Life-threatening superbugs:

how factory farm pollution risks human health

ALLIANCE TO SAVE OUR ANTIBIOTICS

WORLD ANIMAL PROTECTION

Contents

Life-threatening superbugs: how factory farm pollution risks human health

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Preface

Our food system is broken. It is in part causing our climate to change. And now, we are on the edge of, yet another, global human health crisis. Except this is not one we will be able to vaccinate our way out of.

We already know that factory farming is the biggest cause of animal cruelty in the world. Under horrendous conditions, animals are reared, transported, and slaughtered in their billions in a global system driven to produce ever more meat at the cheapest possible price. In the UK, where we pride ourselves on high standards and on being a 'nation of animal lovers' an estimated 80% of our farmed animals are produced in factory farms.

Farm animals, like us, think and feel, they have personalities and needs of their own and the capacity to experience suffering. Science shows this. Our wellbeing is intimately connected to that of animals and our planet. Yet, our demand for cheap meat is causing their suffering, our planet to heat up and now it is causing antibiotic resistance.

We wouldn't take antibiotics if we were not ill. Yet antibiotics are used excessively in farming; given to healthy animals as a preventative measure. This allows animals to be kept in closer quarters than is natural or comfortable for them and often in highly unhygienic conditions. We are seeing a rise in antibiotic resistance in animals, which is also contributing to the public health crisis of antibiotic resistance in humans.

As the world recovers from Covid, scientists are increasingly referring to the spread of antibiotic resistance as a "silent pandemic" [1]. The United Nations Environment Programme (UNEP) says that it is a pandemic hiding in plain sight [2]. It's not hard to understand why concern is so high: an estimated 4.95 million people died of an antibiotic-resistant infection in 2019, and for 1.27 million of these people their death was attributable to the antibiotic resistance of the infection [3]. These huge numbers are already shocking, but unless strong action is taken, a government-commissioned review has forecast that 10 million people could die globally each year by 2050 as a result [4]. This is the hidden public health cost of intensive factory farming.

Resistant bacteria can spread to humans on food [5][6]. High levels of resistance in human Campylobacter infections [7] have been caused by the use of critically important antibiotics in poultry, for example. However, the environment is also key to the development and spread of antibiotic resistance [2]. According to UNEP, up to 90% of antibiotics consumed by humans or animals are excreted into the environment as an active ingredient [8], and can end up contaminating waterways. Antibiotic-resistant bacteria are also present in untreated sewage and animal manure.

This report finds evidence that intensive factory farms are not just having an impact on water quality, but they are also likely to be contributing to the environmental spread of antibiotic-resistant bacteria. The consumption of fruit and vegetables grown with contaminated manure and water helps spread antibiotic resistance to unwitting consumers. The excessive use of antibiotics in livestock production should, therefore, be a concern for all of us.

Various steps can be taken to reduce the environmental spread of antibiotic resistance from livestock production, but the most important of these is to reduce antibiotic use. Whilst the UK livestock sector has made good strides in reducing its reliance on antibiotics, it remains far too high. It is only by making major improvements to animal husbandry, so that animals are no longer kept in unhygienic, stressful conditions where infections spread easily, and by reducing meat production and consumption to more sustainable levels, that truly responsible antibiotic use will be achieved. We need to lead the way on this, by moving the UK to a humane and sustainable farming system to not only ensure farmed animals lead good lives, but for our own health. There is no future for factory farming.

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World Animal Protection

We're World Animal Protection. **We're on a mission to change the way the world works to end animal cruelty and suffering. Forever.**

Alliance to Save Our Antibiotics

The Alliance to Save Our Antibiotics is an alliance of health, medical, civil-society and animal-welfare groups campaigning to stop the overuse of antibiotics in animal farming. It was founded by Compassion in World Farming, the Soil Association and Sustain in 2009. Our vision is a world in which human and animal health and well-being are protected by food and farming systems that do not rely on routine antibiotic use.

Bureau of Investigative Journalism

The Bureau of Investigative Journalism is an independent, not-for-profit organisation that holds power to account. Founded in 2010 by David and Elaine Potter, we tackle big subjects through deep reporting that uncovers the truth. We tell the stories that matter.

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Executive summary

Antibiotic resistance is a deadly threat to people, killing an estimated 1.27 million people a year, and factory farming is a major contributor to the spread of antibiotic resistance in the environment. Testing commissioned by World Animal Protection, the Alliance to Save Our Antibiotics and the Bureau of Investigative Journalism has found bacteria resistant to the highest-priority critically important antibiotics in rivers and waterways in areas with high numbers of factory farms.

Antibiotic-resistant E. coli and S. aureus were found in rivers adjacent to both factory farms and higher-welfare outdoor farms, as well as in slurry run off from intensive dairy farms. E. coli and S. aureus are the two pathogens causing the most deaths worldwide that are associated with antibiotic resistance. Separate testing for a specific gene which makes bacteria resistant to certain antibiotics found more of these genes downstream of intensive farms than upstream.

Resistance was found to the antibiotics cefotaxime in E. coli and vancomycin in S. aureus. Both of these antibiotics are classified by the World Health Organization as highest-priority critically important in human medicine. Resistance was also found to ampicillin, cefazoline and trimethoprim in E. coli, and erythromycin and trimethoprim in S. aureus. All of these antibiotics are classified as highest-priority critically important, critically important, or highly important in human medicine by the World Health Organization.

Testing was also carried out for two antibiotic-resistance genes, *Sul(1)* and *Tet B*, which make bacteria resistant to sulphonamide and tetracycline antibiotics respectively. Evidence was found that factory farms were contributing to the spread of *Sul(1)* in the environment. This gene was found more consistently downstream than upstream of intensive pig and chicken farms.

