Swedish Civil Contingencies Agency

Increased presence of multi-resistant intestinal bacteria

A general overview including a scenario analysis within the Swedish National Risk and Capability Assessment

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Preface

The Swedish version of this report was published in early November 2015. Shortly thereafter it was reported that a colistin-resistant gene (mcr-1) had been identified in China, undeniably confirming the relevance of our report. Colistin resistance has been identified before, but this time it was in a form that could be transmitted between bacteria in the same manner as ESBL, making transmission far easier. Similar reports followed from several more countries, and in February 2016 the Public Health Agency of Sweden reported that the mcr-1 had been identified in Sweden. Colistin is one of the few remaining antibiotics effective even against CPE (carbapenemase-producing Enterobacteriaceae, in Sweden known as $ESBL_{CARBA}$). It is an old antibiotic that has not been recommended due to side effects. The spread of colistin resistance in antibiotics is both feared and anticipated – now it has finally emerged. Hopefully the spread will not occur as quickly and widely as ESBL or CPE in order to provide society time to learn more and adapt routines, and possibly develop new antibiotics.

In Sweden, the Government recently presented a new national strategy for containing antibiotic resistance. According to the strategy, knowledge and awareness of the issue must increase. This is true for professionals within the One Health perspective (humans, animals, food and the environment) and elsewhere, as well as for the general public. As always, knowledge is power – we need to increase our awareness and learn more! This is also confirmed by the British Review on Antimicrobial Resistance who recently published its final report.

The MSB is by way of this report, aims to contribute to this ongoing effort, in hope of increasing awareness of the risks with antibiotic resistance from a civil contingencies' perspective. This report also goes beyond risk awareness, by including what can be done by actors within civil contingencies to prevent and manage antibiotic resistance in Sweden.

Antibiotic resistance is a global issue, and must be addressed as such. We therefore hope that our report will encourage other countries to include the civil contingencies' perspective in the work on containment of antibiotic resistance.

Cecilia Nyström,

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Content

Executive summary

About the report

Antibiotics save lives. An increased resistance to antibiotics for bacteria in the outside world will make this more difficult, and in the extreme case impossible. The MSB has according to its instructions[1] the task of identifying and analysing such vulnerabilities, threats and risks in society that can be regarded as especially serious. MSB considers one such risk to be antibiotic resistance.

In this report antibiotic resistance is analysed from a fictive scenario that describes an increased presence of multi-resistant intestinal bacteria in the population, a situation that develops over several years. This is by definition a so called creeping risk, which differs from more traditional risks in which a sudden event often is in focus.

The report is a basis for a national analysis that MSB has been commissioned by the Government in its 2015 appropriation directive. The report can also be used as a base by responsible actors[2] within civil contingencies to increase awareness of antibiotic resistance in intestinal bacteria and how society can prevent and ultimately manage an increase in the presence of such bacteria.

The situation in Sweden

Sweden has a long standing tradition within the work on containing antibiotic resistance and the prevention of communicable diseases. The Public Health Agency of Sweden and the Swedish Board of Agriculture are currently commissioned by the Government to oversee a National Coordinating Mechanism for the government agencies' effort to contain antibiotic resistance and healthcare-associated infections. A number of government agencies together with various other actors meet regularly to collaborate on Swedish work in the field. The agencies are also commissioned by the Government to produce a joint-agency action plan. The plan was published in March 2015 – *Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections – Base for the Continued Work of the Government Agencies*. The Action Plan provides a description of what a number of central government agencies have committed to in upcoming years in regard to humans, animals, food and the environment.

The type of resistance depicted in this report, ESBL with carbapenem resistance, can be found in various bacteria, many of which belong to the family

[1] Swedish government agencies are governed by a specific category of ordinance called instructions and the annual appropriation directives.

[2] The term *actors* refer to public, private and nonprofit organisations. These can be municipalities, county councils, authorities, voluntary organisations, companies or spontaneous social networks.

Enterobacteriaceae, where *Escherichia coli* (*E. coli*) is included.[3] Many bacteria within this family are present in the intestinal flora of humans and animals. Bacteria with ESBL can be treated with a category of antibiotics called carbapenems, while bacteria producing $ESBL_{CARBA}$ (CPE) are resistant to carbapenems. Apart from carbapenems there are no proven antibiotics or treatment methods available. Carbapenems are therefore considered a "last resort" when treating infections with multi-resistant bacteria. When a bacterium is resistant against carbapenems, very few treatment alternatives remain. In Sweden, it is mandatory to report $ESBL_{CARBA}$ when detected in both humans and animals. Furthermore when a bacterium with $ESBL_{CARBA}$ is discovered in humans, tracing is mandatory.

An *E. coli* that is resistant functions in the same manner as a non-resistant *E. coli* as long as it remains within its natural environment, the intestinal system. It is when certain *E. coli*, resistant or non-resistant, ends up in particular areas of the body where they are not supposed to be that these bacteria may cause infection. It is therefore far from all carriers that become ill due to carriage.

From an international perspective, Sweden is considered as having a low presence of resistant bacteria. Bacteria and resistant genes, including the type used in the scenario (*E. coli* with $ESBL_{CARBA}$), are easily transferred across borders. ESBL-producing bacteria are present in humans as well as animals in Sweden, although the presence is low in international terms. The Public Health Agency of Sweden estimated, in a joint-agency report, that nearly five percent of the human population carries such bacteria. The Agency also warns in particular about the development of $ESBL_{CARBA}$ where 46 cases were documented in 2014, four of which had been infected domestically. A majority of the cases were imported from other countries where care had been received through for example, emergency care or medicinal tourism. No cases of $ESBL_{CARBA}$ have been found so far, in animals in Sweden.

Consequences, probability and capability

The report reveals that the consequences for society may be significant if an increased spread of multi-resistant intestinal bacteria occurs in Sweden. The greatest consequences arise within healthcare as well as human life and health. Tightened hygiene routines may also affect functionality within large parts of society. The concern for infection may result in greater need for information. If the public's expectations of healthcare and information are not met, trust in society's institutions can decline.

In the scenario, the number of individuals in the southern part of Sweden that carry *E. coli* with $ESBL_{CARBA}$ increases to five per cent over a five year period and bacteria with resistance is discovered in animals, food and the environment. Experts reason that a situation where five percent of the Swedish population carries $ESBL_{CARBA}$ could be a reality already within 10-15 years, providing that $ESBL_{CARBA}$ with high likelihood will spread as quickly and widely

[3] In English, these bacteria are often labelled carbapenemase-producing *Enterobacteriaceae* (CPE).

as commonly occurring ESBL. In principle, it is only a matter of time before such a spread will occur. The uncertainties include both how the consequences will appear and how and to what extent resistance mechanism like $ESBL_{CARBA}$ are spread between humans and the environment.

The preventive work is in principle about slowing down the momentum of the spread. This work is mostly comprised of having knowledge and being compliant with rules and regulations. In Sweden, there is expertise concerning the risks of multi-resistant intestinal bacteria and to some extent how it is spread. However, that knowledge and expertise are not widespread. Public and private actors as well as the general public need to increase their knowledge of the consequences of an increased spread of antibiotic resistance and how it can be prevented and contained. Therefore, central government agencies, county administrative boards, county councils and municipalities need to consider whether antibiotic resistance should factor into their respective risk and vulnerability analyses, if not already the case.

In the managing phase, adequate preconditions are required in order to achieve detection and early warning relating to the presence of multi-resistant intestinal bacteria, for example $ESBL_{CARBA}$. This includes both single outbreaks and the increased spread across society. The MSB reckons that such preconditions exist for detection and early warning regarding humans, animals and in meat, but not for other food or the environment. Adequate preconditions for detecting and identifying an increased presence of carriage in the population at an *early* stage are limited, especially if the increase does not result in more people falling ill and thereby being subjected to testing. In the Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections, a number of measures are described, to be executed within the next few years, to enhance the monitoring of the presence of resistant bacteria in society. Thereby the preconditions for early detection of an increased spread are also enhanced.

To enhance the capability to prevent and manage an increased presence of $ESBL_{CARBA}$ and other multi-resistant bacteria, there is a need for additional plans and routines. This is highlighted in the Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections. According to the Action Plan the responsible agencies should develop a suggestion for a cross-sectional strategy for management of $ESBL_{CARBA}$ in humans, animals, food and the environment.

The MSB's recommendations

Based on the conclusions above regarding society's ability to prevent and manage an increased presence of multi-resistant intestinal bacteria, the MSB recommends that:

- concerned parties within emergency preparedness aspire to increase their knowledge of the risks involving antibacterial resistance, especially $ESBL_{CARBA}$.

- government agencies with special responsibilities for emergency preparedness, and counties and municipalities, investigate and

consider including antibacterial resistance in their respective risk- and vulnerability analyses.

- intentions and measures described in the government agencies' Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections are executed according to plan.
- responsible actors enable and develop Swedish government agencies' international work on containment of antibiotic resistance.

1. Introduction

Antibiotics save lives. Increased resistance to antibiotics for bacteria in the outside world will make this more difficult, and in the extreme case impossible. Antibiotic resistance is a global challenge and a major threat to today's healthcare and society, an issue raised by the World Health Organization (WHO)[4]. The presence of resistant bacteria is continually increasing at a relatively slow and creeping pace that appears difficult to prevent and even limit. The Swedish Civil Contingencies Agency (MSB) has previously, within the framework of strategic foresight, analysed antibiotic resistance from a future perspective, focusing on the impact of a more far-reaching antibiotic resistance, in the long run for societal security.

The primary consequence of antibiotic resistance is that modern healthcare can no longer be conducted and administered in the same manner. Morbidity levels and mortality rates resulting from infections will increase. Furthermore some specialised care will be more difficult to administer or impossible to maintain.[5] This also means that Vital Societal Functions will be affected, and ultimately society in general, which makes antibiotic resistance a critical issue for the MSB to address.

In this report antibiotic resistance is analysed based on current preconditions, in contrast to the above mentioned report focusing on an increase in antibiotic resistance as a future event. The analysis is based on a fictive scenario that describes an increased presence of multi-resistant intestinal bacteria in the population, a situation that develops over several years. This is by definition a so called creeping risk, which differs from more traditional risks in which a sudden event often is in focus.

1.1 Purpose of the report

The MSB has according to its instructions[6] [7] the task of

identifying and analysing vulnerabilities, threats and risks in society that can be regarded as especially serious, in cooperation with government agencies[8], municipalities, county councils, organisations, and businesses.[9]

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[4] World Health Organization, 2014, *Antimicrobial resistance: global report on surveillance 2014.*

[5] MSB, *Antibiotic resistance and societal security – What would a more far-reaching antibiotic resistance mean for societal security?*, MSB677 - May 2014.

[6] Swedish central government agencies and county administrative boards are governed by a specific category of ordinance called instructions and the annual appropriation directives.

[7] Förordning (2008:1002) med instruktion för Myndigheten för samhällsskydd och beredskap [Instruction for the Swedish Civil Contingencies Agency]

[8] Central government agencies and county administrative boards are both agencies sorting under the Government and will therefore be referred to as *government agencies* in this report. For more information on the Swedish model of government

MSB considers one such risk to be antibiotic resistance.

In the years 2014 and 2015, the MSB conducted a scenario analysis of an increased presence of intestinal bacteria resistant to several antibiotics (multi-resistance), within the framework of the National Risk and Capability Assessment. The scenario analysis is presented in this report, together with a general overview of the issue, to increase knowledge within civil contingencies. The report is a basis for a national analysis that the MSB has been commissioned by the Government in its 2015 appropriation directive.

"15. The Swedish Civil Contingencies Agency shall present a national assessment of society's capabilities, risks, vulnerabilities and identified and completed actions regarding emergency preparedness, in cooperation with concerned parties. In the assessment, information security shall also be considered. To be submitted to the Government Offices (Ministry of Justice) on the 11th of March 2016 at the latest." [10]

The report can also be used as a basis by actors within civil contingencies to increase awareness of antibiotic resistance in intestinal bacteria and how society can prevent and ultimately manage an increase in the presence of such bacteria.

1.2 Starting points and limitations

1.2.1 About the analysis and the MSB's responsibility

According to the Swedish principle of responsibility, actors are responsible both on a day-to-day basis as well as in a crisis. Regarding issues related to communicable diseases, it is also clearly stated in laws and ordinances which various public authorities, including government agencies, are accountable in the matter. It is not the purpose of this report to review the division of responsibilities and the general capability within the Swedish work on communicable diseases. The report instead focuses on what capabilities society as a whole require in order to prevent and manage an increased presence of multi-resistant intestinal bacteria. Specific segments of the Swedish work on communicable diseases will be reviewed, not communicable diseases in its entirety.

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administration, see http://www.government.se/how-sweden-is-governed/the-swedish-model-of-government-administration/ .

[9] Translated by the author.

[10] Translated by the author. Justitiedepartementet, 2014, *Regleringsbrev för budgetåret 2015 avseende Myndigheten för samhällsskydd och beredskap* [The Ministry of Justice, *The 2015 Appropriations Directive for the Swedish Civil Contingencies Agency*].

1.2.2 Limitations in the scenario

There are many types of antibiotic resistance, within various types of bacteria. While analysing antibiotic resistance within the framework of the national risk and capability assessment, the MSB has chosen to limit the analysis to antibacterial resistance in intestinal bacteria (*Enterobacteriaceae*).

The scenario is set up to be a *worst credible scenario* , in contrast to a *worst case scenario*, which means that it should lead to large or very large consequences and also be perceived as plausible based on best available knowledge and expertise in the field of the scenario.

The scenario assumes a cross-sectional ”One Health”-perspective, a term that incorporates an interdisciplinary method using a holistic approach to humans, animals, food and the environment to promote health and security on all levels.[11] The term is used by the American authorities for communicable diseases, the Centers for Disease Control and Prevention (CDC).[12]

The scenario is restricted to describe *one* kind of bacteria with *a specific type* of antibiotic resistance, in contrast to the MSB's earlier work with a future focus where no clear position was taken regarding bacteria or resistance type.[13] The scenario analysed in this report is therefore one of many possible and relevant scenarios. In reality, the bacteria and resistance described in the scenario will be complemented with other bacteria and other forms of resistance with either similar or completely different effects. The consequences and management described in the report can also be valid for other intestinal bacteria of the same family. However, reality is more complex than the scenario can convey and the consequences of antibiotic resistance can be more widely spread than the consequences described based on the scenario.

In some instances, bacteria carrying certain types of resistance can be spread in other ways, such as MRSA[14], in which the carriage is primarily on the skin, in the nose and where skin flakes can spread disease. Certain bacteria with particular types of resistance and means of transmission can therefore lead to other consequences and require a different course of management than the one accounted for in this report.

1.3 Reading guide

This report is divided into several sections. Chapter two contains descriptions of method and execution. Chapter three provides general background

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[11] For more information on the concept One health, see for example Zinsstag, J. et al., *From “one medicine” to “one health” and systemic approaches to health and well-being*, 2011.

[12] See for example http://www.cdc.gov/ncezid/dhcpp/one_health/mission_statement.html, downloaded 2015-09-16.

[13]MSB, *Antibiotic resistance and societal security – What would a more far-reaching antibiotic resistance mean for societal security?*, MSB677 - May 2014.

[14] Methicillin-resistant yellow staphylococcus (*Staphylococcus aureus*)

information on antibiotic resistance and ESBL, the presence of these bacteria today and an overview of previous assessments on the subject. In chapter four, a review is made of the work on the containment of antibiotic resistance in Sweden. The purpose of chapter three and four is to provide an introduction of the risk itself as well as the prevention and management, thereby describing the context for the scenario and the analysis.

In chapter five the scenario is introduced. In chapter six the analysis of society's ability to prevent and manage the scenario is presented. In this chapter an assessment of the consequences, rationale regarding probability, uncertainties and a sensitivity analysis are included.

Antibiotic resistance is a complex matter that requires knowledge of medicine as well as communicable disease control along with familiarity with various regulations and actors within the area. Since the report focuses on civil contingencies, more detailed descriptions regarding how antibiotic resistance works and the responsibilities within Swedish communicable disease control are found in the appendices in the Swedish version of the report.[15] The appendices have not been translated as they were intended for the benefit of Swedish responsible actors. Some additional information is available through the reference list.

Translations of Swedish publications' titles as well as legislation titles are primarily made by the author of this report. When titles are mentioned in the text the English translation is also given. For titles in footnotes, only translations for acts and ordinances are given. For other titles, the reader is referred to the reference list in chapter 8 for a translation.

For general information on the roles and responsibilities of the government agencies specifically responsible for these matters, we refer to the webpages of the Public Health Agency of Sweden[16], the Swedish Board of Agriculture[17], the National Food Agency[18], the National Board of Health and Welfare[19] and the National Veterinary Institute[20].

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[15] MSB, *Ökad förekomst av multi-resistenta tarmbakterier*, 2015.

[16] http://www.folkhalsomyndigheten.se/about-folkhalsomyndigheten-the-public-health-agency-of-sweden/

[17] http://www.jordbruksverket.se/swedishboardofagriculture.4.6621c2fb1231eb917e680002462.html

[18] http://www.livsmedelsverket.se/en/

[19] http://www.socialstyrelsen.se/english

[20] http://www.sva.se/en

2. Method and execution

The analysis has been conducted in several stages, based on the MSB's methodology for the National Risk and Capability Assessment.

First, a relevant "worst credible scenario" was created, with an overall effect on society. The scenario was created based on existing literature and interviews with experts. The scenario was thereafter analysed together with experts during a workshop. The results from the workshop were then further analysed with additional material from existing literature.

The scenario and the initial analysis were conducted with support from the Swedish Defence Research Agency (FOI).

