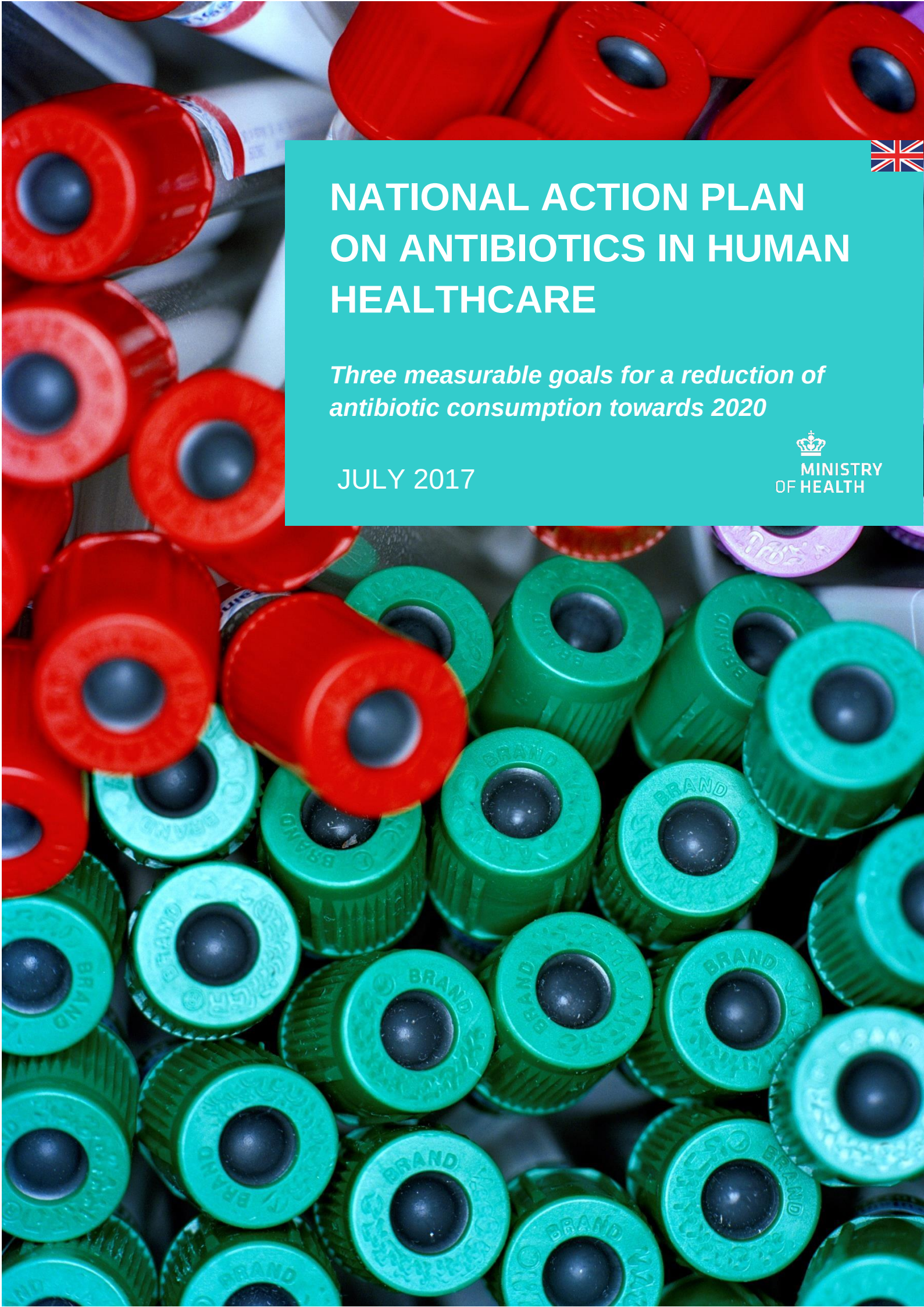

NATIONAL ACTION PLAN ON ANTIBIOTICS IN HUMAN HEALTHCARE

Three measurable goals for a reduction of antibiotic consumption towards 2020

JULY 2017

MINISTRY OF HEALTH

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Foreword: Antibiotics or not?