Testing was also carried out on four slurry samples from dairy farms and on one chicken-litter sample. One of the dairy samples and the chicken-litter sample had E. coli resistant to cefotaxime, a highest-priority critically important antibiotic. All five samples had the sulphonamide-resistance gene *Sul(1)*, and all four of the dairy samples had the resistance gene *Tet B* which confers resistance to tetracycline antibiotics, which are classified as highly important in human medicine.

We also found five cases of vancomycin-resistant S. aureus, four of which came from the Wye Valley area. This is significant as vancomycin is the antibiotic used to treat potentially deadly MRSA infections (a resistant form of S. aureus). Until now, resistance has been uncommon in S. aureus but has been closely monitored in enterococci bacteria. Vancomycin resistance in Enterococci emerged due to the use of avoparcin as a growth promoter on farms in Europe. Although avoparcin was banned as a growth promoter in 1997, the use of macrolide antibiotics is known to have maintained elevated levels of vancomycin-resistant enterococci in some livestock. Further investigation is needed to determine whether the bacteria have the key *vanA* resistance gene which confers full vancomycin resistance.

Residues of antimicrobials widely used in chicken farming to control coccidiosis, a disease which is very common in intensive chicken farming, were found in sediment downstream of an intensive chicken farm in the Wye Valley. Residues of one of the chemicals found is known to be persistent in the environment, and in 2019 the European Food Safety Authority (EFSA) said it was unable to conclude on its environmental safety for this reason.

None of the four higher welfare extensive pig or chicken farms tested had higher levels of any type of resistance downstream than was found upstream.

On the other hand, five of eight intensive pig or chicken farms had higher levels of at least one type of resistance downstream than upstream.

The government needs to implement routine testing of soils and waterways on or adjacent to intensive farms to determine the extent of the spread of antibiotic resistance and antibiotic residues, including those potentially harmful to wildlife.

Even more importantly, the problem must be tackled at the source and farm antibiotic use must be reduced to more sustainable levels. Doing this will require a ban on all forms of routine farm antibiotic use, including preventative group treatments. It will also require major improvements to animal husbandry so that practices known to be associated with higher levels of disease and antibiotic use are phased out.

Introduction – factory farming and the spread of AMR

Water downstream from factory farms harbours an invisible threat to people's health which could eclipse the COVID-19 crisis. The threat? Superbugs – or antimicrobial resistant bacteria - projected to kill up to 10 million people annually by 2050 [4].

Already over one million people a year are dying from infections that cannot be treated with antibiotics. World Health Organisation (WHO) chief Tedros Ghebreyesus has warned that the antibiotic-resistance crisis is just as dangerous as the pandemic [12].

Our 2022 research tested water samples upstream and downstream of factory farms and of extensive farms for the presence of antimicrobial-resistance genes (ARGs) and superbugs. In factory farms, millions of animals are kept in highly intensive and unhygienic conditions where disease spreads easily, whereas in extensive farms animals can lead a more natural life and are free to roam,

Overall, our findings suggest that factory farms are likely to be discharging resistance genes and superbugs into public waterways and the wider environment. Intensive poultry farms are also releasing residues of coccidiostat antimicrobials. Some of these are environmentally persistent and may be harmful to wildlife.

Building Antibiotic Resistance

Antibiotics are medicines used to treat infections caused by bacteria. When they work, they kill or prevent the growth of the bacteria. Achievements in modern medicine, such as major surgery, organ transplantation, treatment of preterm babies, and cancer chemotherapy, which we today take for granted, would not be possible without access to effective treatment for bacterial infections. But some bacteria can develop resistance to antibiotics, making the drugs ineffective. The growth of antibiotic resistance is encouraged by the overuse of antibiotics in human medicine and farming and threatens to undermine much of modern medicine [3].

Resistant bacteria generally have one or more antibiotic-resistance genes (ARGs), which enable them to resist the antibiotics. Copies of ARGs can pass between bacteria, through a process called "horizontal gene transfer", and the bacteria receiving the genes then become resistant. The presence of ARGs in some bacteria therefore increases the chance that others will become resistant, particularly when antibiotics are overused.

Antibiotic use in farming

Factory farms squash billions of genetically uniform animals into stressful, barren environments, with no access to outdoor space or natural light.

Animals may have little or no room to turn around or lie down with their limbs, head or wings fully extended. This highly stressful and often barren environment can lead to injuries and severe behavioural issues. These can include aggression or repetitive behaviour like tail biting in pigs, cage biting or chewing continuously on nothing until frothing at the mouth, feather pecking or even sometimes cannibalism. Stress depresses the immune system and makes animals more prone to infections.

Very densely packed sheds also provide good conditions for disease to spread from animal to animal. Poor hygiene and air quality are also a cause of disease. Antibiotics are used across groups to prevent stressed animals getting sick; they prop up a system of suffering for food production.

Worldwide approximately 65% of antibiotic consumption occurs in farming [13], the figure is lower in the UK at 30% [14].

Despite intensive farming remaining widespread in the UK, the British livestock industry has achieved a welcome 55% reduction in antibiotic use since 2014 [15].

Use in the pig industry has been reduced by about 60%, but despite this, the pig industry is still the largest farm user of medically important antibiotics in the UK. This is because pigs are one of the most intensively farmed species on the planet. Up to 90% of all antibiotics they receive are administered in the first 10 weeks of pigs' lives. Their use is associated with painful mutilations (tail docking and teeth clipping), early separation from mothers, barren and overcrowded environments and related gut and respiratory infections [16].