2.1 The method for National Risk and Capability Assessment

An important objective of the National Risk and Capability Assessment is to work with scenario analyses. The analyses include the ability to prevent and manage an event, consequences and rationale regarding probability. Additionally there are also assessments regarding uncertainty and sensitivity. The analyses will provide conclusions regarding vulnerabilities and shortcomings in capability, consequences for the risks being analysed and suggestions of measures to strengthen the capability to prevent and manage such events. For a more extensive description of the work and methodology of the National Risk and Capability Assessment the reader is referred to *Risker och förmågor 2013 - Redovisning av regeringsuppdrag om nationell risk- och förmågebedömning*.[21] Currently there is no description of the methodology available in English.

2.2 Production of the scenario

The aim of the scenario is to describe the basic characteristics of antibiotic resistance – a creeping passage of events with a global flow and transmission over different areas and functions. The scenario illustrates how a reservoir of intestinal bacteria with $ESBL_{CARBA}$ is accumulated in Sweden through a larger human carriage, presence in animals and spread among humans, animals and the environment. This differs from other scenarios within the National Risk and Capability Assessment in that the chain of events is extracted over several years and no acute phase is identified to clearly indicate the event has taken place.

A central question which emerged during the creation of the scenario was if and when the responsible actors would notice the changed operational picture in which the share of the population carrying *E. coli* with $ESBL_{CARBA}$ increases more quickly than expected.

[21] MSB, *Risker och förmågor 2013 – Redovisning av regeringsuppdrag om nationell risk- och förmågebedömning*, 2014.

There is a long list of critical factors for a scenario involving antibiotic resistance:

- type of bacteria
- the main presence of the bacteria
- who is affected or becomes a carrier
- ways of spreading and knowledge regarding ways of spreading
- type of resistance
- whether the disease caused by the bacteria is treatable with antibiotics
- whether there are new antibiotics under development or alternative treatment methods available
- possibilities for testing and monitoring.

The type of bacteria is connected to whether the bacterium is endogenous and belongs to the normal flora, if it is toxin-producing or pathogenic. *E. coli* is a bacterium considered belonging to the normal flora. It exists among humans and animals as well as in the environment and can be spread institutionally through healthcare, the livestock industry and food production, particularly in cases where there is a lack of knowledge regarding both the origins as well as method of transmission.

$ESBL_{CARBA}$ is considered almost completely resistant (pan-resistant) to antibiotics, given the lack of new antibiotics in development. If *E. coli* leads to infection, the treatment is antibiotics, but in general it is only when the antibiotics are ineffective or the patient is tested that the antibiotic resistance is discovered. Bacteria are generally treated with antibiotics when they cause disease, otherwise the antibiotic resistance provides little beneficial consequences to society (even though there are implications for people or animals who are carriers). The factors listed above show the complexity and the variety of possible scenarios that can be created for antibiotic resistance, before taking specific species of bacteria or resistance mechanisms into consideration.

2.3 The analysis

The analysis in this report began with a workshop conducted with experts on the 25th of September 2014 based on the scenario in the report. Rationale regarding the unfolding of events, probability, consequences and preventive measures were summarised and distributed to the participants, who were given the opportunity to comment on the summary.

The following actors were represented at the workshop: the Public Health Agency of Sweden, the University of Gothenburg, the Swedish Board of Agriculture, the Karolinska Institute, the National Food Agency, the Medical Products Agency, the County Administrative Board of Skåne, The Swedish Civil Contingencies Agency, the Swedish Environmental Protection Agency, the

Region Skåne[22], the Swedish Board of Health and Welfare, the National Veterinary Institute, the Swedish Association of Local Authorities and Regions and the Uppsala University/ReAct.

In addition, the MSB has been in contact with representatives of the Swedish Work Environment Authority, the Swedish Agency for Marine and Water Management and the City of Lund to provide further quality assurance and completeness of the results from the workshop. All parties mentioned above have been given the opportunity to read and comment on the Swedish version of the final report. The translation is made by the author, with assistance from Susan Edner at Executive English.

[22] The County Council of Skåne.

3. Background

The purpose of this chapter is to provide context to the report scenario which is about a creeping increase of multi-resistant intestinal bacteria (*Enterobacteriaceae*) within the Swedish population.

Antibiotic resistance is a cross-sectional, global challenge that stretches across society due to the fact that genes and bacteria carrying resistance can be transmitted between people, animals, food and the environment. If resistance is developed within an area, this resistance potentially spreads and affects other areas and functions despite significant efforts may already have been made within these other areas to limit the spread. The spread knows no boundaries, therefore cross-sectional work (humans, animals, food and the environment) must be conducted nationally, regionally and locally. Resistance is spread across borders, therefore the issue must be viewed in a comprehensive, international perspective.

The chapter provides a description of multi-resistant intestinal bacteria, how they spread, how large the spread is in Sweden, and makes a comparison with the spread in the rest of the world. Furthermore, there is a brief summary of some earlier assessments of the area.

3.1 Antibiotic resistance and ESBL

Since the beginning of time, bacteria have had the ability to make themselves unresponsive, to become resistant, against potential threat. Antibiotic resistance is therefore a natural defence mechanism. As long as alternative antibiotics exist, infections can be treated, but resistance today is so vast that for particular types of bacteria with specific types of resistance, eventually, antibiotics will be ineffective e for treatment. Humans' and animals' ability to fight disease is thereby considerably reduced. This means that, for example certain cases of urinary tract infections and blood poisoning will be difficult to treat resulting in more deaths due to untreatable infections. Also today's livestock industry requires access to effective antibiotics. This also means that events such as influenza pandemics, communicable animal diseases[23] and large scale accidents or terror attacks (situations in which many people are injured and thereby risk developing wound infections), pose the risk of far more serious consequences than today.

The type of resistance depicted in this report, ESBL with carbapenem resistance ($ESBL_{CARBA}$) or CRE (carbapenem-resistant *Enterobacteriaceae* in English), can be found in various bacteria, many of which belong to the family *Enterobacteriaceae*, including *Escherichia coli* (*E. coli*). Many bacteria within

[23] Epizootics and zoonoses. An influenza pandemic is an example of a zoonosis. A zoonosis can be a form of an epizootic in which disease can be transferred between humans and animals. A zoonosis does not have to be an epizootic, for example in cases where animals do not become ill, but still can spread the disease.

this family are present in the intestinal flora of humans and animals.[24] Other bacteria in this family can be found in the environment (water and soil). The analysis is based on *E. coli*, but many of the results can be valid for other bacteria of the family *Enterobacteriaceae*, where another path of transmission is faecal-oral (faeces-mouth) infection. On the other hand, the consequences and required management can vary for other resistant bacteria with differing paths of transmission.

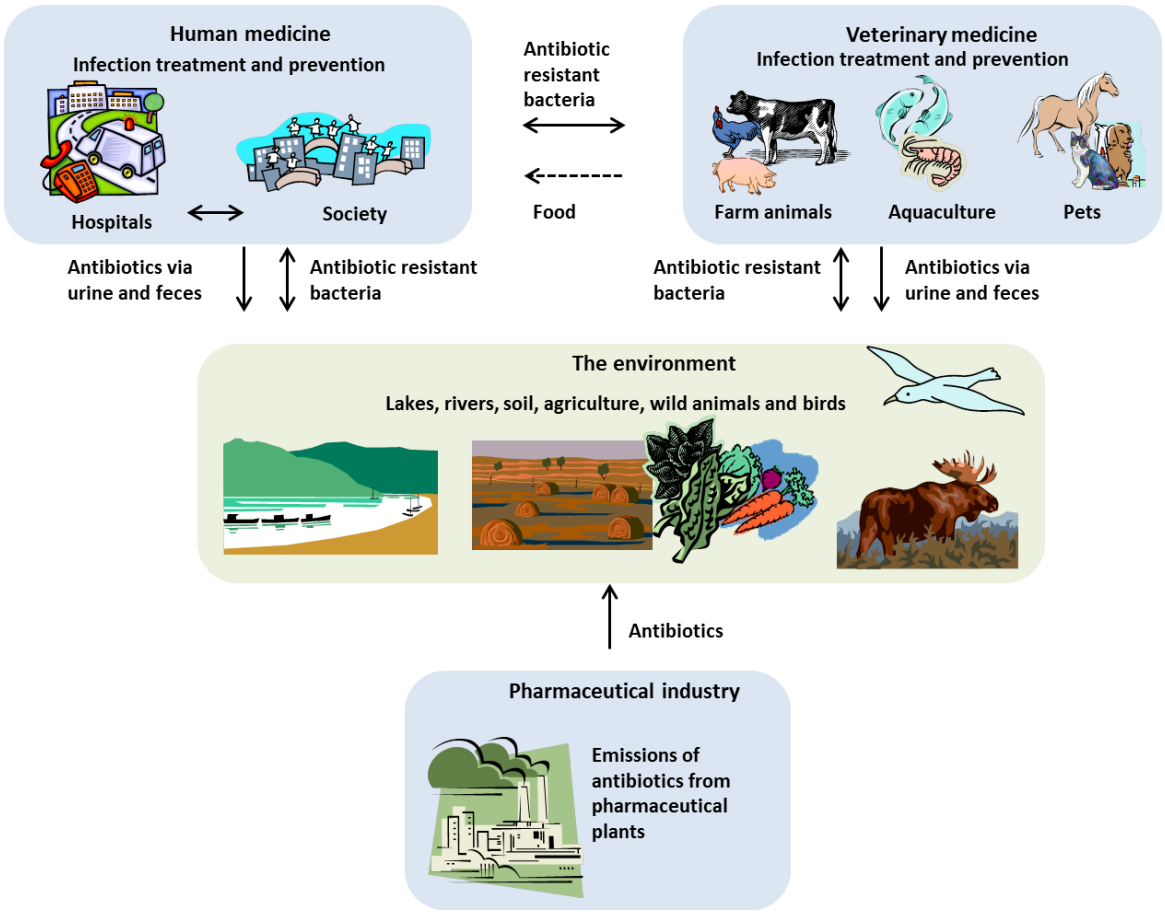
An *E. coli* that is resistant functions in the same manner as a non-resistant *E. coli* as long as it remains within its natural environment, the intestinal system. It is when certain *E. coli*, resistant or non-resistant, ends up in particular areas of the body where they are not supposed to be that these bacteria may cause infection. It is therefore far from all carriers that become ill due to carriage. Also, infection caused by resistant bacteria is more difficult to treat than infection caused by non-resistant bacteria since antibiotics normally used are rendered ineffective.

The analysed scenario describes a situation that has not yet occurred, in which the presence of *E. coli* with a particular type of resistance, $ESBL_{CARBA}$[25], increases more rapidly than expected. The factor that poses the threat is the resistance of the type $ESBL_{CARBA}$. In the scenario, the share of the population in southern Sweden carrying *E. coli* with $ESBL_{CARBA}$ increases to five per cent over five years and resistant bacteria are then discovered within animals, in food and the environment.

The picture below illustrates how ESBL-producing intestinal bacteria can be spread between humans, animals, food and the environment.

[24] Examples of other bacteria in the same family are *Klebsiella pneumoniae*, *Salmonella* and *Shigella*.

[25] $ESBL_{CARBA,}$ (Extended Spectrum Beta-Lactamase and Carbapenems) is a term used for broad-spectrum betalactamase that can break down betalactam antibiotics (penicillins, cephalosporins and carbapenems). In English, the term CRE is more widely used. For more info on $ESBL_{CARBA}$, see http://www.folkhalsomyndigheten.se/amnesomraden/smittskydd-och-sjukdomar/smittsamma-sjukdomar/esblcarba/ (in Swedish). For more info on CRE, see http://www.cdc.gov/hai/organisms/cre/cre-patientFAQ.html



Picture 1. Ways of spreading for ESBL-producing *E. coli*. (Source: Translation from Egervärn, M. et al., 2014)[26]

When ESBL-producing bacteria and their resistant genes have settled in the environment, within animals or humans, it is very difficult to remove them. Studies also show that carriage of ESBL within humans is not something that can be presumed to disappear very quickly, it may take up to a year. Negative tests results are no guarantee that the carriage does not remain, it can appear after several years of negative tests.[27]

3.2 How can the event take place?

The following factors potentially cause an increased spread of multi-resistant intestinal bacteria:

[26] Since bacteria move freely across borders, picture 1. should be interpreted globally, i.e. spread occurring between countries. Exhaust from pharmaceutical plants is mostly emitted in countries with low level of compliance to environmental regulations.

[27] Folkhälsomyndigheten, *ESBL-producerande tarmbakterier – Kunskapsunderlag med förslag till handläggning för att begränsa spridningen av Enterobacteriaceae med ESBL*, 2014.

- Multi-resistant intestinal bacteria spread to Sweden from other countries.
- Multi-resistant intestinal bacteria develop domestically in Sweden.
- Multi-resistant intestinal bacteria already present in Sweden have more extensive transmission.[28]

The first case illustrates travel and tourism (including medical tourism) in which individuals spread multi-resistant bacteria via intestinal flora from countries such as India, Thailand or Egypt. The risk is even greater if the individuals in question have received medical care abroad. In such cases, a trip to southern Europe (for example Italy or Greece) can be sufficient for the individuals to become carriers of multi-resistant intestinal bacteria.

It can also pertain to entry and import of animals, fodder or foodstuff alternatively spreading in the environment, for example via migratory birds.

The second case deals with the use of antibiotics, both for humans and animals, and the handling of fertiliser and waste water. Antibiotic resistance can develop through waste emissions from pharmaceutical production, however Sweden currently has no such production. Regarding the use of antibiotics, the relevant point is whether usage is compliant with official guidelines. For fertilisers and water there are no official guidelines specifically regarding antibiotic resistance. A certain degree of regulation exists based on laws regarding infection control and water quality.

The third case is about preventive efforts within infection control. This work is described in the Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections (only available in Swedish). This report will elaborate on the Action Plan in section 4.3.

3.3 The presence of multi-resistant intestinal bacteria in Sweden and the world

3.3.1 What do statistics tell us?

ESBL-producing bacteria are present in humans as well as animals in Sweden, albeit a low figure on an international scale. The Public Health Agency of Sweden warns specifically about the development of $ESBL_{CARBA}$ in which 46 cases were reported during 2014, four of them infected domestically. The Public Health Agency of Sweden estimates, in a combined report with other agencies that nearly five per cent of the Swedish population carries such bacteria.[29] According to the Public Health Agency of Sweden's compilation of

[28] Since there are different types of ESBL, which also can move between different plasmids, which in turn can move between different bacteria, the reasoning in the text is a simplification.

[29] Egervärn, M. et al., *Slutrapport från ett myndighetsgemensamt projekt – Antibiotikaresistens, ESBL-bildande E. Coli i vår omgivning – livsmedel som spridningsväg till människa*, 2014.

the reports from Swedish doctors and laboratories, the presence of ESBL-producing bacteria in Sweden is increasing.[30] During 2007, just over 2 000 cases of ESBL-producing *Enterobacteriaceae* in humans were reported in Sweden.[31] The corresponding figure for 2014 was 8 902 cases. Most of the cases from 2014 (89 per cent) were *E. coli* with ESBL.[32]

The Public Health Agency of Sweden especially highlights the development of $ESBL_{CARBA}$, in which 46 cases were reported in 2014, four of which were infected domestically.[33] The majority of cases were imported from countries such as Bosnia, Egypt, Greece, India, Iraq, Israel, Italy, Romania and Syria, where medical care had been received in the form of emergency medical care and medical tourism.[34]

Figure 1 below displays the number of cases of $ESBL_{CARBA}$ discovered in Sweden since 2007. The significant increase between 2012 and 2013 is partly due to the fact that discovered cases of $ESBL_{CARBA}$ from that period became mandatory to report, not only from laboratories, but also medical doctors. At the same time, tracing also became mandatory. To what extent this explains the increase in reported cases is not known. Regardless, the trend is steeply on the rise, but so far the number of cases is relatively few.

[30] The Public Health Agency of Sweden and the National Veterinary Institute, *Swedres-Svarm 2014 – Consumption of antibiotics and occurrence of antibiotic resistance in Sweden*, 2015.

[31] Ternhag, A., *$ESBL_{CARBA}$ 2007-2013*, presentation in Swedish during a workshop at the MSB on the 25th of september 2014, Public Health Agency of Sweden.

[32] The Public Health Agency of Sweden and the National Veterinary Institute, *Swedres-Svarm 2014 – Consumption of antibiotics and occurrence of antibiotic resistance in Sweden*, 2015.

[33] The Public Health Agency of Sweden and the National Veterinary Institute, *Swedres-Svarm 2014 – Consumption of antibiotics and occurrence of antibiotic resistance in Sweden*, 2015.