Antibiotics play a key role in the treatment of infections, and not long ago, pneumonia was often considered a fatal disease. However, antibiotics will cease to be effective if we use them too often. For this reason, antibiotics must be used with care. Otherwise, we run the risk of once again becoming powerless to fight infections that are now considered relatively harmless.

For years, Denmark has spearheaded efforts in the field of antibiotics, and we were the first in the world to establish a One Health national monitoring programme for humans and animals in 1995. The Danish National Antibiotic Council was established in 2010 by the Liberal-Conservative (VK) government at the time, and at the same time the former Minister of Health and Minister of Food published a One Health National Action Plan on Antimicrobial Resistance.

The One Health cooperation, which intends to prevent the transmission of resistant bacteria from animals, the environment and food to humans, is highly prioritised by the current government. I have therefore, in July 2017, in cooperation with the Minister of Environment and Food, published a national One Health strategy, to serve as overall guidelines for work in the field of antibiotics, both here in Denmark and through our participation in international networks.

Bacterial resistance to antibiotics means that antibiotics cease to be effective, and each time we use antibiotics, bacteria become more resistant. In the end, these bacteria can become so resistant that antibiotics are no longer able to treat the infection. This cannot be allowed to happen.

With input from the National Antibiotic Council, among others, I have therefore, set up three ambitious and measurable goals that aim at reducing the consumption of antibiotics among humans – and in this way also reducing the development of resistance – by the year 2020. This is also in line with Denmark's EU-commitments, as it follows from EU Council conclusions regarding antibiotics of June 2016, that national measurable goals for antibiotics must be in place by mid-2017.

To briefly summarise the three national goals: Goals 1 and 2 are directed at antibiotic consumption in the primary healthcare sector, while goal 3 is directed at hospitals. The reason that two of three goals are directed at the primary healthcare sector is that most of the antibiotics are prescribed by general practitioners, private specialists, dentists and emergency care physicians. Goals 1 and 2 are closely connected, as goal 1 is directed at reducing the unnecessary consumption of antibiotics in the primary healthcare sector, while goal 2 focuses on a more prudent use of antibiotics in any situation where physicians decide to prescribe antibiotics. Goal 3 aims to ensure that critically important antibiotics in the treatment of serious infections in patients will continue to be effective in the future.

This is the first time that measurable goals have been set up for antibiotic use in human healthcare in Denmark, and I hope that you will join me in supporting these goals, so we can work together to ensure a future where antibiotics continue to play a key role in the treatment of diseases.

Happy reading.

Ellen Trane Nørby
Minister for Health

Introduction: Background for the goals

A threat to modern illness treatment

Antibiotic resistance poses a particular threat to the health of the elderly or individuals with weakened immune systems, and can lead to significant problems in all areas of treatment, including the treatment of cancer or simple hip surgeries. Antibiotic resistance can result in a lengthier course of treatment, or even death. Antibiotic resistance also involves higher expenses for hospitals, as patients with resistant bacteria often require single rooms and longer hospital stays.

In order to treat patients with serious infections in the future, it is essential that the antibiotics utilised in this treatment remains effective – meaning that the bacteria have not become resistant. This especially applies to various critically important antibiotics – meaning the only antibiotic or one of very few kinds of antibiotics that can be used in the treatment of serious infections in humans. It is therefore crucial to avoid the overuse of critically important antibiotics. The development of resistance can be prevented by certain measures, such as restricting the consumption of antibiotics.

The current action plan must be viewed as a follow-up related to several other initiatives, such as the 2010 National Action Plan on Antimicrobial Resistance, the EU Council conclusions on antibiotics which was adopted under the Danish EU Presidency in 2012, and the Nordic Declaration on Antibiotic and Antimicrobial Resistance, adopted during the Danish Presidency of the Nordic Council of Ministers in 2015. Recently, the Ministry of Health launched a national antibiotic strategy in cooperation with the Ministry of Environment and Food in July 2017.