Early weaning is a particularly important cause of antibiotic use in the pig industry, and delaying weaning is one of the most important husbandry improvements which can reduce the need for excessive use [17][18]. A Danish study looked at antibiotic use in all Danish free-range pigs and organic pigs and compared it with average levels of use found in 300 intensive pig farms. It found that use in intensively farmed pigs was 3.75 – 15 times higher than in organic pigs, and 1.3 – 4.1 times higher than in free-range non-organic pigs, depending on the age group examined, see Table 2 [18]. The minimum weaning age for organic pigs is 40 days, compared with 30 days for free-range pigs and just 21 days for intensively farmed pigs.

Table 1. Antibiotic use in organic, non-organic free-range and indoor (intensive) pigs in Denmark in 2016-2018 (mean number of doses per 1000 animal days) [18]

	Organic	Free range	Indoor
Sows and piglets	1.1	4	16.5
Weaners	4.8	33.7	72
Finishers	2.88	8.2	10.5
Min weaning age	40 days	30 days	21 days

The authors said that it was "logical to suspect, that not only strict regulations on antibiotic usage but also improved health related to conditions like being born outdoor[s], higher weaning age and lower stocking density have an effect on antibiotic usage."

Chicken farms have seen the biggest reduction in antibiotic use overall in the UK. Use per bird fell by 80% between 2014 and 2017, but subsequently increased again by 63%, so that in 2020 use was only down by 67% compared with 2014 [19]. In 2016, the British Poultry Council committed to no longer using antibiotics preventatively, which has contributed to the reductions, as has improved antibiotic-use data collection.

However, the highly intensive production methods used in chicken farming means that bird health is often badly impacted. In intensive production systems, chickens are genetically selected for fast growth in order to achieve the target live weight of 2-2.5 kg in 35 to 40 days. Whereas in free-range production, birds live at least 56 days and in organic production they usually live 70–81 days [20][21]. The very rapid growth rate has large impacts on bird health and welfare, and consequently on antibiotic use. Data collected from every chicken farm in the Netherlands show that fast-growing breeds use on average of 6 times more antibiotics per bird than slower-growing breeds [22].

Intensively farmed birds are also kept in cramped conditions in very large numbers in small spaces: industry Red Tractor standards allow for a "stocking density" (number of animals per area) of up to 38kg of bird per square meter, which means that each bird has a space allowance of less than an A4 sheet of paper. Excessively high stocking densities badly impact chicken health and welfare [21] and have been associated with higher antibiotic use [23].

In addition to the use of medically important antibiotics, intensive chicken farming uses enormous quantities of non-medically important antibiotics, called ionophores. Ionophores, and some other antimicrobials, are used in chicken farming as "coccidiostats". Coccidiostats are drugs added to chicken or turkey feed to control a disease called coccidiosis, which occurs when chickens ingest their own faeces. The very cramped conditions of intensive chicken farming result in poor hygiene, which is why coccidiosis is the most common disease problem in intensive chicken farming.

Coccidiostats are extremely widely used in poultry farming. In 2020 the UK poultry industry used 258 tonnes of ionophores and 116 tonnes of non-ionophore coccidiostats [24]. This compares with just 21 tonnes of medically important antibiotics sold for use by members of the BPC [19] , and 226 tonnes of medically important antibiotics sold for use across all animal species [15].

While ionophores are not currently used in human medicine because of their toxicity, some scientists have suggested that it might be possible to develop them for human use in the future [25]. Furthermore, it has been demonstrated that the overuse of ionophores may increase resistance to medically important antibiotics in some bacteria, through a process called co-selection. Co-selection can occur if bacteria that are resistant to one antibiotic also happen to be resistant to another, and then use of the second antibiotic selects for resistance to the first antibiotic. The use of the ionophore narasin is thought to co-select for resistance to a critically important antibiotic, vancomycin, in pathogenic bacteria called enterococci. After the elimination of virtually all ionophore use in the Norwegian poultry industry, no vancomycin-resistant enterococci were found in Norwegian poultry, whereas previously they had been present [26].

Intensive dairy production, where animals may be kept in overcrowded conditions and are bred for maximum production, can compromise animals' immune responses, and enable disease to develop and spread.

The main health problems requiring antibiotic treatment are mastitis (inflammation of the mammary gland and udder tissue, usually due to bacterial infection), foot problems and uterine problems. According to a European Food Safety Authority (EFSA) review, these health problems are greater in "zero-grazing" dairy systems where the cows are kept indoors all year round [27].

In the UK, most dairy cows have access to pasture during the summer months, but increasingly cows are being kept indoors and large, zero-grazing herds are becoming more common in the UK and worldwide.

EFSA also say that genetic selection for high yield is a "major factor causing poor welfare, in particular health problems, in dairy cows", and is positively correlated with the incidence of lameness, mastitis, reproductive disorders and metabolic disorders [27], which are conditions that often require antibiotic treatment.

Falling behind the EU - Calling for a routine preventative antibiotic use ban

The UK and the EU banned the use of antibiotics for growth promotion on 1 January 2006. However, ending the use of antibiotics for growth promotion did not lead to the reduction in antibiotic use that some had been hoping for since it remained legal to use antibiotics for routine disease prevention.

Because of this, on 28 January 2022, the EU introduced new laws banning all forms of routine antibiotics use in farming, and all preventative antibiotic treatments of groups of animals [28].

Furthermore, under the new EU legislation, antibiotics can no longer be used to "to compensate for poor hygiene, inadequate animal husbandry or lack of care or to compensate for poor farm management."

The UK was still a member of the EU when the new farm-antibiotic legislation was agreed in 2018, and the government claimed to support it, and said that it would align with the legislation and implement the new provisions subject to a public consultation [29]. In particular, in 2018 the then Secretary of State for Defra said in Parliament that it would apply the restrictions on preventative antibiotic use [30].