[34] Smittskyddsinstitutet, 2011, *Konsekvenser – $ESBL_{CARBA}$ Konsekvenser och risker med resistensutveckling hos gramnegativa tarmbakterier med karbapenemasproduktion tillhörande familjen Enterobacteriaceae ($ESBL_{CARBA}$).*

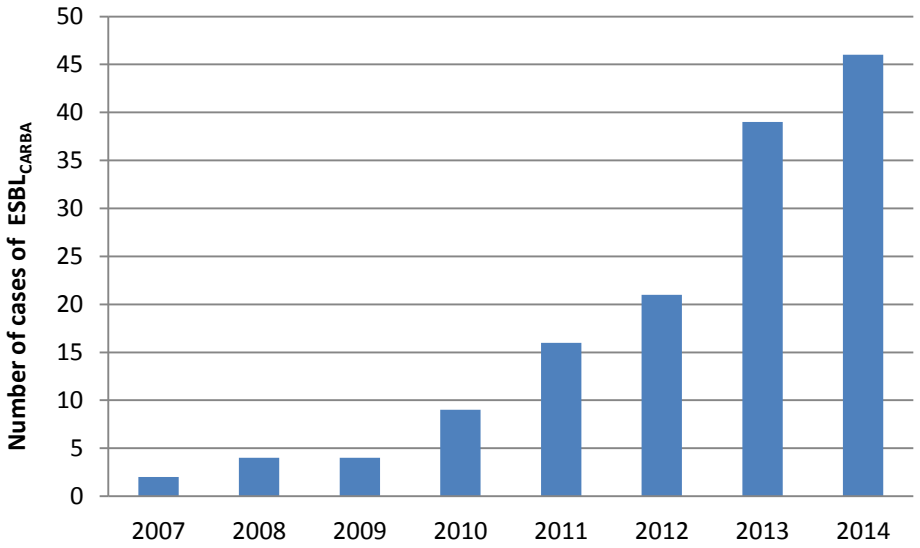


Figure 1 Number of cases of $ESBL_{CARBA}$ in Sweden 2007-2014.[35]

No cases of $ESBL_{CARBA}$ have so far been discovered in animals in Sweden. According to the National Veterinary Institute, ESBL-producing bacteria rarely occur among bovines and pigs, but are common among poultry.[36]

From an international perspective, Sweden is considered as has a low presence of resistant bacteria. Bacteria and resistance genes, including the one used in the scenario (*E. coli* with $ESBL_{CARBA}$), are easily transferred across borders. Knowledge is incomplete in several cases regarding presence and transmission of $ESBL_{CARBA}$ in humans, animals and the environment, globally and within Sweden. Regarding the presence of $ESBL_{CARBA}$ in Sweden, it is only for humans and animals that surveillance provides an adequate picture of the situation. There is cause for concern, as current reports indicate that the presence in Europe[37], Asia and Africa[38] is increasing. The American Centre for Disease

[35] Ternhag, A., *$ESBL_{CARBA}$ 2007-2013*, presentation during a workshop at the MSB on the 25th of september 2014, Folkhälsomyndigheten and The Public Health Agency of Sweden and the National Veterinary Institute, *Swedres-Svarm 2014 – Consumption of antibiotics and occurrence of antibiotic resistance in Sweden*, 2015.

[36] The Public Health Agency of Sweden and the National Veterinary Institute, *Swedres-Svarm 2014 – Consumption of antibiotics and occurrence of antibiotic resistance in Sweden*, 2015.

[37] Hawser, S.P. et al., 2010, *Antimicrobial susceptibility of intra-abdominal Gram-negative bacilli from Europe: SMART Europe 2008.*

[38] Hsueh, P.R., et al. (Asia–Pacific SMART Group), 2010, *Epidemiology and antimicrobial susceptibility profiles of aerobic and facultative Gram-negative bacilli isolated from patients with intra-abdominal infections in the Asia-Pacific region: 2008 results from SMART (Study for Monitoring Antimicrobial Resistance Trends).*

Control (CDC) identifies carbapenem-resistant *Enterobacteriaceae* (CRE) as an urgent threat.[39]

Based on a report from the European Centre for Disease Control (ECDC), in Europe, the situation is generally better in the northern part than the southern part.[40] The report states that for many types of resistance, there has been an increasing trend over time. There is cause for concern that the situation in Sweden may become worse with time and increasingly resemble the situation in certain countries in southern Europe. According to the ECDC, it is critical to have an awareness of how antibiotic resistance in *E. coli* is changing.

3.3.2 Examples of previous events in Sweden and internationally

There should be differentiation between singular outbreaks , for examples within care wards or among particular livestock herds, and endemic situations, which means that the bacteria is continuously present among the population without the need for external inputs. There are several examples of singular outbreaks in Sweden, especially when all forms of antibiotic resistant bacteria are taken into account and not just intestinal bacteria. This holds true regarding hospital outbreaks[41] [42] as well as resistant bacteria at preschools.[43] [44] There are also examples from both Swedish and Norwegian neonatal care.[45] [46] Further examples are presented in Swedres-Svarm 2014 regarding MRSA, *Clostridium difficile*, VRE and others.[47]

A smaller outbreak at a burn unit in Linköping University Hospital reveals that ESBL$_{CARBA}$ is already a serious problem and could potentially become worse in

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[39] Centers for Disease Control and Prevention (CDC), 2013, *Antibiotic resistance threats in the United States*.

[40] European Centre for Disease Prevention and Control (ECDC), 20132014, *Antimicrobial resistance surveillance in Europe 20122013*.

[41] Alsterlund, R., et al., 2009, *Multiresistant CTX-M-15 ESBL-producing Escherichia coli in southern Sweden: Description of an outbreak*.

[42] Akademiska sjukhuset, 2007, *Rapport till Socialstyrelsen angående LexMaria anmälan om utbrott av multiresistenta Klebsiella Pneumoniae ESBL*.

[43] http://www.ystadsallehanda.se/ystad/article764159/Resistenta-bakterier-staumlnger-foumlrskola.html

[44] http://www.svd.se/nyheter/inrikes/symptomfri-2-arig-flicka-nekas-forskola-bar-pa-resistenta-pneumokocker_3915111.svd

[45] http://www.svt.se/nyheter/regionalt/vast/for-tidigt-fott-barn-dog-av-multiresistenta-bakterie

[46] Rettedal, S., et al., 2013, *Risk factors for acquisition of CTX-M-15 extended-spectrum beta-lactamase-producing Klebsiella pneumoniae during an outbreak in a neonatal intensive care unit in Norway*.

[47] The Public Health Agency of Sweden and the National Veterinary Institute, *Swedres-Svarm 2014 – Consumption of antibiotics and occurrence of antibiotic resistance in Sweden*, 2015.

the future.[48] In 2013 there was an outbreak of $ESBL_{CARBA}$-producing *Acinetobacter baumannii*[49] where the bacteria were only treatable with colistin. The outbreak began when two patients transferred from a foreign hospital were discovered to be carriers of *A. baumannii* with $ESBL_{CARBA}$. The outbreak led to a decision from hospital management resulting in zero-tolerance for deviations from the protocol for basic hygiene routines[50] and to stop the inflow of new patients to the burn unit. The conclusion of the Agency for Public Health Control in Sweden (former Institute for Disease Control) was that the event demonstrated the need to monitor bacteria with multi-resistance that have not yet caused problems in Sweden, but that have been brought to attention in other countries.[51]

Several more examples of endemic presence can be found abroad, even for $ESBL_{CARBA}$. There are also several examples of outbreaks with ESBL where transmission routes and consequences are documented.

Examples of findings and hospital outbreaks of colistin-resistant bacteria (that are also resistant to carbapenems) can also be found abroad. In many of the cases, *Klebsiella pneumoniae* is the organism carrying resistance. *Klebsiella pneumoniae* is a bacteria primarily detected as well as transmitted within hospitals. In Italy there is a vast presence of carbapenem resistance and several hospitals have had outbreaks with colistin-resistant *Klebsiella pneumoniae*.[52] In France, colistin-resistant *Klebsiella pneumoniae* had been discovered in a patient who had not been travelling abroad.[53]

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[48] http://www.folkhalsomyndigheten.se/amnesomraden/beredskap/utbrott/utbrottsarkiv/acinetobacter-baumannii-linkoping-2013/smittspridning-pa-brannskadeavdelningen-i-linkoping/

[49] A. baumannii can among patients cause pneumonia, urinary tract infections, blood poisoning and open-wound infections.

[50] The protocol for Basic Hygiene Routines is based on regulations by The National Board of Health and Welfare, *Socialstyrelsens föreskrifter om basal hygien inom hälso- och sjukvården m.m.* (SOSFS 2007:19) and includes rules regarding hand hygiene, clothing etcetera.

[51] http://www.folkhalsomyndigheten.se/amnesomraden/beredskap/utbrott/utbrottsarkiv/acinetobacter-baumannii-linkoping-2013/smittspridning-pa-brannskadeavdelningen-i-linkoping/

[52] Mammina, C., et al., 2012, *Surveillance and outbreak reports. Ongoing spread of colistin-resistant Klebsiella pneumoniae in different emergency wards of a general hospital, Italy, June to December 2011.*

[53] Arpina, C., 2012, *NDM-1-Producing Klebsiella pneumoniae Resistant to Colistin in a French Community Patient without History of Foreign Travel.*

Tourism (traditional and medical) poses the risk of colonisation with resistant bacteria.[54] [55] Another risk factor is natural disaster.[56]A number of tsunami victims in Thailand had received local care and were infected with resistant *Acinetobacter* and were then flown to Sweden for further medical treatment. [57]

3.4 Previous assessments of risks regarding antibiotic resistance

The extent to which antibiotic resistance is mentioned in the government agencies' and the county councils' reports regarding risk and vulnerability analyses (RVAs) is shown below. There are many assessments within disease control, however from an emergency preparedness perspective it is the RVAs that are the primary source of information regarding the risks of antibiotic resistance, including prevention and management. It is also these reports that are submitted to the Government Offices, the National Board of Health and Welfare, and the MSB.

There is a great deal of international material available, but from an emergency preparedness perspective, the MSB has only found one equivalent to the Swedish national risk and capability assessment. The Netherlands have presented a similar assessment that has been brought to the MSB's attention through international cooperation surrounding national risk assessments.

3.4.1 Assessments within the government agencies' reports regarding risk and vulnerability analyses

According to the Emergency Management and Heightened Alert Ordinance[58] all government agencies are obligated annually to analyse[59] vulnerabilities, threats and risks within the agency's authority which could potentially diminish capability within the area. The agencies shall assess and compile the results in a

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[54] Tängdén, T., et al., 2010, *Foreign travel is a major risk factor for colonization with Escherichia coli producing CTX-M-type extended-spectrum β-lactamases: a prospective study with Swedish volunteers*.

[55] Tham, J. et al., *Duration of colonization with extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers' diarrhea*, 2012.

[56] Uçkay, I., et al., 2008, *Multi-resistant infections in repatriated patients after natural disasters: lessons learned from the 2004 tsunami for hospital infection control*.

[57] Petersson, J., et al., 2006, *Vårdrelaterade infektioner med multiresistenta bakterier – inte bara stafylokocker*.

[58] Replaced 1st of April 2016 by Ordinance on Emergency Management and the Measures Taken by Responsible Government Agencies at Heightened Alert (translated by the author). Förordning (2015:1052) om krisberedskap och bevakningsansvariga myndigheters åtgärder vid höjd beredskap.

[59] In the new ordinance in effect from 1st of April 2016, the word "yearly" is removed. Instead it is stated that the report regarding the analysis shall be submitted every other year.

risk and vulnerability analysis (RVA) with the purpose of strengthening its emergency preparedness as well as that of society.[60]

In the appendix of the ordinance, a number of government agencies are listed, as they have a special responsibility to plan and prepare action to create capability to manage a crisis and minimise vulnerabilities in order to mitigate threats and risks. These agencies (in addition to others the MSB may decide upon) are to submit a report based on their risk and vulnerability analysis to the Government Offices, with a copy to the MSB according to the Emergency Management and Heightened Alert Ordinance.[61]

The accountable agencies (as stated above) include central (national) agencies and the 21 county administrative boards[62]. The central agencies that have mentioned antibiotic resistance in their 2014 RVA reports are the Public Health Agency of Sweden, the Swedish Board of Agriculture, the National Food Agency, the National Board of Health and Welfare, and the National Veterinary Institute.

The County Administrative Boards of Gotland, Gävleborg, Halland, Jönköping, Kronoberg, Skåne, Stockholm and Västra Götaland have all addressed antibiotic resistance in their respective 2014 RVA reports. The County Administrative Boards of Skåne and of Västra Götaland have not previously done so. All the above mentioned county administrative boards address the risk of antibiotic resistance as part of the compilation of risks relevant to each county. Among the county administrative boards, none have yet assessed the magnitude of the risk, that is they have made no statements regarding probability, consequences or capability.

3.4.2 Assessments within the county councils' reports regarding risk and vulnerability analyses

The county councils, according to the Act on Municipal and County Council Measures Prior to and During Extra-Ordinary Events in Peacetime and During Periods of Heightened Alert are to carry out a risk and vulnerability analysis. The county councils shall submit the results of the analysis to the National Board of Health and Welfare, with a copy to the MSB, according to the MSB's The Swedish Civil Contingencies Agency's Regulations on County Councils' Risk and Vulnerability Analyses (MSBFS 2015:4). The results are to be submitted every four years. In the interim years, annual updates are required. The most recent report was submitted in December 2015. As the original version of this report was published in November 2015, the most recent results available to the MSB when this report was written were from 2011.

Based on the results that were submitted in 2011, and the updates made in autumn 2014, the MSB concludes that few county councils addressed risks

[60] The Emergency Management and Heightened Alert Ordinance

[61] This is true for the new ordinance as well, with the difference that the reports shall be handed in every other year instead of yearly.

[62] The county administrative boards are also defined as government agencies, governed through ordinances and appropriations directives, but on a regional level.

related to antibiotic resistance. The only county councils that mention the issue are Gävleborg (MRSA) and Uppsala (resistant tuberculosis). This does not mean that the county councils have not addressed the issue, rather that the MSB has no input to make an assessment.

3.4.3 International comparison

In 2014 the Netherlands published an in-depth thematic analysis of antimicrobial resistance and national security within the framework of the Dutch National Risk Assessment.[63] Eight different scenarios were created and analysed based on the method[64] used for the Dutch national risk assessment. Most of the scenarios were set to occur within five years. However, two of them were set to occur within ten years. The scenarios were based on various bacteria and types of resistance ($ESBL_{CARBA}$ included), as well as whether the presence was endemic (the bacteria is maintained in the population without the need for external inputs).

The analysis concludes that antimicrobial resistance poses no threat to societal security in the form of single outbreaks. Instead, the threat is identified in the form of more frequent outbreaks, as well as multiple outbreaks occurring simultaneously.

The analysis also concluded that the probability for these scenarios was relatively high compared to many other scenarios analysed within the framework of the Dutch national risk assessment. Several of the scenarios had already occurred or were deemed to be on the verge of occurring.

The Dutch analysis explains that outbreaks of resistant bacteria can lead to concern among the population and that trust in society's institutions may be weakened. The analysis also reveals that there is a clear difference between social consequences in general (rarely very large) and specific consequences for healthcare. In the case of the latter, large consequences are expected, especially regarding life and health and the costs connected to the consequences. The costs were particularly large, hundreds of millions of euros, for the scenarios with endemic situations.

[63] National Institute for Public Health and the Environment, *In-depth thematic analysis of AMR and national security*, 2014.

[64] Ministry of Security and Justice, *Working with scenarios, risk assessments and capacities in the National Safety and Security Strategy of the Netherlands*, 2012.

4. The work on containment of antibiotic resistance in Sweden

This chapter provides a brief history regarding the effort against antibiotic resistance in Sweden, the most important actors, how Swedish infection control operates and how Sweden works to prevent an increased prevalence of resistant bacteria.

4.1 History in brief

Sweden has a long standing tradition within the work on containing antibiotic resistance and the prevention of communicable diseases. As early as 1986, Sweden was the first country to ban the use of growth promotors for animals. Sweden continues to lead the effort within the EU. In 1998 the EU imposed tight restrictions on the use of antibiotics as growth promotors, and the introduction of a complete ban in 2006.

In 2000, the Swedish Board of Health and Welfare published a proposal for a Swedish action plan combatting antibiotic resistance (SPAR) as part of a Government commissioned task. [65] Based on these suggestions, the Government submitted the proposition (2005/06:50) *Strategi för ett samordnat arbete mot antibiotikaresistens och vårdrelaterade sjukdomar* [*Strategy for coordinated work towards the containment of antibiotic resistance and healthcare-associated diseases*] to the Swedish Parliament. This strategy raises the need for cooperation between various agencies and organisations, within various segments of society.[66]

In 2012, The National Board of Health and Welfare was commissioned by the Government with the task of, creating and managing a National Coordinating Mechanism in conjunction with the above mentioned strategy and in collaboration with the Swedish Board of Agriculture. The task included producing a cross-sectional action plan to coordinate the work on containment of antibiotic resistance and healthcare-associated infections, with a corresponding communications strategy. The deadline for the task is 2017, during which an annual summary is to be submitted to the Government Offices.[67] As of July 1st 2015, responsibility for infection control has been transferred from the National Board of Health and Welfare to the Public Health Agency of Sweden, including the commissioned task mentioned above.

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[65] Socialstyrelsen, *Förslag till utveckling av strategin mot antibiotikaresistens och vårdrelaterade sjukdomar*, 2011.

[66] The Public Health Agency of Sweden, *Swedish work on containment of antibiotic resistance – Tools, methods and experiences*, 2014

[67] Socialdepartementet, *Uppdrag inom strategin mot antibiotikaresistens och vårdrelaterade infektioner*, S2010/7655/FS (delvis).

The National Coordinating Mechanism's task is to support general and cross-sectional cooperation between all actors involved in containing antibiotic resistance and healthcare-associated infections. This includes human and veterinary medicine, public health, livestock production, foodstuff, the environment, research and innovations. The Office of the Cooperation Function is based within the Public Health Agency of Sweden, and a national cooperation group has been formed, with representation from relevant agencies.[68]

The National Coordinating Mechanism and the participating agencies in the National Coordinating Group have been tasked to produce an action plan with the corresponding communication strategy mentioned above. The Communication strategy[69] was published in December 2014 and the Action Plan[70] in March 2015. The Action Plan will serve as a foundation for the new national strategy against antibiotic resistance.

Another major effort worth mentioning is a four-year patient safety initiative launched in 2010 as a result of an agreement between the Government and the Swedish Association of Local Authorities and Regions. The initiative highlights the rational use of antibiotics and healthcare-associated infections as core issues for patient safety. During 2011-2014, the Government made annual investments of 400 million SEK to incentivise the county councils, provided they met certain basic standards and performed measures to increase patient safety in healthcare. [71]

4.2 Who is responsible for what?

The chart in chapter 3.1 illustrates the fact that many actors are involved in preventing and managing the containment of antibiotic resistance in society. The government agencies primarily responsible for this are the Public Health Agency of Sweden, the Swedish Board of Agriculture, the Swedish Food Agency, the National Board of Health and Welfare and the National Veterinary Institute. The Public Health Agency of Sweden and the National Veterinary Institute are responsible for monitoring and providing statistics for the prevalence of ESBL and $ESBL_{CARBA}$ in Sweden. These data are presented annually in the report Swedres-Svarm. The Swedish Board of Agriculture and the Public Health Agency of Sweden are also responsible for the National Coordinating Mechanism mentioned above.