According to the EU Council conclusions of June 2016, Denmark is under the obligation to prepare a national action plan listing measurable goals by mid-2017. The development of the Danish consumption and level of resistance, is summarised below, along with background information providing the content of the three new measurable goals for the reduction of antibiotic consumption in humans.

Antibiotic consumption and resistance in Denmark

Many countries face even bigger problems with resistance than in Denmark, and many of the resistant bacteria were brought to Denmark by humans, animals and food products crossing the border. In 2015, Denmark had the 8th lowest consumption of antibiotics of 25 European countries, determined by total antibiotic consumption as measured by defined daily doses per 1000 inhabitants (DDD).

Denmark has had a restrictive use of antibiotics for humans for many years. Denmark continues to have a low level of resistance in both a European and international context, due to ongoing Danish efforts in this area, on a national, regional and local level, and among individual members of the public.

Consumption in the primary healthcare sector, i.e. pharmacy sales throughout the country, comprises almost 90 % of the total antibiotic consumption, while hospitals are responsible for the remaining 10 % of the total antibiotic consumption. Distribution in the primary health care sector, including hospital physicians, is shown in Figure 1 below.

Figure 1: Distribution of prescriptions by type of physician in the primary healthcare sector 2016

	Prescription percentages
General physicians	75
Dermatologists – Venerologists	1
Hospital physicians	12
Dentists	7
Ear-nose-throat physicians	2
Other specialist physicians	1
Unknown medical specialty	3

Note: *A small percentage of the prescriptions contain inadequate or incorrect information, where records show varying percentages.*
Source: *Antibiotic statistics from esundhed.dk (Danish e-Health portal)*

From 2000 to 2011, there was a sharp increase in the consumption of antibiotics in the primary healthcare sector, measured by DDD/1000 inhabitants, although this has since stagnated. At the same time, there has been a decline in the use of narrow-spectrum antibiotics, which makes antibiotic consumption even more inexpedient. There has been an especially sharp decrease in the consumption of narrow-spectrum penicillin, while broad-spectrum penicillin combinations have strongly increased until 2015. In addition, the primary healthcare sector has shown a somewhat inexpedient use of antibiotics. Here antibiotics have been prescribed for viral infections, despite the inefficacy of antibiotics against such infections. Both factors – the overuse of broad-spectrum antibiotics and antibiotics used to treat infections on which they have no effect – may lead to increased resistance.

Not all antibiotics are equally important in the treatment of humans. Several antibiotics have been designated “critically important” by the World Health Organization (WHO), because they are the only antibiotics, or one of the few that can be used to treat serious and potentially life-threatening infections in humans. These types of antibiotics should only be used with caution, and should be limited to situations where treatment is considered relevant and significant. For certain groups of antibiotics this means that they should be reserved for specific infections with resistant bacteria, and infections in seriously ill patients.

The Danish Health Authority in Denmark has designated three groups of antibiotics as critically important; these are cephalosporins, fluoroquinolones and carbapenems. Though the consumption of these critically important antibiotics has declined over the past years, the rate of consumption is still of concern and it is important to keep a continued focus on restricting the use of these critically important antibiotics, especially in hospitals.

Three measurable goals for antibiotic consumption in humans
Several criteria were specified prior to drafting the three national goals. Among others the goals must be nationally relevant, they must be valid from 2017 to 2020, they must be directed at both the primary healthcare sector and hospitals, it must be possible to implement them immediately, and it must be possible to follow their progression by means of existing digital surveillance.

The three measurable goals were drafted with input from the Danish National Antibiotic Council, and are based on the most important principles used when drafting guidelines on the rational use of antibiotics. Furthermore, Danish conditions have been taken into account as assessed through Danish surveillance of antibiotic consumption and resistance via DANMAP (Danish Programme for Surveillance of Antimicrobial Consumption and Resistance) and the Danish National Prescription Registry. Current regional and local initiatives were considered when drafting these goals. All three goals apply to the use of antibiotics for systemic use (WHO ATC medicinal product J01 and P01AB01), which means that locally delivered antibiotics, such as eye drops, ointments and creams are not included.