Unfortunately, the promised public consultation on new UK veterinary medicines regulations has been repeatedly delayed and no new restrictions on preventative antibiotic use have been introduced. The government has also replaced its commitment to align with the new EU legislation with a seemingly weaker commitment to implement "similar provisions" [31]. The UK is therefore now one of the only countries in Western Europe which still permits routine antibiotic use and preventative group treatments.

Despite this, the UK has made significant progress in reducing its farm antibiotic use by 55% since 2014. The threat of much stricter EU regulations was one of the factors which motivated the farming industry to take voluntary action, as was the increased focus on the issue brought about by the government-appointed Review on Antimicrobial Resistance and growing media attention [4]. The introduction of stronger supermarket policies on farm antibiotics has also helped drive reductions [32].

All of these factors contributed to farming organisations such as the British Poultry Council and the National Pig Association taking voluntary action, some of it led by the industry group the Responsible Use of Medicines in Agriculture (RUMA) [33]. The pig and poultry industry began collecting antibiotic-use data, RUMA set targets for reducing antibiotic use and the British Poultry Council voluntarily chose to end preventative antibiotic use.

The UK's reductions in farm antibiotic use have had a positive effect in reducing antibiotic resistance in some bacteria from livestock [15]. However, reductions in use have stagnated since 2018, and much greater reductions are still achievable.

Unlike the EU, the UK has not introduced any laws which say that antibiotics cannot be used to compensate for inadequate husbandry or poor hygiene. There are concerns that many EU countries will not fully abide by this new law in practice [34], but its existence does mean that pressure now exists to significantly improve European animal husbandry. Similar attempts to improve animal husbandry in the UK would likely lead to much larger reductions in antibiotic use.

In organic farming, minimum husbandry standards are higher, including the use of much later weaning of piglets, slower-growing broiler breeds, much lower stocking densities, appropriate diets, and access to the outdoors. As a result of these differences, antibiotic use tends to be significantly lower in organic farming [18]. Data from UK organic farms certified by the Soil Association shows that these farms use on average four times less the amount of antibiotics than the UK national average [35], demonstrating the potential for further reductions in overall UK farm antibiotic use.

Moving to more sustainable, high-welfare food systems and lower animal production overall is critical in addressing the unsustainable overuse of antibiotics and farming and protecting public health and the environment. Reducing consumption of animal products and increasing consumption of plant-based foods is also vital.

Environmental testing

According to UNEP, antibiotic resistance could have "potential catastrophic consequences on global health", and the natural environment plays a significant role in its spread [36]. Up to 90% of antibiotics by humans or animals are excreted into the environment in an active form [8] and the environment can also be a reservoir for resistant pathogens and antibiotic-resistance genes. Research has found that previously susceptible pathogens are able to acquire resistance genes from environmental bacteria [36].

Many antibiotic-resistance genes occur naturally in soils and can spread to pathogens affecting humans and animals [37]. However, a study of long-term soil archives in the Netherlands demonstrated that the abundance of antibiotic-resistance genes significantly increased since the 1940s, when antibiotics began to be used in humans and animals [38].

Furthermore, a study of archived soils in Denmark found higher levels of antibiotic-resistance genes in manured soils than in soils receiving only chemical fertilisers. The dominant resistance genes varied over time and the dates when specific genes became dominant were roughly similar to when these types of resistance first appeared in human clinical samples. The scientists said that their findings suggested "ARGs in animal manure and humans are historically interconnected" [39].

World Animal Protection, the Alliance to Save Our Antibiotics, and the Bureau of Investigative Journalism decided therefore to carry out testing of environmental samples for antibiotic residues, antibiotic-resistant bacteria, and ARGs.

Samples were collected on public land adjacent to various chicken, pig, and cattle farms. Samples were collected near factory farms (intensive farms) and near higher-welfare farms (extensive farms, which were free-range or organic).

Factory farms, or intensive farms, are farms where large numbers of animals are confined indoors in very small spaces for their entire lives. For example, up to 50,000 chickens may be kept in one shed, with an average space per bird of less than an A4 sheet of paper. Breeding and husbandry practices are focused primarily on productivity, rather than health and resilience. High levels of stress and poor hygiene increase the risk of disease.

Higher-welfare farms, or extensive farms, are farms where each animal has far more space when kept indoors, and more enrichment materials such as straw bedding are used. Free-range and organic farms provide animals with access to the outdoors, and more resilient and slower-growing breeds are used. Minimum husbandry standards on organic farms are far higher than legal minimums, including much later weaning of piglets and no mutilations such as tail docking or teeth clipping are permitted.

Testing of chicken and pig samples

Water and sediment samples were collected from watercourses adjacent to four intensive chicken farms, four intensive pig farms, two extensive pig farms and two extensive chicken farms. The extensive farms were free-range or organic. Two of the intensive pig and poultry farms were in the Wye Valley, with the other two in Norfolk. One sample of poultry litter from an intensive farm was also tested.

Four samples were tested from each farm, two upstream and two downstream, making 48 water or sediment samples in total. Samples were tested for the presence of antibiotic-resistant E. coli and antibiotic-resistant Staphylococcus aureus and for ARGs.

E. coli and S. aureus are the two pathogens causing the most deaths worldwide that are associated with antibiotic resistance. In high-income countries, these two bacteria cause approximately 50% of all deaths associated with or caused by antibiotic resistance [3].

The ARGs tested for, *sul(1)* and *Tet B*, provide resistance to sulphonamide and tetracycline antibiotics respectively. Sulphonamides and tetracyclines are two families of antibiotics classified as highly important in human medicine. Samples from chicken farms were also tested for residues of coccidiostats.