There are additional actors in the public realm, depending on the topic and relevance to preventive work or managing an outbreak of resistant bacteria.

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[68] http://www.folkhalsomyndigheten.se/amnesomraden/smittskydd-och-sjukdomar/antibiotika-och-antibiotikaresistens/nationell-samverkansfunktion/

[69] Socialstyrelsen och Jordbruksverket, *Kommunikationsstrategi för antibiotikaresistens och vårdrelaterade infektioner*, 2014.

[70] Socialstyrelsen och Jordbruksverket, *Handlingsplan mot antibiotikaresistens och vårdrelaterade infektioner – Underlag för myndigheternas fortsatta arbete*, 2015.

[71] The Public Health Agency of Sweden, *Swedish work on containment of antibiotic resistance – Tools, methods and experiences*, 2014

The table below shows *a selection* of such actors with responsibilities linked to antibiotic resistance based on various perspectives and regulations. It should be noted that the table below includes only a partial list and includes selected representation. .

	Prevent	**Detect, report and trace**
Human	The Public Health Agency of Sweden The National Board of Health and Welfare County councils Municipalities (Care)	The Public Health Agency of Sweden County councils (County Medical Officers for communicable disease control, treating physicians, clinical microbiological laboratories)
Animal	The Swedish Board of Agriculture The National Veterinary Institute Animal health professionals County administrative boards (Regional veterinarians) Animal owners	The National Veterinary Institute The Swedish Board of Agriculture County administrative boards (Regional veterinarians) Veterinary laboratories Animal health professionals
Food	The National Food Agency Livestock and food producers	The National Food Agency The National Veterinary Institute The Public Health Agency of Sweden Municipalities (environmental and health inspectors)
Environment	The Swedish Environmental Protection Agency The Swedish Agency for Marine and Water Management	Municipalities (environmental and health inspectors)

Table 1 Examples of responsible actors

In addition, the Swedish Work Environment Authority and the Medical Products Agency along with a number of private actors are important to add to the list. The private actors play a large role with respect to animals since the Swedish Board of Agriculture and the National Veterinary Institute cooperate closely with the producers' associations when disease outbreaks occur in animal populations.

Other actors worth mentioning are the network of the Swedish Strategic Programme Against Antibiotic Resistance (Strama), Strama VL (Strama for veterinary medicine), the European Centre for Disease prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the global network ReAct[72].

The effort in the prevention and management of antibiotic resistance has many components. What makes antibiotic resistance an issue for societal security is the clear connection to communicable disease control. The regulation of communicable disease control related to humans can primarily be found in the Communicable Disease Control Act[73]. The work on containment of antibiotic resistance falls under a number of other laws, ordinances and regulations, depending on the specific topic. Examples of such regulations include a law regulating the taking of samples from animals etc.[74] and the Swedish Environmental Code[75].

When crises or other extraordinary events occur, municipalities and county administrative boards have a responsibility on both a local and regional level according to the Emergency Management and Heightened Alert Ordinance[76] and the Act on Municipal and County Council Measures Prior to and During Extra-Ordinary Events in Peacetime and During Periods of Heightened Alert[77]. Also the MSB has a responsibility to coordinate the actors responsible for preventing and managing accidents and crises.

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[72] ReAct is a global, independent network working for action against antimicrobial resistance. The network was founded in 2011 and is based in Uppsala, Sweden. http://www.reactgroup.org/who-we-are.html

[73] Smittskyddslagen (2004:168) [the Communicable Disease Act]

[74] Lagen (2006:806) om provtagning på djur, m.m. [Ordinance on Animal Testing etc.]

[75] Miljöbalken (1998:808) [the Swedish Environmental Code]

[76] Förordningen (2006:942) om krisberedskap och höjd beredskap, Replaced 1st of April 2016 by Förordning (2015:1052) om krisberedskap och bevakningsansvariga myndigheters åtgärder vid höjd beredskap (Ordinance on Emergency Management and the Measures Taken by Responsible Government Agencies at Heightened Alert, translated by the author).

[77] Lagen (2006:544) om kommuners och landstings åtgärder inför och vid extraordinära händelser i fredstid och höjd beredskap

4.3 The government agencies' Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections

Most of the central aspects identified in this report are addressed in the Action Plan published in March 2015 by the Swedish Board of Agriculture and the Public Health Agency of Sweden.[78] The Action Plan has been produced with the cooperation of a number of agencies and various other actors, based on the National Cooperating Mechanism for containment of antibiotic resistance and healthcare-associated infections. The Action Plan describes the commitments of a number of agencies over the next few years. The Action Plan does not include commitments made by municipalities, county councils and other private actors since the Government does not have a mandate for such governance. The Action Plan however, is very clear in stating that a commitment from these actors is a prerequisite for success.

The commitments in the Action Plan are divided into six target areas:

- International work
- Knowledge and ability
- Prevention, identification and measures of action
- Prudent and rational use of antibiotics
- Data collection and analysis
- Diagnostics and effective treatment

The report outlines specific commitments for each target area, where it is noted which actors are responsible as well as the timeframe for such measures to be taken. Examples of commitments are:

- A cross-governmental working group to be formed, with the aim of continuously developing and harmonising the monitoring and analysis of resistance data from humans, animals, food and the environment, with the purpose of facilitating integrated analysis. (The National Veterinary Institute, the Swedish Board of Agriculture, the Public Health Agency of Sweden, the National Food Agency, the National Agency for Environmental Protection, the Swedish Chemical Agency and the Swedish Agency for Marine and Water Management, 2015-2019)
- Identify and prioritise which data on resistant antibiotics in food, not included in current monitoring, should be monitored and develop a plan for the method in which this data should be collected. (The National Food Agency in collaboration with the Public Health Agency of

[78] *Handlingsplan mot antibiotikaresistens och vårdrelaterade infektioner – underlag för myndigheternas fortsatta arbete*.

Sweden, the Swedish Board of Agriculture and the National Veterinary Institute, 2016)

- Develop a proposal for a cross-sectional strategy for managing $ESBL_{CARBA}$ in humans, animals, food and the environment. (Minor national cooperating group will initiate work in 2015 to develop a proposal in 2016)

4.4 Planned and ongoing actions regarding antibiotic resistance from an emergency preparedness perspective

Listed below are examples of ongoing work within the emergency preparedness sector pertaining to antibiotic resistance.

4.4.1 The CBRNE strategy

CBRNE is an acronym used to define hazardous material – chemical, biological, radiological, nuclear and explosive substances. Even if antibiotic resistance is not a biological substance in itself, it is to be viewed as a biological threat, and is therefore regarded as a part of CBRNE.

The MSB is commissioned by the Government to develop a strategy for CBRNE, for all parties concerned. The strategy includes guidelines outlining how the aims of the strategy will be realised by local and regional actors as well as government agencies. The guidelines also note aspects of cooperation that require further development.

4.4.2 Common Guidelines for Collaboration and Command in Societal Disruptions

To facilitate various actors' efforts regarding cooperation and management, the MSB has developed common guidelines for collaboration and command. The guidelines include approaches as well as methods for the management of societal disruptions.

The intention of Common Guidelines for Collaboration and Command in Societal Disruptions is to provide guidance to actors that facilitate a common direction and coordination when working with other actors. Actors working together in a structured and similar manner strengthen their capacity to manage societal disruptions.[79]

4.4.3 Other examples

Within MSB there are other efforts related to antibiotic resistance. In 2007 an agreement between the Swedish Ministry of Defence and the American Department of Homeland Security (DHS) was signed regarding research and development within societal security. The MSB is responsible for coordinating Sweden's national effort. This includes the coordination of a group consisting

[79] MSB, *Gemensamma grunder för samverkan och ledning vid samhällsstörningar*, 2014. An English version will be available in 2016.

of the Public Health Agency of Sweden, the National Food Agency and the National Board of Social Welfare, among others. The agreement provides opportunities for joint research projects, exercises and education, exchange of information, methodology and equipment. The agreement's link to antibiotics can primarily be found regarding hazardous materials (CBRNE).

The MSB is also responsible for managing governmental research funds within the Emergency Preparedness Appropriation[80]. In the adjoining research strategy, the increased presence of antibiotic resistance is included among the trends particularly emphasised.

The MSB is responsible for coordinating the cooperation areas defined in the emergency preparedness ordinance, in which the relevant agencies responsible for crisis management are identified. Antibiotic resistance is a relevant topic for the Cooperation Area Protection, Relief and Healthcare (SOSUV)[81] and the Cooperation Area Hazardous Materials (SOFÄ)[82]. The participants of the Cooperation Areas meet regularly to plan and coordinate current work and activities as well as to exchange experiences.

The agencies responsible for emergency preparedness have the opportunity to apply for funds from the Emergency Preparedness Appropriation[83] for specific initiatives within emergency preparedness. The MSB manages the appropriation, with this report being used as input for how the funds will be allocated in the future. The appropriation has also funded an initiative dealing with the presence of *E. coli* in food, collaboration between the National Food Agency, the National Veterinary Institute and the Public Health Agency of Sweden. The initiative resulted in a report, *ESBL-bildande E.coli i vår omgivning – livsmedel som spridningsväg till människa*[84], a report used as reference material in this report.

[80] Anslag 2:4 Krisberedskap, translated by the author.

[81] Samverkansområde Skydd, undsättning och vård (SOSUV), translated by the author.

[82] Samverkansområdet Farliga ämnen (SOFÄ), translated by the author.

[83] Anslag 2:4 Krisberedskap, translated by the author.

[84] Egervärn, M. m.fl., *Slutrapport från ett myndighetsgemensamt projekt – Antibiotikaresistens, ESBL-bildande E. Coli i vår omgivning – livsmedel som spridningsväg till människa*, 2014.

5. Scenario

5.1 Time and weather

The scenario depicts a steep increase in the presence of multi-resistant intestinal bacteria (*E. coli* with $ESBL_{CARBA}$) in the Swedish population over a five year period. This is a so-called creeping scenario, which means that the scenario is depicted over a longer time-period compared to other scenarios describing a sudden event.

5.2 Location

The scenario is primarily set in the southern parts of Sweden, even though other areas of Sweden can be affected by such events in the scenario. In the region there are producers of poultry, fodder, dairy and livestock (beef). The area is often flooded when exposed to heavy rainfall.

5.3 Chain of events: in the beginning

The summer is warm and dry. Beaches are heavily frequented and barbecuing is a preferred method of cooking food such as poultry and hamburgers from minced beef. The heat is periodically interrupted by thunderstorms with heavy downpour.

Heavy rainfall in the southwest of Sweden disenables the water grid to fully absorb all the water. This leads to flooding, including from sewage and wastewater pipes (combined sewer overflow). The rain also causes surfaces and farmland to be flooded, resulting in surface water contaminated with intestinal bacteria. Wet weather conditions also contribute to intestinal bacteria being introduced into the environment from manure. Surface water used in agricultural production is thereby contaminated and when used for large cultures of vegetables and strawberries, the transmission of the intestinal bacteria *E. coli* increases. The quality of water in the lakes is affected, sometimes deemed unfit for bathing. This is not always detected since not all lakes are tested. Cattle and other livestock graze in fields previously flooded. In combination, this increases the presence of intestinal bacteria in the environment.

In a large fodder production facility supplying a significant area of southern Sweden, situated in a frequently flooded area, a cooler and the exhaust air canal in a production line becomes contaminated by *E. coli* with $ESBL_{CARBA}$. The contamination occurs through the air intake and comes from resistant intestinal bacteria that originate from sewage treatment plants and agricultural facilities in connection with the heavy rain. There is a possibility that raw materials used in the fodder factory were contaminated. This is not detected since it is not customary for fodder to be tested for *E. coli*.

Chickens bred in several of the large production facilities in southern Sweden receive fodder contaminated with *E. coli* with $ESBL_{CARBA,}$ building reservoirs of intestinal bacteria carrying $ESBL_{CARBA}$. The chickens do not exhibit signs of

illness and hence contamination is undetected. The contaminated chickens reach consumers upon distribution to retail stores after slaughter.

During warm weather conditions, the public frequently grills outdoors, grilling poultry and beef. Recommended hygiene routines are not complied with. The meat is inadequately cooked and utensils and grills are not always handled correctly, potentially leading to contamination. Some may experience stomach pains but dismiss them attributing them to food spoilt in the summer heat. Due to a relatively speedy recovery, they will fail to seek medical care, and therefore no further investigation will ensue. Therefore no *E. coli* with $ESBL_{CARBA}$ are discovered. This results in the number of individuals carrying the multi-resistant bacteria silently increasing by a rate that is considered beyond the acceptable norm.

During the warm summer, produce, for example lettuce and strawberries in the southern parts of Sweden are watered with contaminated water. The water comes from streams, containing *E. coli* with $ESBL_{CARBA}$ due to previous floods and heavy rains that have contaminated several watercourses in southern Sweden. When the lettuce and strawberries reach retail stores, the number of human carriers of *E. coli* with $ESBL_{CARBA}$ continues to increase…. Because the level of *E. coli* is too low to cause illness, it is undetected.

When the National Veterinary Institute conducts its examination of $ESBL_{CARBA}$ in poultry within the framework of the EU Commission's mandatory surveillance programme, a high presence of $ESBL_{CARBA}$ is discovered at a facility with more than 50 000 chickens. The tracing of the contamination leads to the fodder factory and the contaminated cooler is discovered.

At the same time as the contamination via Swedish poultry, produce and beef there are other pathways of transmission increasing the number of individuals carrying *E. coli* with $ESBL_{CARBA}$ with varying levels of virulence. People continue with holiday travel to warm climate destinations where they risk becoming carriers of intestinal bacteria with $ESBL_{CARBA}$. Also, the rate of planned surgeries abroad increases. There is also a continuing increase in the import of food from regions with a high presence of resistant bacteria, including $ESBL_{CARBA}$, in production and in the environment. Entry and import of fertilisers and raw materials for fodder production also increases.

5.4 Chain of events: development during the subsequent three years

Healthcare institutions in southern Sweden have increasingly noticed a higher occurrence of poultry industry employees being carriers of $ESBL_{CARBA}$. This is discovered when the employees are treated for work-related injuries or have been admitted to hospital for testing due to other causes.

Two years after the warm summer, a water study reveals a six per cent presence of *E. coli* with $ESBL_{CARBA}$ downstream from a sewage treatment plant. This has been noted within research on environmental protection as it increases the risk of transmission to humans and animals.

Within the healthcare sector an ”unusual” increase in multi-resistant intestinal bacteria, including *E. coli* with $ESBL_{CARBA}$, is noted two years after the hot summer. A smaller screening study is initiated, with results expected within two years.

Small outbreaks of *E. coli* with $ESBL_{CARBA}$ are detected throughout the country, mostly in the southern parts, however county councils have failed to notice the pattern. The outbreaks occur both within hospitals and other healthcare facilities and are caused by both bacteria in the form of Klebsiella (*K. pneumoniae*) and *E. coli*. In many of the cases, the bacteria are ESBL-producing, and $ESBL_{CARBA}$ is discovered on a much larger scale than expected. There are also cases with $ESBL_{CARBA}$ present in clinical tests from animals. A larger study of calves in southern Sweden reveals a high presence of $ESBL_{CARBA}$.

In elderly care facilities, both residents and staff are exhibiting signs of carrying *E. coli* with $ESBL_{CARBA}$. Earlier, the residents have primarily fallen ill due to infections of Klebsiella with $ESBL_{CARBA}$, but this now appears to have changed. In elderly care facilities, the staff provides care for the residents, but also handles food, which facilitates transmission.

Within primary care, cases of urinary tract infections are discovered, both in younger women and elderly people, in which the bacteria causing the illness in most cases is *E. coli* with $ESBL_{CARBA}$. Some cases with pneumonia, caused by multi-resistant Klebsiella (*K. pneumoniae*) have been reported, along with cases caused by *E. coli* with $ESBL_{CARBA}$. The infected individuals have, in some cases been abroad during the last six months, but others have not left Sweden.

A large Swedish hospital has an outbreak of *E. coli* with $ESBL_{CARBA}$. Approximately 70 individuals are confirmed to be carrying $ESBL_{CARBA}$ and are admitted to various wards in the hospital. It is primarily the surgical and emergency/rehab wards that are affected. The hospital is overcrowded and therefore infected individuals may have been transferred to medical facilities in other counties, to elderly care facilities or to their homes.

Within neonatal care, several minor incidents have been reported, in which premature infants carrying *E. coli* with $ESBL_{CARBA}$ have been discovered. The result of the carriage has varied results, however this variation has not been noted by the media. Now, media is focusing on a contained and controlled outbreak of $ESBL_{CARBA}$ in a hospital in a medium sized town. $ESBL_{CARBA}$ is found in a premature infant, causing transmission to other infants in the neonatal intensive care unit. Twenty infants were receiving treatment in the unit, with approximately 25 per cent infected and one infant dead. The media attention is significant. The pressure on primary care increases as the public demands testing to determine carriage.