Figure 2: Three measurable goals for antibiotics in humans 2017-2020

Goal 1: The number of redeemed prescriptions for antibiotics should be reduced	Goal 2: There should be a change in the use of broad-spectrum to narrow-spectrum antibiotics	Goal 3: The consumption of antibiotics that are critically important for the treatment of infections should be reduced
The number of redeemed prescriptions for antibiotics in the primary healthcare sector should be reduced from 460 prescriptions per 1000 inhabitants per year in 2016 to 350 prescriptions per 1000 inhabitants per year in 2020.	Narrow-spectrum antibiotics should be used more frequently in illness treatment. The use of Penicillin V should be increased from approx. 31 % in 2016 to constituting 36 % of the total antibiotic use in the primary healthcare sector in 2020, measured by the number of prescriptions per 1000 inhabitants.	The consumption of critically important antibiotics should be reduced by 10 % by 2020 measured by DDD/100 bed-days for hospitalised patients, compared with consumption in 2016.

For goal 1 and goal 2 it is noted that the number of prescriptions per 1000 inhabitants per year is estimated based on reports of antibiotics dispensed from Danish pharmacies. The primary healthcare sector is in this case, defined as prescriptions written by general practitioners and private practice specialists, including emergency physicians and dentists.

For goal 3 it is noted that consumption is estimated in DDD (defined daily dose), which is a standard dose per antibiotic group per primary indication determined by WHO´s ATC group. DDD is the recommended unit of measurement used to quantify the use of the same medicinal product group over time. DDD is an international system, and as such it is used to compare the consumption of a certain group of antibiotics between countries. Consumption is adjusted for hospital activity by estimating the use per 100 bed-days.

The year 2016 is the baseline for all three goals.

Follow-up and implementation of the national goals will be carried out within the existing financial framework for this area.

Goal 1. Most infections resolve on their own

Background for goal number one
The purpose of antibiotic treatment is to destroy pathogenic bacteria. However, the use of antibiotics also causes bacteria to protect themselves by developing a resistance to the antibiotic agent over time. It is therefore essential to avoid the overuse of antibiotics.

Surveillance figures show that approx. one in four Danes were given one or more prescriptions on antibiotics in 2016. There was a sharp increase in the consumption of antibiotics in the primary health care sector from 2000 to 2011, but this increase has since stagnated.

It has been assessed that there is a potential for reducing the consumption of antibiotics in the primary health care sector by reducing the unnecessary use of antibiotics. Antibiotics are ineffective against virus infections, and most respiratory infections are caused by viruses. In such cases, antibiotics do more harm than good. In case of mild and moderate bacterial infections, antibiotics may also be harmful, for instance, in the treatment of middle ear infections in children.

A reduction in the total consumption of antibiotics in the primary health care sector can be achieved:

Goal 1

The number of redeemed prescriptions for antibiotics in the primary healthcare sector should be reduced from 460 prescriptions per 1000 inhabitants per year in 2016 to 350 prescriptions per 1000 inhabitants per year in 2020.

Definition of the goal
The primary health care sector is, in this goal, defined as general practitioners, private practice specialists, dentists and emergency physicians (including prescriptions from physicians in emergency units). This goal does not include prescriptions written by physicians in hospitals for out-patient contact, or when discharging patients from hospital.

Antibiotics referred to in goal 1 are from the antibiotic statistics found at esundhed.dk (Danish e-Health portal) and are defined as antibiotic groups J01 + P01AB01. This refers to reduced consumption of systemic antibiotics, and does not include locally applied antibiotics such as antibiotic eye drops, ointments and creams.

Initiatives to achieve the goal
Numerous national and local measures , that can facilitate the achievement of goal 1 have already been initiated. However, a single initiative would be insufficient on its own, as the reduction of antibiotic consumption requires a wide range of measures. At the same time, it will differ from region to region, which measures should be used.

Below different examples of how to work with goal 1 is described, keeping in mind that the decision on whether to prescribe antibiotics or not, always must be based on a physician's assessment in each case.