There was a period of extreme drought prior to sampling, and as a result water courses and river flow rates were very low which made the collection of the samples more difficult. The drought also undoubtedly reduced the amount of runoff that would normally have been occurring, and it therefore likely had an impact on the findings.

Despite this, in total 28 (58%) of the water/sediment samples were positive for E. coli, with higher levels generally being found from samples taken from intensive farms.

Resistant bacteria or ARGs were found from at least one sample from all of the intensive farms, and from three of the four extensive farms.

None of the extensive farms had more resistant E. coli or resistant S. aureus in downstream samples than upstream samples, and no ARGs or residues of coccidiostats were found in any of these samples. Therefore, no clear evidence was found that these farms were contributing to higher levels of antibiotic-resistance in the environment. See Table 2.

Table 2. Results from testing of extensive farms

Farm	Type of farm	Location	Results
1	**Extensive pig**	Warwickshire	Resistant E. coli in sediment upstream, two samples, both ESBL and one cefotaxime intermediate resistant and one full cefotaxime resistant, resistant S. aureus in sediment upstream
1	**Extensive broiler**	Herefordshire	
2	**Extensive pig**	Norfolk	Resistant E. coli in sediment upstream, resistant E. coli in liquid downstream
2	**Extensive chicken**	Devon	Resistant E. coli in liquid upstream, resistant S. aureus (MRSA) in sediment upstream

However, while samples from two intensive farms in the Wye valley, one pig one chicken, and one intensive broiler farm from Norfolk, had no more resistant bacteria or ARGs downstream than upstream, and had no coccidiostat residues, the other five intensive farms all had more of at least one type of resistance downstream than was found upstream. See Table 3.

Table 3. Results from testing of intensive farms

Farm	Type of farm	Location	Results
1	**Intensive pig**	Wye	Resistant S. aureus in sediment upstream. Resistant S. aureus in sediment downstream. More resistant S. aureus downstream than upstream.
2	**Intensive broiler**	Wye	Resistant S. aureus (vancomycin-resistant) in sediment upstream. Resistant S. aureus (vancomycin-resistant) in liquid downstream.
3	**Intensive pig**	Wye	Resistant S. aureus (vancomycin-resistant) in liquid upstream. Sulphonamide resistance gene in liquid upstream
4	**Intensive broiler**	Wye	Resistant E. coli (ESBL and intermediate cefotaxime resistant) in sediment upstream. Resistant S. aureus in liquid upstream. Sulphonamide resistance gene in sediment upstream and downstream with more ARG downstream than upstream. Sulphonamide resistance gene in liquid upstream and downstream, with more ARG downstream than upstream. Dinitrocarbanilide (nicarbazin) 74 microg/kg, narasin 1 microg/kg.
1	**Intensive broiler**	Norfolk	Resistant E. coli in liquid upstream and downstream (lower levels downstream). ESBL E. coli that is cefotaxime resistant in liquid downstream sample. No ESBL or cefotaxime resistance upstream.
2	**Intensive broiler**	Norfolk	Resistant E. coli in sediment and liquid upstream and downstream (lower levels downstream). Sulphonamide resistance gene in sediment upstream and downstream (more upstream than downstream). Sulphonamide resistance gene in liquid downstream but none upstream.
3	**Intensive pig**	Norfolk	Resistant S. aureus in sediment downstream. Sulphonamide resistance gene in sediment upstream.
4	**Intensive pig**	Norfolk	Resistant S. aureus (MRSA) in sediment upstream. Sulphonamide resistance gene in sediment downstream.
Poultry litter sample	**Intensive broiler**	Sussex	ESBL E. coli which is fully cefotaxime resistant. Sulphonamide resistance gene.

The findings at these five intensive farms were:

- Two intensive pig farms (one Wye, one Norfolk) had more resistant S. aureus bacteria downstream than upstream (one had no such bacteria upstream).
- One intensive chicken farm (Norfolk) had E. coli resistant to a cefotaxime downstream but not upstream. Cefotaxime is an antibiotic classified as highest-priority critically important in human medicine (HPCIA).
- Another intensive chicken farm (Wye) had more sulphonamide resistance genes downstream than upstream.
- The final intensive pig farm (Norfolk) had more sulphonamide resistance genes downstream than upstream.
- The chicken farm in the Wye valley with the higher levels of sulphonamide resistance genes downstream than upstream also had residues in downstream sediment of dinitrocarbanilide (a component of the coccidiostat nicarbazin) and of the ionophore coccidiostat narasin.

In addition to the above findings, two samples from two farms (an intensive pig farm in Norfolk and an extensive chicken farm) were positive for methicillin-resistant Staphylococcus aureus (MRSA), although the presence of a methicillin-resistant gene was not tested for, so it is possible the bacteria were not full MRSA. Both samples were taken upstream of the farms in question.

Remarkably, five isolates of S. aureus were resistant to the HPCIA vancomycin, although no genetic testing for the *vanA* resistance gene was carried out, so full resistance to vancomycin was not confirmed. Two of these resistant isolates were downstream of an intensive pig farm in the Wye Valley, and two isolates were found upstream and downstream of an intensive chicken farm in the Wye Valley. An isolate was also found downstream of an extensive pig farm. The finding is surprising as only 52 cases of vancomycin-resistant S. aureus (with *vanA* gene) have been found in human infections worldwide [40].

Furthermore, another two farms (one intensive chicken farm in the Wye Valley and an extensive pig farm) had isolates of E. coli that were resistant to the HPCIA cefotaxime. However, in both these cases the isolates were found upstream of the farm.