Three children, siblings, one in diapers, just returned from holiday abroad are diagnosed to be carriers of *E. coli* with $ESBL_{CARBA}$ after being ill. They have attended preschool before being diagnosed as carriers. The two youngest children attend a preschool in southern Sweden together with approximately 100 other children, where various groups of children use the same facilities, including nursery rooms. The preschool has two bathroom facilities, resulting

in approximately 50 children using the same toilets and nursery rooms. During periods when children are brought to the preschool early or collected late, groups of children from various wards are combined. During certain activities, other facilities are used with adjoining toilets in the school across the yard. The eldest child attends a school with 700 pupils between the ages of seven and twelve. Several children from both the preschool and the school are diagnosed as carriers of *E. coli* with $ESBL_{CARBA}$ after tests, but it is discovered to be a separate form of $ESBL_{CARBA}$ than that carried by the other three children initiating the screening.

Despite stricter enforcement of hygiene routines by the healthcare sector since the hot summer, there is an increase in the workload, due to an increase in patients as carriers. A large population study is scheduled to commence immediately, as preliminary results from a minor study reveal that approximately five per cent of the screened population, taken from the general population in southern Sweden, is discovered to be $ESBL_{CARBA}$ carriers. The media interprets the results by stating that treatment is “made impossible” when one is infected with bacteria with $ESBL_{CARBA}$. The media also illustrates through colour-coded charts how “alarming” the situation in Sweden is, compared to other Nordic countries. Public concern and speculation grow around the potential consequences; as individuals, family members and as a part of society, personally and professionally. In light of this, the Government Offices begins to respond by demanding information from the government agencies.

6. Analysis

The purpose of this chapter is to analyse society's capability to prevent and manage an event corresponding to the scenario presented in chapter 5. This would include how the consequences would impact society. The chapter also weighs the probability of the scenario or a similar event.

6.1 Society's capability to predict and prevent an increased presence of multi-resistant intestinal bacteria

Swedish society has solid capabilities to predict such events and in principle, already have. The difficulties lie not in the prediction of increased presence, but the early discovery and commencement of preventive efforts to limit further transmission.[85]

Ultimately, there is consensus among actors leading the effort on containing antibiotic resistance that it is a question of *when*, and not *if*, such an event takes place – and that it is close at hand. Thus prevention is simply about delaying such an event.

6.1.1 Central aspects from a communicable disease control perspective

The MSB concludes that to prevent a crisis generated through an increased presence of multi-resistant intestinal bacteria, Sweden needs the following capabilities:

To have an international impact in the prevention of existent forms of resistance as well as the development of further resistance. The responsibility for this lies with government agencies and the Government, in cooperation within the EU, with WHO and bilateral measures. Various NGO's can also have an impact, such as ReAct.

To understand the risks with multi-resistant intestinal bacteria and to have knowledge regarding communicable disease control. To increase society's preventive capability, the transmission of resistant intestinal bacteria in society must be reduced. Therefore the individual, both in a professional and private capacity, must have an awareness of how and why transmission of such bacteria needs to be prevented. Generating and communicating such information is mainly the responsibility of scientists, governmental agencies and care professionals. All functions in society, especially those considered Vital Societal Functions, should reflect upon how prevention and reduction of the presence and transmission of resistant bacteria can be achieved.

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[85] Increasing presence is already a fact. The seriousness of the events analysed in this report is comparable to the events described in the scenario in chapter five, which states that five per cent of the population in southern Sweden becoming carriers of $ESBL_{CARBA}$. Society requires adequate capability to be able to detect such presence.

To understand the risk of becoming a carrier of multi-resistant intestinal bacteria when travelling abroad, especially when receiving medical care. Here the responsibility lies with the individual, but also with governmental agencies and county councils. The Swedish Ministry for Foreign Affairs also shares the responsibility to inform the public about the risks. The National Food Agency has published guidelines for foreign travel, addressing the risks of resistant bacteria.[86]

To comply with rules and recommendations for entry and imports of animals and agricultural products. Here there are various categories of actors with varying degrees of responsibility: for rules and compliance (public actors), for recommendations (private actors supported by public ones) and for entry or imports of animals and food (usually private actors or individuals).

To comply with guidelines and recommendations about the use of antibiotics in Sweden. This applies to those responsible for prescribing antibiotics to humans and animals, such as medical doctors, dentists and veterinarians. Patients also have a responsibility to closely follow doctors' instructions regarding medication. Similarly, animal owners have the same responsibility to follow instructions from the veterinarian.

To separate the remnants of antibiotics and resistant bacteria, from manure and wastewater to the greatest extent possible. The treatment of manure and wastewater is currently regulated, however there are no specific rules outlining acceptable levels of trace elements of antibiotics or resistant bacteria. The responsibility to reduce the levels of trace elements lies mainly with actors responsible for regulation (public actors) and those responsible for treatment of manure and wastewater. Also, each individual is responsible for submitting unused medication to pharmacies in accordance with the responsibility of the producers as opposed to disposal into the public sewage system.

To comply with rules and regulations regarding communicable disease control. Communicable disease control in Sweden is highly regulated and includes rules defining which bacteria are mandatory to report to the authorities and how the involved parties should act when an outbreak occurs. The aim of communicable disease control is defined in the Swedish Communicable Disease Control Act[87]: "Society's communicable disease control shall meet the needs of the population for protection against the transmission of communicable diseases".[88]

To comply with basic hygiene standards or equivalent, based on regulations set by authorities. Within healthcare and social services, basic hygiene principles shall be applied in accordance with the regulations of the National

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[86] http://www.livsmedelsverket.se/matvanor-halsa--miljo/sjukdomar-allergier-och-halsa/matforgiftning/rad-vid-utlandsresa/

[87] Smittskyddslagen (2004:168)

[88] Translated by the author.

Board of Health and Welfare.[89] According to regulations, it is the management's responsibility to ensure employee compliance with routines. The Swedish Work Environment Authority has hygiene rules which apply to all occupational environments in which employees are exposed to communicable diseases and other toxic substances.[90] Concerning the housing of animals, for example in the livestock industry, there are hygiene standards for all actors (with exemptions for animals kept in private residence, including those in which visitors have the opportunity to come into direct contact with animals.[91] As of 2014, veterinary facilities are required to produce and comply with a hygiene plan, in accordance with the above regulations. The plan is to state how transmission and healthcare-associated infections will be contained and how basic hygiene routines will be upheld.[92]

6.1.2 Central aspects from an emergency preparedness perspective

A prerequisite for society's capability to prepare for an increased presence of multi-resistant intestinal bacteria is that all concerned parties, including actors responsible for emergency preparedness, are aware of the risk. Additionally, all concerned parties need to analyse, or at least reflect upon, what the risk implies for them. Such an impact assessment includes examining the interdependencies with other actors, revealing the need for further knowledge and routines necessary for emergency preparedness.

Risk awareness regarding the increased presence of multi-resistant intestinal bacteria, is generally found among experts on a national level and in professions linked to communicable disease infection control. There is also risk awareness at the political level, manifested through an outspoken support for measures to prevent and manage the risks. However, the level of risk awareness is low with emergency preparedness actors and the general public. The government agencies' Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections specifically addresses the need for increased knowledge, but mainly focuses on research, the public and relevant professionals within healthcare and veterinary medicine. Due to the experiences of avian flu and ebola in recent years, society has become more aware of the risks and consequences of communicable diseases and the effort to mitigate the effects.

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[89] The National Board of Health and Welfare, *Socialstyrelsens föreskrifter om basal hygien inom hälso- och sjukvården m.m.* (SOSFS 2015:10).

[90] Arbetsmiljöverkets föreskrifter (AFS 2005:1) om Mikrobiologiska arbetsmiljörisker – smitta, toxinpåverkan, överkänslighet.

[91] Statens jordbruksverks föreskrifter och allmänna råd om förebyggande och särskilda åtgärder avseende hygien m.m. för att förhindra spridning av zoonoser och andra smittämnen (SJVFS 2013:14, ”K112”).

[92] Statens jordbruksverks föreskrifter och allmänna råd om förebyggande och särskilda åtgärder avseende hygien m.m. för att förhindra spridning av zoonoser och andra smittämnen (SJVFS 2013:14, ”K112”).

Assessments of consequences and interdependence are mainly produced by actors working with communicable disease control for humans, animals, agriculture and the environment. Other actors often have pandemic planning, however antibiotic resistance rarely factors into such planning. For intestinal bacteria, the transmission is often undetected since carriers rarely become ill.

The need for knowledge and routines has almost exclusively been identified by actors working with communicable disease control. Within the framework of the government agencies' Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections, extensive work has been accomplished. The Action Plan has identified a need for raising awareness regarding the risks of antibiotic resistance in society overall. The Action Plan also includes the task of coordinating a cross-sectional strategy for managing $ESBL_{CARBA}$ in humans, animals, food and the environment.

Education regarding antibiotic resistance exists within healthcare and veterinary health. However, within emergency preparedness, the availability of education and information is insufficient, according to the experience of the MSB. In contrast to other types of risks, information relating to antibiotic resistance is seldom available within the emergency preparedness area. However, further information may be accessed through the websites of the agencies responsible for communicable disease control. In contrast, the communicable disease control sector offers a great deal of information online. An ambitious effort regarding education on antibiotic resistance within healthcare is the Patient Safety Initiative based on collaboration between the Government and the Swedish Association of Local Authorities and Regions. The initiative stretched over four years from 2011 to 2014, with the aim of encouraging, strengthening and reinforcing patient security in the county councils. In total, 2.2 billion SEK was allocated to the county councils, incentivising the reduction of antibiotic prescriptions and the presence of healthcare-associated infections (where resistant bacteria are common).[93] The initiative focused on preventive measures.

6.1.3 Assumptions regarding preventive capability that were made when creating the scenario

In the scenario there are assumptions made both regarding humans as well as animals, food and the environment. The trigger to the scenario is an overflow of wastewater due to heavy rains, resulting in flooding. Via the environment *E. coli* with $ESBL_{CARBA}$ is transferred to animals, food and then on to humans. Other forms of transmission also contribute to further spread, such as travel, entry and import of food, animals, fodder, fertilisers and Swedish residents who have received medical care abroad and return to Sweden as carriers of bacteria with $ESBL_{CARBA}$. The inadequate application of hygiene routines by the general public, primarily when cooking, heavily contributes to the probability of the scenario.

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[93] For example, see The Public Health Agency of Sweden, *Swedish work on containment of antibiotic resistance – Tools, methods and experiences*, 2014.

The scenario assumes that if carriers of $ESBL_{CARBA}$ come into contact with healthcare, the carriage will be detected. It is also assumed that Swedish communicable disease control is generally effective, especially regarding tracing and confirming the carriage of $ESBL_{CARBA}$. When a higher presence of $ESBL_{CARBA}$ is suspected, further studies will be carried out for confirmation.

Similar assumptions are made regarding animals and food, where testing of animals and meat are presumed to lead to the detection of $ESBL_{CARBA}$. The scenario also assumes testing for animals that become ill. Healthy animals are tested according to EU regulations, which means every other year for poultry and every other year for bovine and pigs.

Purification of wastewater is presumed in general to be effective. Tests for detecting *E. coli* with $ESBL_{CARBA}$ are presumed to be done only in specific studies. When such bacteria are detected, the scenario assumes that this will be noted.

The scenario assumes that the increased presence of $ESBL_{CARBA}$ is undetected in early stages, among humans, animals and the environment. This is mainly due to the fact that most animals and humans are unlikely to become ill and hence are not tested. Additionally, systematic tests in the environment are not carried out. Ultimately, this results in the failure to establish early detection, and therefore the extent of the transmission goes undetected.

In the workshop and the analysis, colistin and tigecycline (other antibiotics) are presumed to be effective. These antibiotics are, as far as the MSB is aware, effective in the treatment of infections with $ESBL_{CARBA}$ in Swedish healthcare. However, there are countries within Europe where resistance to these antibiotics is already present.[94] [95]

During the workshop an assessment was made that *E. coli* with $ESBL_{CARBA}$ would be found with chickens in the first part of the scenario. This is not in line with the development of the events in the scenario.

6.2 Society's capability to manage an increased presence of multi-resistant intestinal bacteria

The prerequisites for managing an increased presence of multi-resistant intestinal bacteria have several aspects: early detection and subsequent warning of the trend (surveillance and alarm), reducing transmission in society (infection control), reaching a common operational picture and in a

[94] Mammina, C. et al., 2012, *Surveillance and outbreak reports. Ongoing spread of colistin-resistant Klebsiella pneumoniae in different wards of an acute general hospital, Italy, June to December 2011.*
[95] Giani, T., et al., 2013, *Surveillance and outbreak reports. Epidemic diffusion of KPC carbapenemase-producing Klebsiella pneumoniae in Italy: results of the first countrywide survey*.

coordinated manner, communication and information in response to the situation, including the ability to treat those infected.

The preconditions to manage a crisis can be improved by exercises. There have been no exercises based on scenarios regarding antibiotic resistance in intestinal bacteria, nor are there currently any plans for such exercises, to the knowledge of the MSB. Various forms of communicable diseases, including epizootic and zoonotic diseases, are the subject of regular exercises on a national level. These exercises include the participation of the National Board of Agriculture, the National Veterinary Institute, the Public Health Agency of Sweden and the National Food Agency. The County Administrative Boards have regional exercises where contagion sometimes is included in the scenarios. The MSB has no knowledge of any central or regional exercise being carried out that included intestinal bacteria, let alone multi-resistant ones.

6.2.1 Detection, common operational picture and early warning within sectors

There are two different aspects to surveillance and early warning (early detection): first, the detection of the trend of a higher presence in society and second, the detection of single outbreaks. Additionally, knowledge and experience are required to determine when the surveillance should signal the need for early warning, along with routines for doing so. A common operational picture is a prerequisite for detection and early warning, as well as for coordination and communication in a crisis.

There are various methods for detection: screening, testing when the patient exhibits symptoms, specific testing when presence is suspected or discovered by researchers in a study. The work within each sector regarding detection, common operational picture and early warning is described below. Finally, a similar description for society as a whole, using the One Health approach for humans, animals, food and the environment, will be presented.

For early detection of an increased prevalence, an overview of the present prevalence is required for comparison purposes. This corresponds by a necessary level of surveillance. In Sweden this is equivalent to the data presented annually by the Public Health Agency of Sweden and the National Veterinary Institute in the Swedres-Svarm reports.

For transmission of communicable diseases there are early warning systems defined by law. Regarding early warning within the emergency preparedness system, Duty Officers are most commonly used. All government agencies responsible for emergency preparedness, and those additionally designated at the suggestion of the MSB, are obliged to have a Duty Officer available around the clock. Municipalities and county councils are not required to have a Duty Officer, but many maintain such a service.

The Duty Officer of the MSB is also an official point of contact for a number of international forums for the purpose of sharing national common operational pictures. These forums can also serve as support when national resources are scarce.

Detection, common operational picture and early warning among humans (healthcare)

The annual results of Swedish antibacterial resistance surveillance, published in the Swedres-Svarm reports, are based on tests conducted within healthcare. Approximately two thirds of patients in hospital care receiving antibiotics are tested. For example, blood cultures are used to confirm suspected cases of invasive infections[96]. Within primary care, the test rate is significantly lower. Diagnoses such as urinary tract infections and upper respiratory infections do not immediately induce the use of bacterial cultures to determine which bacteria are causing the infection unless deemed to affect the treatment method.[97] The first cases are therefore likely to be detected in hospitals.

Carriers without detectable symptoms would therefore only be discovered when the bacteria are traced due to a patient exhibiting symptoms of infection. The Public Health Agency of Sweden will monitor and analyse the development of the registered samples.

There is no regular screening among the healthy population in Sweden. Only risk patients[98] are screened with regard to multi-resistant intestinal bacteria. As only a small portion of the population is tested, it is difficult to establish the level of presence for $ESBL_{CARBA}$ in the general population. Instead, separate population studies have been conducted to measure this, which is also the case in the scenario. According to a recent study, the prevalence of ESBL-producing bacteria in the Swedish population is nearly five per cent.[99] In a global perspective, this is a very low figure. Regarding $ESBL_{CARBA}$, resistance was only found in two samples out of over 5 000 in the study. The conclusion is that the current level of prevalence of $ESBL_{CARBA}$ in the Swedish population is likely to be very low.

Early detection of sporadic outbreaks in humans is facilitated by the fact that it is mandatory for laboratories to report ESBL-producing bacteria upon detection. In the case of $ESBL_{CARBA}$, physicians are also required to report findings of such bacteria. Furthermore, detection of $ESBL_{CARBA}$ also requires tracing the bacteria to its origins. Tracing implies a search for the original source of the bacteria, and additionally whether the bacteria have been transmitted to other individuals. If laboratories used by the county councils find $ESBL_{CARBA}$ in their analyses, they are obligated to inform the treating

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[96] Infections spreading within the body, for example into the blood stream or other internal organs.

[97] When individuals with weak immune systems are infected, clinical infections will be detected earlier than for those who were otherwise healthy when infected. One workshop participant comments that it would probably take years before the *E. coli* with $ESBL_{CARBA}$ results in urinary tract infection in a young woman otherwise healthy.

[98] For example if the patient has received care abroad within the past six months.

[99] Egervärn, M. m.fl., *Slutrapport från ett myndighetsgemensamt projekt – Antibiotikaresistens, ESBL-bildande E. Coli i vår omgivning – livsmedel som spridningsväg till människa*, 2014.

physician, the local infection control unit, including the County Medical Officer, and the Public Health Agency of Sweden. Tracing is conducted locally with support from the Public Health Agency of Sweden. Patients infected by or carrying $ESBL_{CARBA}$ are required to be documented as such in their medical records.

Within healthcare, the common operational picture on a national level is compiled by the Public Health Agency of Sweden, based on the reports in SmiNet, ResNet and Svebar.[100] It might take some time before a pattern emerges from the reports. This is partly due to the fact that it takes time to determine which kind of $ESBL_{CARBA}$ is present in each case. The more varieties involved, the longer it will take.[101] This may in turn affect which actions will be taken by the responsible actors. At a certain point in the scenario the Public Health Agency of Sweden will inform the County Medical Officers regarding the increased presence of *E. coli* with $ESBL_{CARBA}$ and it will be the responsibility of each County Medical Officer to decide which measures should be carried out within their respective county councils.

