even though the literature review spanned five years, only one article was found that provided reasons against genome editing of animals from the ethics of care. Earlier, care ethics had been criticized as vague and underdeveloped (Engster, 2006) with a lack of rule of reason (Franklin, 2005), which might explain its underrepresentation in the scientific debate. Furthermore, a limitation of care ethics could be that its argumentation is not as easy to handle as argumentation from utilitarianism or duty ethics. Even though there is ongoing debate within utilitarianism and duty ethics regarding a variety of matters, the debate within care ethics seems to be even more diverse. For example, in general there seems to be agreement within the animal rights movement by Tom Regan about consumption of meat, while opinions in care ethics are much more divided on that matter. It could be that the principles provided by utilitarianism and duty ethics, (e.g. principle of equality or mini-ride principle) help to provide guidance and therefore more unanimity but that could be doubted given the criticism that also exists on these principles. Anyway, the lack of agreement on matters within care ethics could hinder the debate on genome editing.

### Reasoning from virtue ethics

At first sight, virtue ethics seemed also underrepresented in the genome editing debate because only few arguments were presented in the literature review containing concepts like virtues or telos. However, some arguments might be underlying an virtue ethical perspective, for example the ‘Playing God’ argument that was put forward as an objection against genome editing. According to Swierstra & Rip (2007), this argument has a virtue ethical nature because it touches upon the ‘good life’ where certain boundaries have to be respected. Another example is the argument of naturalness that was put forward as an objection against genome editing. Bovenkerk & Nijland (2017) argued

that several arguments are usually behind this argument. It is therefore possible that the argument of naturalness was presented from a virtue ethical perspective, for example when the thought behind the argument was based on the virtue of respect (we should respect nature and should therefore not get involved in processes that we do not completely understand).

Furthermore, some overlap was observed between virtue ethics and care ethics, where Murphy & Kabesenche (2018) put forward an argument from virtue ethics that originally came from care ethics, by describing care as a virtue. Such agreements between virtue ethics and care ethics could be used as a starting point in a genome editing debate.

A limitation of virtue ethics in the genome editing debate could be that virtue ethical arguments are not always recognizable as being arguments from virtue ethics. Examples are the 'Playing God' argument or the argument of naturalness that are discussed above. Especially the argument of naturalness runs the risk of being underappreciated or even discarded due to its complexity, because the criteria of naturalness are difficult to determine (Bovenkerk & Nijland, 2017). However, valuable arguments from virtue ethics could be behind this argument but they risk to remain unnoticed.

## Improvement of the debate on genome editing of animals

First of all, it is important that ethics is involved in all areas related to the genome editing of animals, such as animal research regarding genome editing or actual application in, for example, farm animals. As noticed before, the literature is lacking interdisciplinary reasoning which could lead to a limited debate within disciplines because valuable arguments from other disciplines are missing. It would therefore benefit the debate on genome editing of animals if the debate would have a more central position in which multiple disciplines are involved. An example from the literature review where the debate had a more central position was the article of Eriksson et al. (2018), who chose an interdisciplinary approach, thereby connecting both ethical and animal breeding perspectives.

Secondly, as interdisciplinary reasoning is currently lacking in the debate on genome editing of animals, a difference was noted in the type of arguments presented by different authors. The different types of arguments (e.g. practical arguments vs. beyond-welfare arguments) could possibly be caused by a lack of ethical knowledge among scientists, as well as lack of genomic knowledge among ethicists. To stimulate understanding in the debate of genome editing, education could play an important role. For example, teaching students the value and importance of ethical reasoning in research. Although this measure does not necessarily affect the current debate on genome editing of animals, it could help to improve debates in the future.

Thirdly, as observed before, ethical theories could sometimes put forward the same argument but based on different premises. This convergence is very valuable as it could be used to stimulate the debate on genome editing of animals. For example, the use of similarities as starting points in debates between proponents of different ethical theories could boost understanding and communication, and therefore improve the ethical debate on genome editing of animals.

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