In addition to the water and sediment samples tested, one sample of chicken litter was tested. E. coli was found which was resistant to the HPCIA cefotaxime. Sulphonamide resistance genes were also found in the sample.

Testing of cattle samples

Four solid slurry samples from intensive dairy farms and one liquid slurry sample from a beef farm were tested, as well as one water sample from an intensive dairy farm. The samples were tested for resistant E. coli and S. aureus and for sulphonamide and tetracycline resistance genes.

All four slurry samples from dairy farms had E. coli, but the beef sample did not. No S. aureus were found in any of the cattle samples.

One dairy sample had resistant E. coli. The E. coli were resistant to cefotaxime, a HPCIA antibiotic in human medicine.

Furthermore, all four slurry samples from intensive farms were positive for sulphonamide and tetracycline ARGs.

Overall incidence of antibiotic resistance found in testing

In total, two hundred and eighty-one *E. coli* isolates were susceptibility tested against the panel of 10 key antibiotics and 25 (8.9%) were resistant to one or more of them. Of these, 22/25 were ampicillin resistant, 8/25 were cefotaxime resistant, 5/25 were resistant to trimethoprim and 2/25 were resistant to cefazoline. Farm types from which these resistant isolates were found were mainly intensive and either poultry or pig.

A total of twenty-three isolates of S. aureus were taken forward for susceptibility screening. Of these, 11/23 (48%) were resistant to one or more antibiotic, and 8/11 of these were found from upstream locations.

Significance of testing findings

Superbugs and antibiotic resistance genes do not remain on the farm. Intensive animal production generates large quantities of animal waste, which is often spread on land for use as a fertiliser or discharged into public water ways. It can also seep into groundwater.

Waterways can act as reservoirs where superbugs accumulate. This is because they harbour discharge from agricultural runoff and human wastewater treatment plants [12][41].

Once in the environment, superbugs can reach humans in multiple ways. This ranges from recreation, water used for drinking and washing, consumption of fish and bivalves from contaminated water, and consumption of crops produced with contaminated manure or water [4][41].

The problem also affects soil health. Manure sludge contaminated with superbugs can enter soil and alter the balance of bacteria. Once in the soil, superbugs can persist there even if there is no further contamination with antibiotics. Studies have shown higher levels of ARGs in soil where manure has been applied for up to six months following application. This suggests ARGs can accumulate in soil over time [41][42].

Antibiotic-resistant bacteria can also be found in the air surrounding livestock farms. Flies and insects also have contact with livestock and manure, contract antibiotic resistant bacteria and transmit it to people. Research from Johns Hopkins University in the USA found that many houseflies near chicken operations carried antibiotic resistant bacteria strains [43].

This is not just a problem for land-based farming. Up to 75% of antibiotics used in aquaculture may also be lost into the surrounding environment [36].

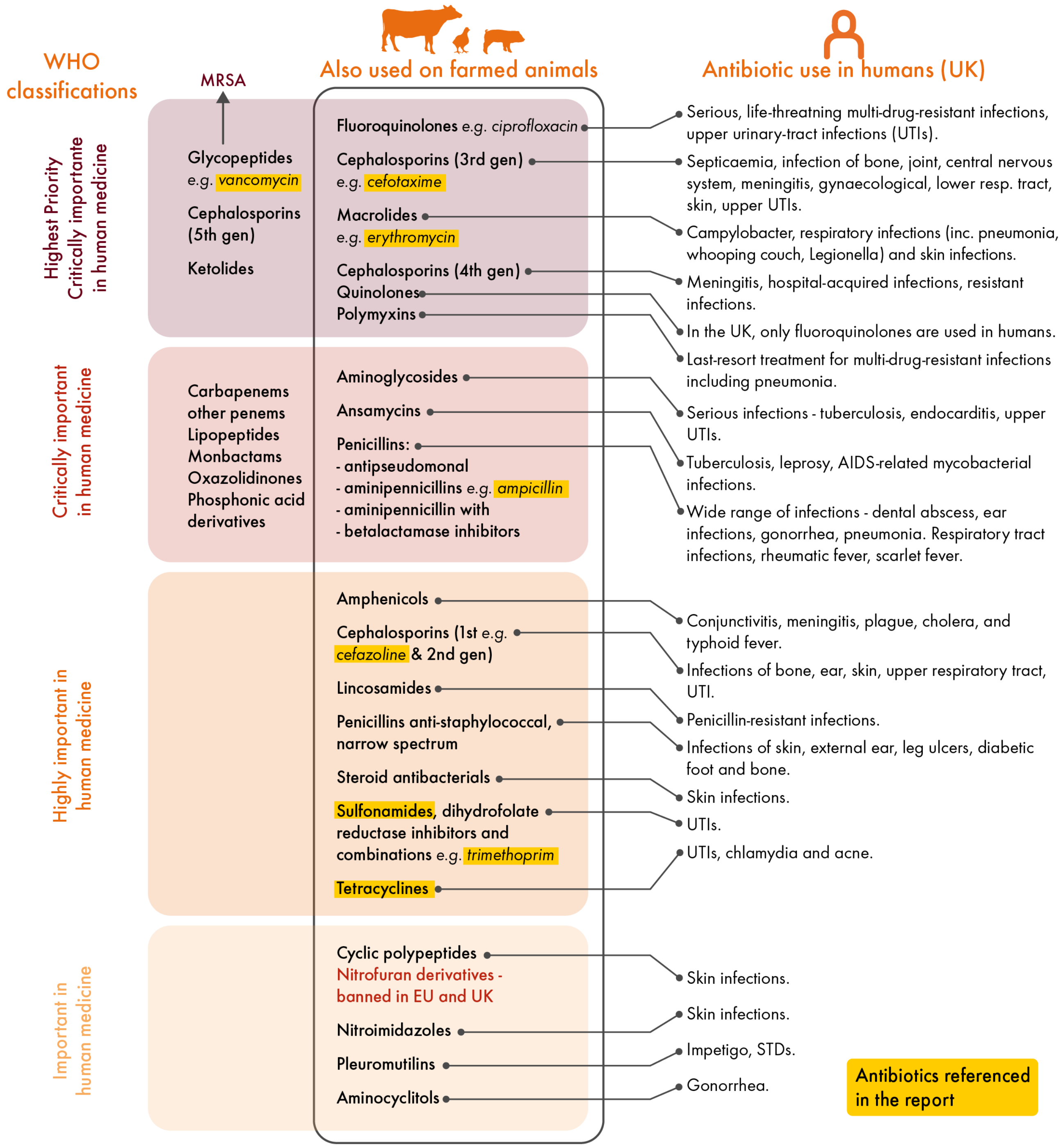
The water and sediment samples tested for this project were collected after a period of extreme drought. This meant that runoff from the farms would have been at a much lower level than usual. Despite this, we found significant numbers of samples had bacteria showing resistance to antibiotics, such as cefotaxime and vancomycin, which are classified by the WHO as critically important in human medicine.