Detection, common operational picture and early warning among animals and in meat

It is mandatory to report $ESBL_{CARBA}$ in animals as well as in humans.[102] The National Board of Agriculture has the mandate to determine further actions.[103] For livestock and meat, the statistics are based on a screening program within the EU where healthy animals are tested regularly. For pets, the statistics are based on tests taken from animals that are ill, as it is for humans. Multi-resistant intestinal bacteria will therefore be detected within the EU screening program for livestock and meat mentioned above, or when tracing such bacteria when detected in individual animals or pets. Foreign animals and foodstuff are not subject to any form of screening.

If cases were detected among animals, this would be reported to the National Board of Agriculture and the County Veterinarian at the county administrative board, which is responsible on a regional and local level. It is not mandatory to inform the National Veterinary Institute. However, as the Institute offers free verification[104] on index cases at its own expense, it is plausible that this would

[100] Various databases for reporting findings in clinical test analyses.

[101] Determining the type means verifying whether it is the same type of resistance that has been transmitted or if the resistance has several origins. It can also provide information on how the transmission has occurred and thereby give guidance regarding how to contain the spread.

[102] Statens jordbruksverks föreskrifter om anmälningspliktiga djursjukdomar och smittämnen (SJVFS 2012:24) Saknr K4.

[103] The National Board of Agriculture has the mandate to make decisions regarding testing, isolation or for animals to be put down, according to förordning (2006:815) om provtagning på djur, m.m. [Ordinance on Animal Testing etc.].

[104] http://www.sva.se/antibiotika/anmalningspliktig-resistens/verifiering-av-misstankta-esblcarba-mrsa-mrsp-och-andra-mrs

increase the chances of the Institute being informed. This is also according to practice.

The County Medical Officer is also informed, and determines whether tracing is required among humans. The National Board of Agriculture would also inform the National Food Agency and the Public Health Agency of Sweden if $ESBL_{CARBA}$ has been found in livestock. In the scenario, the animals do not become ill, which means animal health professionals could potentially fail to detect $ESBL_{CARBA}$.

Testing within the EU screening programme is anonymous, hence the National Veterinary Institute is only able to inform the National Board of Agriculture of detected presence, not obligated to provide identification of the source. The National Food Agency and the Public Health Agency of Sweden would be informed. The National Board of Agriculture can decide on further tests to locate the contagion. Should the National Board of Agriculture receive reports on cases of $ESBL_{CARBA}$, it has the mandate to act immediately for tracing and containment.

The National Board of Agriculture is responsible for compiling the reports from veterinary and laboratory findings among animals. The National Veterinary Institute will verify and characterize the findings from a molecular biological perspective, and then analyse and report. Acting as risk manager regarding animal issues, the National Board of Agriculture determines future measures to take. The National Veterinary Institute will also compile, analyse and report findings uncovered in the monitoring of meat. In this context, the National Food Agency act as risk managers, however since this also relates to primary production, the National Board of Agriculture shares responsibility.

Detection, common operational picture and early warning for food (excluding meat) and in the environment (including drinking water)
Presence in other food than meat, as well as in fertilisers and sewers, is only documented as a result of tracing required when multi-resistant bacteria have caused illness. Tracing is therefore mandatory. In drinking water, producers monitor the general presence of *E. coli,* not specific types of resistance.[105] Point prevalence studies have been made, but there is no screening. Presence in raw water (surface water) or drinking water will therefore not be detected unless specific tests are ordered.

Food (excluding meat) and drinking water are measured for the presence of *E. coli* as an indicator to detect traces of bacteria, viruses or parasites from faeces. Hence, the type of resistance is not determined. *E. coli* generally does not cause illness, however it is possible that noroviruses will be present in faeces. A high level of *E. coli* indicates a risk for such viruses in the water and often results in recommendations to boil water before consumption. In the scenario, this results in failure to detect increased presence as the amount of *E. coli* is not

[105] Livsmedelsverkets föreskrifter om dricksvatten (SLVFS 2001:30) [the National Food Agency's regulations on drinking water].

increasing. The exception is the initial flooding of wastewater due to heavy rains.

There are no tests performed on wastewater for the presence of resistant bacteria. The regulations of the Swedish Environmental Protection Agency regarding sewage plants have been reviewed with the aim of modernising and simplifying them. The new regulations will not contain any demands on tests for *E. coli* in the effluent water.[106] There is no party responsible for systematic screening of the microbial quality of sewage or other parts of the environment, even though the Swedish University of Agricultural Sciences performs certain environmental analyses.

Fodder is problematic from a detection aspect. Although fodder producers should detect contagions in their internal control systems, they do not test for the presence of $ESBL_{CARBA}$. The workshop participants raised the issue that contagions can be transmitted through contaminated manure on the fields. In the fields, crops can be contaminated and as fodder transmit the contagion further into livestock production.

Cases of illness due to consumption of food or water contaminated with $ESBL_{CARBA}$ would be detected by healthcare, resulting in reports to the Public Health Agency of Sweden via routine procedure. Food controls by municipalities and the National Food Agency monitor only for specific resistance, therefore a creeping increase of $ESBL_{CARBA}$ is unlikely to be detected.

For food (excluding meat) and for the environment detection of the spread is unlikely since reporting of detected cases is not mandatory and there is no screening for $ESBL_{CARBA}$. A local increase in the level of *E. coli* in drinking water might be detected as a result of flooding by wastewater, as well as in food where tests are made due to suspected contamination. The responsible actors are the National Food Agency and the Swedish Environmental Protection Agency. Only the National Food Agency has a special responsibility for emergency preparedness.[107] A common operational picture is unlikely to be produced since the spread would be undetected. Any findings will however be forwarded to actors responsible for infection control for humans and animals.

Conclusions regarding detection, common operational picture and early warning within sectors

In conclusion, when testing is carried out due to indications of infection, whether routine or when presence is suspected, *E. coli* with $ESBL_{CARBA}$ will be detected among humans and animals. Cases will be discovered by various actors. In the environment, presence is unlikely to be detected. Even upon

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[106] http://www.naturvardsverket.se/Stod-i-miljoarbetet/Remisser-och-Yttranden/Remisser/Remisser-2014/Forslag-till-nya-foreskrifter-om-rening-och-kontroll-av-utslapp-av-avloppsvatten-fran-tatbebyggelse-samt-andring-av-Naturvardsverkets-foreskrifter-NFS-20069-om-miljorapport/

[107] Förordning (2006:942) om krisberedskap och höjd beredskap, [Emergency Management and Heightened Alert Ordinance].

detection, it was concluded in the workshop that it would not necessarily result in actions being taken.

The local and regional levels will monitor development within their respective areas, however will probably lack the benefit of the national picture. This will instead be delegated to the county councils (the County Medical Officer) by the Public Health Agency of Sweden, as the County Veterinarians will have from the National Board of Agriculture.

Early warning systems with corresponding routines for infection control exist for both humans and animals, but since testing is limited and mandatory monitoring systems could be improved, a common operational picture is unlikely to be produced, which reduces the functionality (effectiveness) of the early warning systems. Since there are few clinical cases with $ESBL_{CARBA}$, the Public Health Agency of Sweden does not focus on regularly following development within the healthy population.

Despite early warning systems for detection among both humans and animals due to mandatory reporting and tracing, the MSB concludes that with the current system for surveillance, it is uncertain whether the responsible agencies would detect a creeping increase of $ESBL_{CARBA}$ in the healthy population as well as among animals, food and the environment. Although perhaps with the exeption of the animals included in the EU screening programme. The actors responsible for infection control (for humans, animals, food and in the environment) also have plans and routines for producing a common operational picture within their sectors respectively, based on relevant regulation.

6.2.2 Cross-sectional common operational picture

The way in which a common operational picture is produced depends on within which particular sector cases are first detected and measures therefore are taken to inform the other sectors. It is thereby difficult to estimate the time required to discover whether resistance has spread throughout society, not being limited to separate sectors. This means in turn that it will be difficult to determine when a warning will be issued from a One Health-perspective and the situation therefore, as in the scenario, becomes an issue for the entire society.

National level
A forum for cooperation that can be used for producing a common operational picture for national responsible actors within infection control is the Coordinating Group for Zoonoses. The group consists of the National Board of Agriculture, the National Veterinary Institute, the National Food Agency, the National Board of Health and Welfare, the Public Health Agency of Sweden and the Work Environment Authority. The MSB, the Swedish Association of Local Authorities and Regions, the county administrative boards and the Association of County Medical Officers are affiliated on an adjunct basis. In the case of an event, the National Board of Agriculture would assemble a group for both public and private actors in the same way as for zoonoses and other contagions.

The MSB is tasked to facilitate, based on its operational responsibility. The MSB's operational assignment includes daily surveillance focusing on societal security. Reports from other government agencies, as well as traditional and social media, are included in the surveillance through multiple systems, on a large variety of subjects.

Typically, the MSB arranges national cooperation conferences once a week. The aim of the conferences is information gathering in order to produce a national common operational picture, coordinate resources and create a forum for decision-making. The MSB compiles a national common operational picture based on collected information and its own assessment of the situation. The common operational picture is shared via WIS (web-based information system). The common operational picture can also be used in reports from the MSB to the Government Offices (the Ministry of Justice). Such reports can also be requested from other government agencies by their respective supervising ministries.

The MSB does not take over responsibility from other actors during a crisis, however can offer support by serving as a coordinating function on a variety of issues. Supporting central, regional and local authorities by providing information and common operational pictures is an example. Coordination can also be achieved through designated coordination conferences.

Local and regional levels
Regional common operational pictures are produced in cooperation with county veterinarians, County Medical Officers and representatives from various municipal operations. The assumption is that actors have access to regional and local reports regarding presence, along with indications of a connection between them. The county administrative boards and the municipalities have a regional and local jurisdictional responsibility to report.[108]

How this works in practice may differ between the county administrative boards and the municipalities, depending on their respective current preconditions. The County Medical Officer's responsibility is also a factor, including his or her responsibility to plan, organize and lead the effort on infection control and strive towards efficiency, coordination and compliance within the county. [109]

Conclusions on cross-sectional common operational picture
The responsible actors within infection control (humans, animals, food and the environment) have established common cooperation forums. The MSB has a role in supporting the responsible actors by coordinating cooperation conferences and compiling a national cross-sectional common operational

[108] Förordning (2006:942) om krisberedskap och höjd beredskap, lagen (2006:544) om kommuners och landstings åtgärder inför och vid extraordinära händelser i fredstid och höjd beredskap and förordningen (2006:637) om kommuners och landstings åtgärder inför och vid extraordinära händelser i fredstid och höjd beredskap
[109] Smittskyddslagen (2004:168).

picture. The common operational picture of the MSB is published in WIS and is therefore available for other actors, including municipalities and county administrative boards. On a regional and local level, the county administrative boards and municipalities have a coordinating role, based on geographic responsibility within emergency preparedness. The county veterinarian and County Medical Officer also serve important roles. Coordination and cooperation are based on the individual set preconditions of each county and municipality.

Compiling cross-sectional common operational pictures in an efficient manner depends on relevant actors having mutual knowledge of responsibilities and routines.

6.2.3 Coordinated communication

The difference between managing an increase in the presence of multi-resistant intestinal bacteria compared to preventing it from happening is the elevated level of public anxiety. Society's capability to manage this higher presence will to a large extent be determined by how well the authorities communicate with the public. This holds true for both the information regarding how people should act and to what extent the public in turn accepts and applies this information. Trust in public authorities is of great importance for containing the spread. The importance of communicating and retaining public trust has previously been cited by the MSB, as being two of the most important strategic challenges for societal security preparedness.[110]

The MSB has a supportive role in providing coordinated communication to the public through networks for communication professionals and cooperation conferences with concerned parties. These conferences contribute to laying the foundation for producing a common operational picture and coordinating communication activities. The information generated in the conferences may also be used for producing questions and answers in a web-based tool linked to krisinformation.se, a communal webpage for information from the authorities, administered by the MSB.

In connection to the Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections, the agencies within the National Coordinating Mechanism have produced a communications' strategy. The strategy includes a platform for communication including primary and supporting messages.[111]

The experts participating in the MSB workshop deliberated over whether the National Coordinating Mechanism should be involved in managing the situation, based on an action plan and communications' strategy. However, no definitive conclusion was reached. The Action Plan mainly focuses on preventive measures and only where government agencies are responsible. The

[110] MSB, *Strategic challenges for societal security*, 2013.

[111] The Swedish Board of Health and Welfare and the Swedish Board of Agriculture, *Kommunikationsstrategi för antibiotikaresistens och vårdrelaterade infektioner*, 2014.

MSB can provide support in the distribution of information to the regional and local level as well as to the public, for example using krisinformation.se. It has not been determined to what extent the support of the MSB would be utilised.

The media and the public would react to the events in the scenario, creating demand for information from the authorities. This would create significant pressure for the communications departments of various actors, also demanding coordinated messages. This might be achieved through the cooperation conferences held by the MSB. A large increase in fatalities would be reported by the media and potentially cause concern and anxiety, hence creating a greater need for information to the public. It is a particularly difficult communication challenge to establish true understanding of the distinction between being a carrier and being ill. Managing information regarding animals, food and manure can affect public confidence in these industries.

The communications' strategy for containing antibiotic resistance and healthcare-associated infections is by definition a strategy, not an action plan for crisis communication. Therefore it is not sufficient to constitute the entire foundation for coordinating communication for such events described in the scenario. It is however a foundation for the development of such an action plan. The need for information in a crisis is immense and the capability to coordinate responsible public as well as private actors requires a level of coordination that currently does not exist in the case of multi-resistant intestinal bacteria.

Conclusions on coordinated communication
Within each sector there are often routines for coordinated communication, however cross-sectional coordination lacks such routines.

6.2.4 Containing the spread of contagion

The same principles apply to both prevention and containment of the spread, see chapter 6.1. Society's capability to contain the spread of these bacteria and thereby manage the crisis depends on the level of knowledge found in various levels of society. The public as well as various professionals in all parts of society need sufficient knowledge of both how transmission of resistant intestinal bacteria occurs as well as what carriage and illness implies. The level of knowledge on these matters will determine society's capability to contain the spread and manage the situation.

The recent influenza pandemic (AH1N1 or swine flu) and the outbreak of ebola in Western Africa has perhaps made the public more aware of infection control in general. However, it is also a challenge to explain the difference between transmission routes and consequences of being a carrier of resistant intestinal bacteria, compared to influenza and ebola which spread and create consequences in an entirely different manner.

The central aspect of managing the scenario is to contain the spread among both humans as well as among animals, in food and in the environment. This is mainly achieved by tracing, along with more rigorous hygiene routines by concerned professionals and the public. This capability requires knowledge regarding how *E. coli* with $ESBL_{CARBA}$ is transmitted and how it can be prevented. Therefore, a very important aspect of society's capability to manage

the scenario is the effective distribution of information to the public as well as to concerned professionals, explaining transmission routes and hygiene routines.

Containing the spread within human healthcare
Most county councils have routines on a regional level for managing detection of *E. coli* with $ESBL_{CARBA}$. On a regional level the County Medical Officers are responsible for tracing. The County Medical Officer responsible would interview patients surrounding food consumption. When animal contact is suspected, the county veterinarian would be consulted. The County Medical Officer can order tests for humans. The National Board of Agriculture as well as County Veterinarian can do the same for farm animals. The municipalities are also involved, however during the workshop, the issue of whether the municipalities' channels are as adequately established as the regional level, was posed. The Public Health Agency of Sweden compiles information on a national level and assists County infection control units during outbreaks. This includes determining the type of bacteria or epidemiological studies to ascertain the source of the contagion.

Most county councils have routines for detecting and managing outbreaks of *E. coli* with $ESBL_{CARBA}$. However the expertise in infection control and antibiotic resistant bacteria in Sweden is mostly in MRSA and VRE[112]. According to experts, there are knowledge gaps concerning transmission of resistant gram-negative bacteria (such as *E. coli*) within healthcare, despite a relatively high level of knowledge when compared globally. This applies to both ESBL-producing and $ESBL_{CARBA}$-producing bacteria. The events in the scenario represent the dilemma of ESBL, in which actors have yet to successfully manage.

On a regional and a local level, there is some uncertainty as to the treatment of carrier and infected patients in the healthcare system. Access to reports and monitoring of how infections develop in patients carrying resistant bacteria is difficult to obtain, but can be accessed through laboratories within the county councils' system. According to the workshop participants, no such access exists today, nor is there any funding to facilitate such access. There is also a lack of procedural uniformity in how County Medical Officers in various counties provide instructions pertaining to handling carriers, as there are no clear restrictions for carriers of *E. coli* with $ESBL_{CARBA}$. Medical care facilities, primary care facilities and nursing homes are also thought to have inadequate hygiene routines.

Containing the spread within the animal sector, including food of animal origin
In the scenario, chickens are likely to be put down and destroyed, a decision made by the National Board of Agriculture. The decision would be made after determining the extent of the transmission. The procedure and handling would match that of an incident with salmonella, involving the handling of potentially contaminated manure. The decision-making process is made more complex by

[112] Other kinds of resistant bacteria.

the risk of $ESBL_{CARBA}$ already present in other herds, in imported chickens and in imported meat in the retail chain.

Private actors, including trade organisations, have a vital role in the livestock industry. These actors are involved in infection control and preventive containment of antibiotic resistance, primarily via the National Board of Agriculture, the National Veterinary Institute and the National Food Agency.

Containing the spread within the environment, including drinking water
There is uncertainty surrounding the presence of $ESBL_{CARBA}$ in the environment, both in terms of where the presence may be found and the level of such presence. In addition there is also uncertainty regarding the division of responsibility between actors. Due to these uncertainties, it is difficult to assess how the presence of $ESBL_{CARBA}$ in the environment could be contained. The handling of manure, as previously mentioned, is potentially problematic. In terms of drinking water, the producers can extend mandatory testing on their own initiative, but there is no obligation to report findings unless the general presence of *E. coli* in the end product exceeds normal levels. Such discoveries of *E. coli* are reported to the municipal department for public health and environmental protection (or equivalent) and usually only results in recommendations to the public to boil the water before consumption.

Conclusions on containing the spread
In summary, routines for containment exist, however further planning is necessary to manage extraordinary situations as well as efforts to increase knowledge, especially at local and regional levels. There are uncertainties as to how the scenario would in fact be managed. Many of the action plans need to be coordinated on a central (national) level before the event occurs.

6.2.5 Treating infected patients

Treating infected humans and animals requires knowledge of transmission paths for resistant bacteria, routines for preventing such transmission and treatment options. Concerning transmission, the knowledge is incomplete. Routines are established, but there is no uniformity on a national level. Additionally there is a question of whether adequate resources exist for guideline and routine compliance, for example the use of cohorting[113] when needed. Regarding treatment options, it is necessary to have access to a variety of trained professionals, in medical care as well as for laboratories.

There are few treatment options for infections with $ESBL_{CARBA}$. In the scenario in chapter 5, the MSB assumes the antibiotics colistin and tigecycline to be effective, but this will not always be the case. The remaining options include trying different combinations of antibiotics, inventing new forms of antibiotics or allowing the body to fight the infection on its own. A great deal of research is

[113] In Sweden, cohorting in the case of $ESBL_{CARBA}$ constitutes specially assigned staff for each patient. The staff within the cohort is not allowed to handle food or to visit the kitchen area. Additionally, for $ESBL_{CARBA}$ the routines also include designated single rooms for each patient and individual bathrooms for the purpose of minimising the spread of infection.

in progress and there are some new pharmaceuticals soon available in the market. One example is a combination of enzyme inhibitors and antibiotics.[114] The Public Health Agency of Sweden, in conjunction with the Medical Products Agency was commissioned in 2014 by the Government to evaluate existing antibiotics from new angles to investigate whether further effect can be derived and whether the effect might be optimised to preserve the possibility of efficient treatment with antibiotics. The results are to be submitted to the Government Offices (Ministry of Health and Social Affairs) by the 31st of May, 2017.[115]

The workshop addressed that due to lack of feedback on the treatment of infected patients, for example from specialists to general physicians, the county council had inadequate information to assess the level of morbidity in infections caused by for example $ESBL_{CARBA}$. This knowledge gap is a challenge in the treatment and management of patients with infections caused by $ESBL_{CARBA}$. The knowledge gap could also be explained by a shortage of particular categories of professionals, for example microbiologists or physicians specialising in infections. However, expertise within Swedish healthcare is considered very high in an international comparison. Swedish physicians are recognised as having established routines for consulting infections' specialists in cases of uncertainty regarding how to proceed in treating infections with resistant bacteria.

Workshop participants also deliberated over whether Swedish healthcare could successfully manage such an extensive spread as described in the scenario, with respect to the challenges routines consisting of cohorting involving specially assigned staff, as well as single rooms and individual bathrooms.

Conclusions on treating infected patients
The resource capacity within Swedish healthcare is considered inadequate for cohorting and routines with single rooms and individual bathrooms. Knowledge of treatment required for patients with multi-resistant intestinal bacteria is considered satisfactory. Sweden, just as the rest of the world, is dependent upon both knowledge of how to combine existing antibiotics for more efficient treatment, as well as research to develop new antibiotics.

6.3 Consequences' assessment

In this section there are descriptions of the consequences for the core societal values for civil contingencies[116]:

- Society's Functionality (Vital Societal Functions)

[114] See for example http://www.drugdevelopment-technology.com/projects/ceftazidime-avibactam-urinary-tract-intra-abdominal-infections/

[115] The Ministry of Health and Social Affairs, *Regleringsbrev för budgetåret 2014 avseende Folkhälsomyndigheten*.

[116] These core societal values are described in *Övergripande inriktning för samhällsskydd och beredskap* by the MSB (2014).

- Human Life and Health
- Democracy, Rule of Law and Human Rights and Freedom
- The Environment and Economic Values
- National Sovereignty

The scientific publications in the assessment often refer to and include the entire family of *Enterobacteriaceae* with carbapenem resistance ($ESBL_{CARBA}$). This is a broader definition than used in the workshop scenario, which only included *E. coli* with $ESBL_{CARBA}$.

6.3.1 Core societal value 1: Society's Functionality

This core societal value includes functionality and continuity in operations which, directly or indirectly, affects Vital Societal Functions in a significant way. These values, if interrupted or upset, could bring about consequences for humans, businesses and other organisations. Society's Functionality can be divided into eleven societal sectors in which each sector contains several Vital Societal Functions. These functions are maintained by one or more Critical Infrastructures. For example, a drinking water facility (a Critical Infrastructure) maintains the Vital Societal Function drinking water supply, which in turn is a part of the societal sector Municipal Technical Services. The structure of this section is based on the eleven societal sectors. For more information on Vital Societal Functions, Critical Infrastructure and the societal sectors, in English, the reader is referred to the *Action Plan for the Protection of Vital Societal Functions & Critical Infrastructure*.[117]

Health, Medical and Care Services
This sector includes several Vital Societal Functions in which both direct and indirect consequences materialise due to the events in the scenario. The functions are dependent upon access to effective antibiotics and treatment of those with infections where antibiotic treatment is necessary. For care services, this mainly applies to preschools, domestic services, elderly care homes and other forms of care facilities. In general, the sector is heavily dependent upon its staff, which in this case is subject to a higher workload and psychosocial risks in the form of anxiety over the risk of personal infection.

Within hospitals, treatment includes elevated risk. It will be more difficult to provide highly specialised care, such as neonatal care, organ transplants and cancer treatment.[118] Treatment options for infections with carbapenem resistant *Enterobacteriaceae* are further limited compared to when bacteria are "only" ESBL resistant. Infections with carbapenem resistant bacteria result in

[117] MSB, *Action Plan for the Protection of Vital Societal Functions & Critical Infrastructure*, 2014.
[118] Aldeyab, M.A., et al., 2011, *The impact of antibiotic use on the incidence and resistance pattern of extended-spectrum beta-lactamase-producing bacteria in primary and secondary healthcare settings.*

higher mortality rates and the medications used for treatment can potentially cause severe side effects. [119]

A prevalence rate of five per cent increases the number of individuals needing hospital care[120], requiring lengthier treatments, and prolonging hospitalisation. Given the current situation, more hospital beds would be needed. This will pose a significant challenge since many medical care facilities are already strained and thereby forced to forego protocol, partly due to an insufficient supply of beds. When lengthier treatments are required, the supply of available beds decreases further. Based on current preconditions, hospitals are unlikely to succeed in upholding patient safety. It is particularly difficult to treat carrier patients while managing infection control, which requires designating single rooms, cohorting and access to individual bathrooms. Due to the strained situation, clinics would be forced to forego protocol, simply to treat the patient for the initial ailment for which medical attention was originally sought. This increases the risk for further spread of the contagion. Longer waiting times for medical care can be expected, as well as for prolonged sick leave.

Primary care will be affected by higher prevalence due to a larger proportion of patients being carriers of resistant bacteria, presumably affecting which kind of treatment will be given. For example, treatment of urinary tract infections will be considerably more difficult and costly due to the possibility of being caused by $ESBL_{CARBA}$. Elderly care homes as well as other forms of care facilities with permanent residents will have an increased workload. An increasing proportion of elderly will become carriers, demanding more care than the average patient. To contain the spread, better hygiene routines[121] as well as cleaning routines are required within preschools, schools and healthcare facilities, leading to greater costs for municipalities and others.[122]

Foodstuffs

Food production can be affected both by efforts to contain the spread as well as changes in consumption patterns for certain types of food in which contagion

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[119] Smittskyddsinstitutet, *Konsekvenser – $ESBL_{CARBA}$. Konsekvenser och risker med resistensutveckling av gramnegativa tarmbakterier med karbapenemasproduktion tillhörande familjen Enterobacteriaceae*, 2011.

[120] Partly due to that some antibiotic treatments need to be given intravenously thereby requiring hospitalisation.

[121] Hygiene routines for staff working in preschool and other care facilities currently exist and are included in the Swedish Work Environment Authority's provisions on microbiological working environment hazards – contagions, toxin effects and hypersensitivity (AFS 2005:1). Title translated by the author, only available in Swedish.

[122] The fecal-oral transmission route can be controlled by sufficient hygiene. Therefore, routines from the healthcare sector may be implemented in preschools. Considering the Communicable Disease Act, restrictions should be proportionate and based on the risk for further transmission, as advised by a participant at the MSB's workshop.

has been detected. The trade effects are unlikely to be long term, as consumers will return to their habitual patterns or substitute with similar products.

The consequences for agriculture and food producers will mainly be determined by decisions made by the National Board of Agriculture to control and manage the spread. For food production linked to agriculture, there will be costs, and in certain cases environmental consequences, when it is necessary for individual animals or entire herds to be put down and disposed of. The measures taken do not necessarily mean that animals have become ill, but rather that the animals carry resistant bacteria and are therefore regarded as a hazard to human health. In conclusion, measures can be taken to contain the spread among animals, regardless of whether the animals become ill. In Sweden, animals with carbapenem-resistant bacteria are unlikely to be treated with antibiotics. However, it is not a given that an animal with mild symptoms or carrying the resistant bacteria would be put down, partly depending on what kind of animals are affected. While chickens might be put down and disposed of, a pet or a horse might be placed in isolation, in an effort to contain the spread (which is the routine for MRSA in pets[123]).

Also relevant to mapping the consequences is the question of which measures would be relevant when cows and chickens in neighbouring farms are identified as carriers. Would such livestock be put down and destroyed? In the MSB workshop it was uncertain whether there is an upper limit for presence in which putting down and destroying the animals would no longer be an administrable solution, or if particular kinds of animals would be treated differently. The presence of *E. coli* with $ESBL_{CARBA}$ among animals is currently unknown, both for livestock and pets. Presumably the presence is minimal, at least for farm animals, where no cases have been detected, despite screening. For pets, the situation is more unclear.

Municipal Technical Services
In the case of antibiotic resistance, municipal technical services are relevant in two aspects: drinking water supply and wastewater management.

The production of drinking water is primarily affected when tracing reveals that drinking water is a source for further transmission of the contagion. In such cases, consequences are potentially extensive for the municipality in question, primarily due to restrictions imposed on inhabitants in the use of the drinking water, but also the need of further tracing. It is uncertain whether any restrictions would be imposed if the level of *E. coli* in the water is so low that it would only mean carriage of *E. coli* with $ESBL_{CARBA}$ for drinking water consumption. This should be compared to a case where the level of *E. coli* in the water is so high that it indicates contamination from norovirus, posing a risk of causing gastroenteritis for those who consume it. The municipality would potentially need to invest in additional purification equipment if the contagion originates from raw water in the form of surface water. This could be the case if the water plant's treatment of the raw water does not suffice to

[123] The National Board of Health and Welfare, *MRSA hos häst, hund och katt – Rekommendationer för handläggning*, 2011.

reduce the presence of *E. coli* with $ESBL_{CARBA}$, and the municipality has not yet invested in apparatus for UV-treatment of the water.

Wastewater management is affected since wastewater treatment can be linked to transmission of contagions. However, the type and extent of the consequences are uncertain. Treated effluent from wastewater treatment plants includes bacteria and elements of resistance, resulting in presence in our waters despite efficient purification in general. For consequences for the environment, see core societal value 3.

Other Sectors
Other sectors are not deemed to be as affected, if at all. Consequences are often determined by imposed measures to contain the spread.

Energy Supply is deemed to be unaffected. There is an uncertainty in handling biological waste, for example retting or gas production as they could be affected since it is a potential transmission route for spreading resistance.

Trade and Industry are potentially affected when coming into contact with food or other businesses affected by the spread of resistance or bacteria.

Public Administration (Management Functions, Support Functions) is deemed to be affected through the need for management and decision-making, for example to produce common operational pictures and coordinating information to the public.

Protection, Safety and Security are deemed to be affected, depending on which measures are decided upon to manage the situation. For example, special routines may be necessary within rescue services and the police to contain the spread.

Social Services are affected primarily through an increase in sick leave. The extent is uncertain.

Transports may be affected if measures of infection control are established to contain the spread of bacteria and resistance. Examples of such measures could be restrictions in animal and food transports or in public transport. Travelling patterns might also change due to anxiety among the public regarding the risk of becoming infected.

Concluding assessment of the effect on society's functionality
Consequences for society's functionality due to an increased presence of *E. coli* with $ESBL_{CARBA}$ will be extensive, especially within the societal sector of Health, Medical and Care Services. The consequences within the Foodstuffs' sector might also be large. Several other societal sectors are affected, to a lesser extent. The total extent of the consequences is primarily dependent on which measures are established to contain the spread.

6.3.2 Core societal value 2: Human Life and Health

The core value Human Life and Health includes physical and mental health among those individuals who suffer directly or indirectly (for example next of kin) by the course of an event. This core societal value includes all individuals permanently or temporarily residing in Sweden or are Swedish citizens residing

abroad. Individuals in other countries who are not Swedish citizens or who are not residing in Sweden are included in certain cases.

An increase in antibiotic resistance means that individuals in certain cases will be unable to receive medical treatment, as the case is today. It may be applied to various common infections, routine surgical operations (such as hip replacement operations and caesarean operations) and specialised medical care services (such as cancer treatment). The individual will be at greater risk of injury or death from infections that are currently treatable. Treatments currently taken for granted will become so risky as to be fatal, or such that physicians decide not to proceed, which can result in people having to live with diseases and difficulties that are currently treatable. In the case of caesarean operations, a reduction in procedures can lead to an increase in complicated deliveries with higher risk of injury and death among women and infants. The extent of the consequences from the scenario in chapter 5 depends largely on which decisions are made to contain the spread of the resistant bacteria.

Mental health could be affected based on the scenario, mainly in three aspects: the concern for resistant bacteria, potential stigma due to reception from healthcare and society in general and finally decreasing trust in healthcare.

A positive consequence potentially resulting from the scenario is the public's increased awareness of hygiene, for example the importance of hand washing and ensuring that children with diarrhoea stay home from preschool etcetera.

6.3.3 Core societal value 3: The Environment and Economic Values

This core societal value includes economic value in the form of private and public property and the value of goods and services. It also includes the environment defined as land, water and the physical environment, biodiversity, valuable natural and man-made environments, and other examples of cultural heritage in the form of property.

Economic Values
For all the consequences identified for the previous two core societal values there are corresponding costs. The greatest costs arise within medical care services due to the increasing need for tracing, more testing and more extensive demands for cleaning, longer hospital stays and more resource-intensive care, for example, single rooms, individual bathrooms and cohorting with specially assigned staff. The costs for sick leave, temporary parental benefits[124] and more extensive hygiene routines will also increase.

The costs for society overall will depend, as the consequences for society's functionality, on which decisions are made regarding improved routines to contain the spread.

[124] Care of a child (VAB) is a social benefit for absence from work in order to take care of a sick child. The compensation received when caring for a child is referred to as temporary parental benefits.

The Public Health Agency of Sweden has presented a report based on a Government commission of economic consequences based on modelling of resistance mandatory to report (the bacteria *Enterobacteriaceae* with ESBL, MRSA, VRE and PNSP).[125] The final report concludes that the additional cost on top of standard medical care for the resistance of these bacteria is estimated at approximately SEK 160 million per annum, based on today's presence of resistant bacteria. The sum takes into account extra costs for antibiotics and miscellaneous medical expenses caused by resistant bacteria. These are costs that would not have arisen if the bacteria were treatable with ordinary antibiotics (not been resistant). This can be regarded as a comparative or additional sum for resistance, where the largest costs are attributed to medical care services and tracing. Indirect costs, such as sick leave, reduced productivity etcetera, are not included. The Public Health Agency of Sweden has been commissioned to calculate, based on the method in the final report, the cost of resistance based on various scenarios. The scenarios are designed for guidance purposes in the appropriate measures to manage resistance development within healthcare and in society. The final report is to be submitted to the Ministry of Health and Social Affairs on the 31st of December 2017 at the latest.[126]

In the Dutch scenario analysis of antimicrobial resistance, the equivalent of the Swedish national risk and capability assessment, a scenario in which resistant bacteria become endemic as in the MSB's scenario, reveals that the resulting costs would mount to several hundred million euros.

Economic consequences of resistant bacteria can also induce a slow-down in economic growth and a reduction in GDP, based on reduced production of medical care services such as hip replacement operations and caesarean operations.[127] It is uncertain whether the scenario in chapter 5 would have such effects.

In conclusion, an increased presence of $ESBL_{CARBA}$ in society can result in great financial cost. The costs would arise primarily within medical care services, for example due to an increased need for single rooms. The extent to which the scenario will produce cost in other areas of society depends on the decisions made to contain the spread, inducing further consequences.

The Environment

In the scenario in chapter 5, *E. coli* with $ESBL_{CARBA}$ has spread to the environment via wastewater flooding, creating contaminated surface water sources. The consequences of the scenario relating to the environment are not extensive and are primarily about *E. coli* identified in raw water and

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[125] Folkhälsomyndigheten, *Samhällsekonomiska konsekvenser av antibiotikaresistens - Modellering av anmälningspliktig resistens i Sverige – slutrapport av regeringsuppdrag till Folkhälsomyndigheten 2013*, 2014.

[126] Socialdepartementet, *Regleringsbrev för budgetåret 2015 avseende Folkhälsomyndigheten*, S2015/04530/RS (delvis).