Perhaps because of the drought, there was not always more resistance downstream than upstream. More resistant S. aureus were found upstream than downstream. On the other hand, more sulphonamide resistance genes were generally found downstream than upstream. Also, five of the eight intensive farms had more of at least one type of resistance downstream than upstream, whereas this was not the case for any of the extensive farms.

One intensive chicken farm had cefotaxime-resistant E. coli downstream and not upstream, and two further intensive poultry farms and an intensive pig farm had more sulphonamide resistance genes downstream than upstream. Generally higher levels of sulphonamide resistance genes were found downstream of intensive farms than upstream, and the fact that single chicken litter sample tested also had sulphonamide resistance genes are consistent with findings suggesting that intensive farms are releasing sulphonamide resistance genes into the environment. The chicken litter sample was also positive for cefotaxime-resistant E. coli.

Sulphonamides are widely used in farming and are classified as highly important antibiotics in human medicine by the WHO (see Figure 1) and as critically important in human medicine by the US Food and Drug Administration.

Figure 1. WHO classification of the importance of antibiotics in human medicine [42]



Sulphonamides are usually used in conjunction with another antibiotic, trimethoprim; this combination drug is used to treat urinary-tract infections in humans. Urinary-tract infections are the most common bacterial infection in the world, affecting nearly 25% of all infections in women and resulting in 250 million infections annually. One in three women will need antibiotic treatment by the age of 24.

However, sulphonamides/trimethoprim are used even more widely in farm animals than in humans in the UK. In 2017, 17.4 tonnes of active ingredient were used in humans, whereas 31 tonnes were used in farm animals [44]. There is therefore good reason to believe that farm use is contributing to the sulphonamide-resistance genes found in our testing.

Cefotaxime is a third-generation cephalosporin antibiotic, and these antibiotics are classified as HPCIA in human medicine by the WHO. These broad-spectrum antibiotics are used for treating some cases of sepsis, pneumonia, and meningitis.

Modern cephalosporins (third and fourth generation) were used off-label in some of the poultry industry, but Red Tractor standards no longer permit such use [45]. It seems unlikely that UK chicken farms are still using modern cephalosporins. The presence of cefotaxime-resistant bacteria in poultry litter may be due to previous use years earlier, or due to ongoing selection caused by the use of other related antibiotics.

The finding of several S. aureus resistant to the HPCIA vancomycin requires further investigation to see if the isolates have the *vanA* resistance gene and are fully vancomycin resistant. Vancomycin is in the Glycopeptide family of antibiotics and is the antibiotic of choice for treating most human MRSA infections, so widespread vancomycin resistance in the environment is of concern. It is also surprising as vancomycin is only used in hospitals in human medicine. A closely related Glycopeptide antibiotic, avoparcin, was used very widely as a growth promoter in the UK and the EU in intensively farmed livestock, but this use was banned in 1997.

An important finding was the presence of coccidiostat residues in a sediment sample downstream of an intensive broiler farm in the Wye valley. One chemical found, dinitrocarbanilide, is a component of the coccidiostat antimicrobial nicarbazin. A residue of the ionophore antibiotic narasin was also found. Nicarbazin and narasin are often used together in the coccidiostat product Maxiban [46]. These substances are not used in human medicine, so it is clear that the residues originate from chicken farming.

A 2019 review by the European Food Safety Authority (EFSA) of the safety, including the environmental safety, of nicarbazin provides reasons for being concerned about the residue of 74 microg/kg found in our study. According to EFSA, exposure in water for 21 days at 14 microg/L to dinitrocarbanilide reduced the size of crustaceans called *Daphnia magna*, at 35 micro/L reproduction and weight was reduced and at 85 microg/L none of the crustaceans survived. Our finding was in sediment, and not water, and chemicals may be less bioavailable in sediment than in water and therefore less likely to cause harm. Nevertheless, our finding raises concerns.

No toxicology tests were carried out with sediment-dwelling organisms for the EFSA review, so this is a significant omission and makes the significance of the residue found more difficult to interpret.

The same EFSA review states that dinitrocarbanilide is highly persistent in soil (but is hydrophobic, which is perhaps why it was not found in water but in sediment). For this reason, EFSA says harm to terrestrial organisms cannot be excluded and that the potential of dinitrocarbanilide to bioaccumulate in soils over years should be investigated through field monitoring. Clearly this is not being done at present.