[127] Review on Antimicrobial Resistance, *Antimicrobial resistance: Tackling a crisis for the health and wealth of nations*, 2014.

wastewater to a larger extent tend to carry $ESBL_{CARBA}$. It is worth noting that the scenario does not depict a larger presence of *E. coli* in the environment in general, except after initial heavy rains. However, to a larger extent the detected *E. coli* carries $ESBL_{CARBA}$.

The consequences of a larger spread in the environment are instead found in wild and farm animals which become carriers of $ESBL_{CARBA}$ to a greater extent. The animals then transmit the resistant bacteria through their faeces (manure) and into food production. Additionally, contaminated water is used for the cultivation of produce.

The opportunity for the public to enjoy and utilise the environment can be affected, for instance swimming in lakes, even though resistant bacteria have no direct effect on the environment. There is great uncertainty regarding transmission routes between the environment, animals and humans, making it difficult to assess the consequences.

In conclusion, an increased presence of $ESBL_{CARBA}$ in the environment leads to an increased risk for further spread among humans, animals and food. Additional consequences may occur, however they are uncertain and therefore difficult to assess.

6.3.4 Core societal value 4: Democracy, Rule of Law and Human Rights and Freedoms

This core societal value includes public confidence in democracy, rule of law and trust in public institutions, including the political decision-making process. The leadership ability on various levels, lack of corruption and preventing miscarriages of justice are also included in this core value.

Antibiotic resistant bacteria, similar to other contagion, are invisible to the human eye and visible only on a microscopic level. This can lead to uncertainty among the public in identifying when the bacteria are present and if one has taken adequate measures to remove them, for example by cleaning and washing one's hands. Such uncertainty leads to anxiety as well as a greater demand for information from responsible authorities. If the authorities are unable to meet this demand, there is a risk of losing public trust. It is difficult to predict how the public will react to the course of events in the scenario and the information on the spread of $ESBL_{CARBA}$ in society. Therefore it is also uncertain to what extent fear and concern will affect the public.

In the case of multi-resistant intestinal bacteria, it is primarily among businesses, institutions and other facilities where the contagion is discovered and spread that risk a potentially declining public trust. Examples would include medical care services, farmers and food producers. If more individuals become infected with resistant bacteria while in contact with for example healthcare, it can potentially reduce public trust in healthcare. Public trust in medical care services related to patient safety is already an issue. Another issue is whether healthcare institutions could be made accountable for the continued spread and the consequences for individuals who become infected through contact with such institutions, for instance, complications due to prolonged hospitalisation or postponed assessments or treatment.

There is potentially a risk for stigmatisation and discrimination. For example, carriage could potentially affect employment opportunities. The fear of infection and ignorance regarding transmission routes and hygiene routines can affect children in preschool who are carriers. It is also vital how patients are received in healthcare when they as carriers seek initial treatment.

6.3.5 Core societal value 5: National Sovereignty

This core societal value includes control over national territory, national control of the political decision-making processes in the country and national supply chain resilience for essential goods and services. National sovereignty can be seen as a prerequisite for protecting the other core societal values.

The scenario is deemed to affect this core societal value only to a negligible extent. The supply of pharmaceuticals is however relevant, given the necessity of efficient antibiotics and not having any Swedish production. The scenario is not deemed to affect this supply since in this case we are much more dependent upon the creation of new antibiotics rather than the method in which they are delivered.

6.3.6 Assessments in conclusion

In conclusion, Human Life and Health (physical and mental) along with Society's Functionality (primarily the societal sector of Health, Medical and Care Services) are the core societal values in which the scenario results in the most serious consequences. For example, the individual can become seriously ill or die as a result of infections which are currently treatable. These consequences appear due to deteriorating conditions for administering treatment, reduced access to treatment and an increased workload in healthcare. The health of the individual is also affected since certain specialised care is unable to be administered due to elevated risk of infection. The reduced capability of medical care services to treat patients can also cause mental suffering and anxiety for contracting infections difficult to treat. It is reasonable to believe that with a five per cent prevalence of *E. coli* with $ESBL_{CARBA}$ among the population, other sectors of society will be affected. It is probable that everyone will be acquainted with someone who is affected. There will be economic consequences for both medical care services and individuals, hence for sick leave, pensions, temporary parental benefits etcetera. Reduced productivity due to prolonged sick leave, death and diminished quality of life as a result of non-treatment will also result in economic costs for society.

Livestock production in Sweden will primarily be affected by measures taken to contain the spread of resistant bacteria. This is also true for other actors required to modify their production processes or routines to contain the spread. These consequences are uncertain, especially for actors outside animal and food production sectors. Measures to prevent and contain the spread of antibiotic resistant bacteria can incur costs, for example the demand for tighter hygiene and cleaning routines in addition to other investments.

The costs of antibiotic resistance have been calculated in various ways in several reports. The use of various methods and assumptions also leads to varied results, depending on which factors and limitations are used. The Public

Health Agency of Sweden has recently presented cost calculations relating to resistant bacteria which are mandatory to report when detected (*Enterobacteriaceae* with ESBL, MRSA, VRE and PNSP). The sum, approximately SEK 160 million, is the additional cost for resistance in these bacteria besides basic medical care. The costs include antibiotics and medical care arising from the resistant bacteria, costs that would not have arisen if the bacteria were treatable with ordinary antibiotics (not been resistant). The result can therefore be regarded as a comparative sum for resistance where the largest costs occur within medical care facilities and in tracing. Indirect costs are not included, for example sick leave, production losses etcetera.[128]

Resistant bacteria will spread within the environment. It is uncertain how this will affect cultural heritage and enjoyment of and access to the environment. The reduced capability to treat patients and measures necessary to contain the spread can potentially affect public trust and cause anxiety in society. The events in the scenario depict a clear need for efficient and coordinated decision-making, both for preventive measures and crisis management. There will be a great need for information and communication, with questions considered difficult to communicate. Many of the consequences are uncertain since they depend upon which decisions are made in managing the crisis and containing further spread.

6.4 Rationale regarding probability

When producing the scenario, the respondents have had differing opinions regarding how rapidly the presence of $ESBL_{CARBA}$ in Sweden may increase. There is however consensus that the situation outside Sweden is worse and deteriorating. The discussions in the workshop centred on the likelihood of the scenario being a reality within 10-15 years.

$ESBL_{CARBA}$ is sometimes compared to ESBL. In 2007, approximately 2 000 cases of ESBL were reported in Sweden.[129] During 2014 nearly 9 000 cases were reported.[130] A recent study states that approximately five per cent of the Swedish population carries ESBL-producing *E. coli*.[131] The detected cases of $ESBL_{CARBA}$ are far from the 2 000 cases of ESBL reported in 2007, however the development in the reports of both ESBL and $ESBL_{CARBA}$ demonstrates that the spread of ESBL-producing bacteria is rapid.

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[128] The Public Health Agency of Sweden, *Samhällsekonomiska konsekvenser av antibiotikaresistens - Modellering av anmälningspliktig resistens i Sverige – slutrapport av regeringsuppdrag till Folkhälsomyndigheten 2013*, 2014.

[129] Ternhag, A., $ESBL_{CARBA}$ 2007-2013, presentation during workshop on the 25th of September 2014 in MSB, the Public Health Agency of Sweden, MSB dnr 2015-4537.

[130] The Public Health Agency of Sweden and the National Veterinary Institute, *Swedres-Svarm 2014 – Consumption of antibiotics and occurrence of antibiotic resistance in Sweden*, 2015.

[131] Egervärn, M., m.fl., *Slutrapport från ett myndighetsgemensamt projekt – Antibiotikaresistens, ESBL-bildande E. Coli i vår omgivning – livsmedel som spridningsväg till människa*, 2014.

This conclusion is confirmed by the Dutch national risk assessment, stating that the probability of the assessed scenarios is relatively high compared to the probability of other risks previously analysed using the same method. In some cases the scenarios had already occurred. The scenario with an endemic spread of *Klebsiella pneumoniae* with $ESBL_{CARBA}$ was deemed likely to occur within ten years' time.

In conclusion, it is not possible to make a definitive assessment of the probability for presence of $ESBL_{CARBA}$ in five per cent of the population in the southern parts of Sweden. Experts deem it highly likely that $ESBL_{CARBA}$ will spread as quickly and extensively as ESBL. When such a spread might occur is very difficult to assess, however the discussions among the experts in the MSB workshop revolved around it becoming a reality within 10-15 years.

6.5 Uncertainty and sensitivity in assessing the scenario

All of the assessments incorporate a degree of uncertainty, due to the lack of quality and access to available material. Additionally there is the sensitivity[132] of the results of the analysis, relating to how the output varies with the input given the uncertainties. The uncertainties of the scenario analysis are mainly due to lack of experience in managing such events, as no such event has occurred in Sweden to date. Also, to the MSB's knowledge, there have been no comparable scenarios used in exercises. Containing antibiotic resistance has mainly focused on preventive measures. It is only recently that the emergency preparedness area has brought attention to antibiotic resistance as a threat to societal security.

There are currently structures and working methods in place within emergency preparedness to manage events from an all-hazard approach. Specialist actors are capable of managing situations within their field. However there is less certainty when collaborating with other actors who do not possess the same expertise knowledge, for example the MSB and the emergency preparedness units of the county administrative boards. On the other hand, there is a degree of uncertainty in the level of knowledge within the MSB and the emergency preparedness units of the county administrative boards, with respect to the structures and working methods in the relevant fields of expertise.

The extent to which food and the environment will act as vectors[133] for spreading *E. coli* with $ESBL_{CARBA}$ is also uncertain. The joint-agency study on ESBL-producing bacteria in food, published in late 2014 by the National Food Agency and others, concludes that food within the Swedish market is, only to a limited extent, a source of *E. coli* with ESBL within Swedish medical care. The study also concludes that there are three separate groups of *E. coli* with ESBL in Sweden – one for food and livestock, one for animals, whether through

[132] Sensitivity in a statistical sense, i.e. not regarding for example public reaction.
[133] A vector can be described as an organism, an object or a substance that in itself is not a contagion, but the conduit transmitting them. Examples of vectors are fluids, tics, humans, vehicles etcetera.

import or entry, and one for humans. The last group includes the environment, including wastewater. The study clearly states that monitoring the spread of *E. coli* with $ESBL_{CARBA}$ in society is vital, since the situation may change rapidly due to antibiotic resistance being a global as well as a dynamic problem.[134]

Access to effective antibiotics is the most important factor for consequences arising from the scenario. This applies to both core values of Human Life and Health and Society's Functionality (mainly the societal sector of Health, Medical and Care Services). If there had been an assumption in the scenario regarding the development of effective new antibiotics or treatment methods, the consequences for both the individual and health and medical care would have been less severe due to an improved situation. However, it is very likely that resistance would develop against new antibiotics.

It should be noted that the antibiotics colistin and tigecycline were still deemed effective during the scenario analysis. This assumption was made during the workshop and analysis and reflects the current situation in Sweden. There is already resistance against colistin and tigecycline in Europe.[135] If no antibiotics are effective (pan-resistant bacteria), a far more dangerous situation would arise than analysed in our scenario. Likewise, with new effective antibiotics, the consequences of the scenario would be less serious. New pharmaceuticals are under way. However, the MSB cannot assess what kind of effect new antibiotics will have in regard to the consequences of an increased spread of $ESBL_{CARBA}$ in Sweden.

How early the spread is detected is another important factor determining the extent of the consequences. In the scenario, the spread may have been detected earlier if triggered by hospital outbreaks, facilitating infection control.

The extent of consequences will also be determined by the level of concern and anxiety in the reaction of the public. Equally important is which actions are taken to contain the spread. The scenario also assumes that the situation outside Sweden does not change. Although, the scenario could have taken into consideration international aspects impacting the consequences, since bacteria spread across borders and the fight against antibiotic resistance is global.

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[134] Egervärn, M. m.fl., *Slutrapport från ett myndighetsgemensamt projekt – Antibiotikaresistens, ESBL-bildande E. Coli i vår omgivning – livsmedel som spridningsväg till människa*, 2014.

[135] Giani, T., 2013, *Surveillance and outbreak reports. Epidemic diffusion of KPC carbapenemase-producing Klebsiella pneumoniae in Italy: results of the first countrywide survey, 15 May to 30 June 2011.*

7. Conclusions and recommendations

In this chapter, conclusions are drawn regarding consequences, probability and society's capability to prevent and manage an increased presence of multi-resistant intestinal bacteria. Finally the MSB provides recommendations for the continued work towards strengthening society's capability to prevent and manage such a spread. The recommendations are primarily aimed at the public sector.

7.1 Consequences and probability of an increased presence of multi-resistant intestinal bacteria

Antibiotics save lives. Resistant bacteria mean that we risk losing the tool of antibiotics. This analysis reveals that the consequences for society may be significant if an increased spread of multi-resistant bacteria in Sweden occurs. The greatest consequences arise within medical care and human life and health. Tightened hygiene routines may also affect functionality within large parts of society. The concern for infection may result in greater need for information. If the public's expectations of healthcare and information are not met, trust in society's institutions can decline.

At the MSB workshop, the experts' discussions revolved around a situation in which five per cent of the Swedish population carrying $ESBL_{CARBA}$ could be a reality within 10-15 years, based on the assumption that $ESBL_{CARBA}$ will spread as quickly and extensively as ordinary ESBL. Principally, it is only a matter of time before such an extensive spread will occur. However, there are significant uncertainties regarding both the type of consequences that will arise and how and to what extent resistance mechanisms such as $ESBL_{CARBA}$ are spread between for example humans and the environment.

7.2 The capability to prevent and manage an increased presence of multi-resistant intestinal bacteria

For civil contingencies, society's capability to prevent and manage an increased presence of multi-resistant bacteria is a critical issue, as depicted above. This is also true for antibiotic resistance as a whole. Antibiotic resistance is therefore not only a concern for the fields included by the One Health approach (humans, animals, food and the environment). These fields constitute the front line and a great deal of work is in progress, as described in the agencies' Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections. This work should be encouraged and supported, with further measures required to prevent and manage an increased spread of multi-resistant intestinal bacteria.

Antibiotic resistance is a global issue, bacteria knows no borders. Preventive efforts are required on a global level, among which Sweden is a leading country.

Sweden's international commitment in this area needs to continue to be prioritised in the future. In the agencies' Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections a number of measures are described.

The preventive work is in principle about slowing down the momentum of the spread. This work is mostly comprised of having knowledge and being compliant with rules and regulations. In Sweden, there is expertise concerning the risks of multi-resistant intestinal bacteria and to some extent how it is spread. However, that knowledge and expertise are not widespread. Public and private actors as well as the general public need to increase their knowledge of the consequences of an increased spread of antibiotic resistance and how it can be prevented and contained. Therefore, central government agencies, county administrative boards, county councils and municipalities need to consider whether antibiotic resistance should factor into their respective risk and vulnerability analyses, if not already the case.

Adequate preconditions are required in order to achieve detection and early warning relating to the presence of multi-resistant intestinal bacteria, for example $ESBL_{CARBA}$. This includes both single outbreaks and the increased spread across society. The MSB reckons that such preconditions exist for detection and early warning regarding humans, animals and in meat, but not for other food or the environment. Adequate preconditions for detecting and identifying an increased presence of carriage in the population at an *early* stage are limited, especially if the increase does not result in more people falling ill and thereby being subjected to testing. In the Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections, a number of measures are described, to be executed within the next few years, to enhance the monitoring of the presence of resistant bacteria in society. Thereby the preconditions for early detection of an increased spread are also enhanced.

Forums and channels for cooperation exist for both the actors working with infection control, as well as within emergency preparedness as a whole. Examples of this are Duty Officers, cooperation conferences, the Swedish forums for crisis preparedness, the Zoonosis Cooperation's Group and the National Coordinating Mechanism on containing antibiotic resistance and healthcare-associated infections. The capability to manage events regarding multi-resistant intestinal bacteria could be improved by responsible actors increasing their knowledge on these forms of cooperation, along with their respective roles in a crisis. There is ongoing work on both CBRNE-related issues[136] and the *Common Guidelines for Collaboration and Command in Societal Disruptions* [137] that to a larger extent could be used to further develop cooperation. Such development should be kept within existing forms of cooperation.

[136] MSB, *Vägledning till den svenska aktörsgemensamma CBRNE-strategin*, 2014.
[137] MSB, *Gemensamma grunder för samverkan och ledning vid samhällsstörningar*, 2014. An English version will be available in 2016.

To enhance the capability to prevent and manage an increased presence of $ESBL_{CARBA}$ and other multi-resistant bacteria, there is a need for additional plans and routines. This is highlighted in the Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections. According to the Action Plan the responsible agencies should develop a suggestion for a cross-sectional strategy for management of $ESBL_{CARBA}$ in humans, animals, food and the environment.

7.3 The MSB's recommendations

Based on the conclusions above regarding society's ability to prevent and manage an increased presence of multi-resistant intestinal bacteria, the MSB recommends that:

- concerned parties within emergency preparedness aspire to increase their knowledge of the risks involving antibacterial resistance, especially $ESBL_{CARBA}$.
- government agencies with special responsibilities for emergency preparedness, and counties and municipalities, investigate and consider including antibacterial resistance in their respective risk- and vulnerability analyses.
- intentions and measures described in the government agencies' Action Plan for Containment of Antibiotic Resistance and Healthcare-Associated Infections are executed according to plan.
- responsible actors enable and develop Swedish government agencies' international work on containment of antibiotic resistance.

8. References

8.1 Legal documents

Translations are provided, however the reader should be aware that the translations are made by the author and therefore must be regarded as non-official translations.

8.1.1 Acts and ordinances

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8.1.2 Agencies' regulations

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Myndighetens för samhällsskydd och beredskaps föreskrifter om landstings risk- och sårbarhetsanalyser (MSBFS 2015:4), The Swedish Civil Contingencies Agency's Regulations on County Councils' Risk and Vulnerability Analyses.

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