One of the dairy samples was resistant to the HPCIA cefotaxime, which is a third-generation cephalosporin. The antibiotic ceftiofur, another third-generation cephalosporin, has been widely overused in dairy farming in the UK and worldwide because it can be used with a zero-milk withdrawal period: it does not leave residues in milk as some other antibiotics do, so milk produced during treatment can be sold for human consumption. However, more recently, there has been a significant reduction in the use of HPCIAs in dairy farming as Red Tractor dairy standards now restrict the use of these antibiotics [15]. The resistance detected may be due to ongoing use but could also be because of previous use before restrictions were introduced.

Key findings

1. In total, 44% of E. coli and 66% of S. aureus bacteria isolated during testing were resistant to antibiotics. Seven strains of E. coli and five strains of S. aureus were found with resistance to highest-priority critically important antibiotics. E. coli and S. aureus are the two pathogens causing the most deaths worldwide that are associated with antibiotic resistance.

2. The sulphonamide resistance gene *Sul*(1) was found in all cattle slurry and chicken litter samples tested, and was found in greater numbers downstream than upstream of factory farms. This suggests that factory farms are contributing to the environmental spread of resistance to this sulphonamide antibiotics, which are highly important in human medicine.

3. Residues of coccidiostat antimicrobials, which are very widely used in chicken farming, were found downstream of a chicken factory farm in sediment. One of the chemicals found is highly persistent in soil and the European Food Safety Authority says it may be harmful to terrestrial organisms.

Safeguarding public health, ending unhealthy animal husbandry

The most important and effective strategy for minimising antibiotic resistance spreading from farms is to keep antibiotic use at a minimum, and this inevitably must involve major improvements to animal husbandry and animal health.

According to EFSA, the most important way in which resistance spreads from farms is through the spreading on land of manure or slurry containing antibiotic-resistant bacteria or antibiotic residues - although antibiotic-resistant bacteria can also be released into the environment by air. Furthermore rodents, flies, and insects that have contact with livestock and manure can be vectors for transmission of antibiotic resistance [47].

Proper composting for a sufficient period time of animal manure, or the use of anaerobic digesters can reduce, but not eliminate, the number of resistant bacteria or residues in manure. In addition, anaerobic digestion can also sometimes increase horizontal gene transfer of resistance genes [47]. This is why reductions in antibiotic use are essential.

An EFSA report published in 2021 about the role played by the environment in the spread of antibiotic resistance through the food chain said that the main factor linked with antibiotic resistance at the farm level is current or historic antibiotic use in livestock breeding and production. According to EFSA "prevalence and diversity of antimicrobial resistance in livestock associated bacteria are a function of antimicrobial use and husbandry/biosecurity practices" [47].

In this report, EFSA referred to a previous conclusion that they had come to in a 2017 joint report with the EMA, which was that "animal husbandry and disease prevention measures that could be implemented to improve animal health and welfare, and therefore reduce the need to use antimicrobials, should be implemented" [47][48].

Clearly improved regulation of antibiotic use, aimed at ending all forms of routine use and all purely preventative group treatments, is essential, and would lead to even greater reductions than those already achieved by voluntary action. However, as stated by EFSA and the EMA, action on husbandry is also required.

The problem must be addressed at its source – the wholesale dependence of factory farming on antibiotic overuse to cover up cruel, outdated practices. Reducing farm antibiotic use to truly sustainable levels means building the wellbeing and immunity of farm animals. This means putting an end to the worst animal-welfare abuses in factory farming, including poor hygiene, the early weaning of young animals, the use of non-resilient high-productivity breeds, excessively high stocking densities, and painful mutilations. Farm animals in higher-welfare systems have reduced stress and improved immunity and resilience to disease. This in turn, requires fewer antibiotics [22][49][50][51].

In their 2017 report the EMA and EFSA stated that "Farming systems with heavy antimicrobial use should be critically reviewed, to determine whether/how such systems could sustainably reduce the use of on-farm antimicrobials. If a sustainable reduction in the use of on-farm antimicrobials is not achievable, these systems ideally be phased out" [48].

The world's retail, animal production, and finance sectors, and governments and intergovernmental organisations must act now to protect our animals, people, and planet.

Recommendations

1. The government must introduce new Veterinary Medicines Regulations which:

    - Prohibit all forms of routine farm antibiotic use
    - Prohibit purely preventative antibiotic group treatments
    - Restrict group antibiotic treatments to exceptional cases, where disease has been diagnosed within the group, and where there is a high risk it will spread to other animals, and where no appropriate alternative treatments are available
    - Prohibit antibiotics being used to compensate for poor hygiene or inadequate husbandry.

2. Measures must be taken aim at improving animal health and welfare so that further large reductions in antibiotic use can be achieved. These should include reducing stocking densities to ensure that animal health is not compromised, improving piglet health at weaning, ending routine mutilations such as tail docking, and avoiding the use of non-resilient breeds of animals which require particularly high antibiotic use.

3. There is a need for a national surveillance programme of the spread of antibiotic resistance and antibiotic residues from farms into the environment. A recent cross-departmental programme has been launched, "Pathogen Surveillance in Agriculture, Food and the Environment", which will test the application of genomic technologies in the surveillance of foodborne pathogens and antimicrobial resistant (AMR) microbes in all four nations of the UK [52]. This is a welcome development and will involve testing for antibiotic resistance in several river catchment sites [53]. However, it is important that this pilot project leads to an ongoing national environmental surveillance programme of antibiotic resistance. There is also a need for testing for antimicrobial residues in the environment, including for residues of those antimicrobials known to be toxic to wildlife or to be at risk of bioaccumulating.

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