Focus on specific target groups
Goal 1 may be achieved by focusing on the reduction of antibiotic consumption in specific target groups, where an inappropriate use of antibiotics has been determined, such as in the treatment of respiratory infections in children, coughs in adults, or urinary tract infections in women.

Research studies have shown that in cases of mild and moderate bacterial infections in children, the probability of adverse reactions to antibiotics is greater than the beneficial effect of antibiotics: 1 in 14 children who receive antibiotics for middle ear infections experience adverse reactions, while only 1 in 20 children benefit from this treatment.

Studies show that 9 out of 10 cases of coughs in adults are caused by viruses. Antibiotics are ineffective against viral infections. They only have an impact on bacterial infections. If the patient is generally healthy, it is best to let the body fight a mild bacterial infection. For patients who take antibiotics, the chance of quicker recovery is very small – typically just 1 day earlier. In return, the patient may experience adverse reactions to the medicine. 1 in 8 patients receiving antibiotics for coughs will experience adverse reactions in the form of stomach pain, diarrhoea, vomiting or rash.

Urinary tract infection is a common disease that affect most women once or several times during their lives. Studies have shown that only 50 % of all women with symptoms of urinary tract infections have pathogenic bacteria in their urine. Only half of this group would therefore experience any effect of antibiotics. For the remaining 50 %, antibiotics is considered to be overtreatment, as the symptoms are due to other factors, such as yeast infection, where antibiotics would be ineffective. It is therefore essential that the physician conduct an examination of women's urine – for example by carrying out a urine culture.

Wait-and-see prescriptions

Foreign studies have shown that the use of wait-and-see prescriptions can reduce the consumption of antibiotics in general practice. A wait-and-see prescription is a regular prescription, but the physician instructs the patient not to redeem the prescription the same day. The prescription should only be redeemed if symptoms remain unchanged for a certain number of days (the physician determines the waiting period). If the symptoms disappear, the patient should not use the prescription. For patients with bronchitis, middle ear infections or sinus infections, physicians may consider the use of a wait-and-see prescription. Wait-and-see prescriptions are already being used by some physicians in Denmark.

Cooperation with regional pharmaceutical consultants

Experience from the Danish regions indicate that cooperation between physicians and regional pharmaceutical consultants regarding a more rational use of antibiotics, such as focusing on reducing antibiotic consumption in specific target groups, has a positive effect on the progression of rational antibiotic consumption.

It varies from region to region, in terms of frequency and the manner in which the regional pharmaceutical consultants cooperate with physicians on rational use of antibiotics.

Facts about antibiotics

Children

Antibiotics can lead to adverse reactions. 1 in 14 children who receive antibiotics for middle ear infections experience adverse reactions, while only 1 in 20 children benefit from this treatment. The most common adverse reactions include vomiting, diarrhoea and rash. Antibiotics do not relieve pain. In middle ear infections, there is no change in pain after 24 hours of treatment with antibiotics compared with placebos.

Coughs

Studies show that 9 out of 10 cases of coughs in adults are caused by viruses. Antibiotics are ineffective against viral infections. They only have an impact on bacterial infections. 1 in 8 patients receiving antibiotics for coughs will experience adverse reactions in the form of stomach pain, diarrhoea, vomiting or rash.

Urinary tract infections

Studies have shown that approx. 50 % of all women with symptoms of urinary tract infections have pathogenic bacteria in their urine. Therefore, only half of this group would experience any effect of antibiotics.

The above information can be found in the chapter "Inspiration for antibiotic alternatives" including the paragraph "Facts about antibiotics", and at www.antibiotikaellerej.dk

Ordiprax and diagnostic tests

The national presentation tool, Ordiprax, is a tool that can give general practitioners an electronic overview of their own prescribing practices and prescriptions of antibiotics, along with the opportunity to compare these with the practices of other physicians. This can help to prevent the unnecessary use of antibiotics. The Danish Health Data Authority is now working to discover how to replace the current IT system with a new presentation tool that could give physicians an electronic overview of their own prescriptions of medicines such as antibiotics in a way, so it can be used for quality development, and to define and indicate the quality of treatment. This could include the number of antibiotic prescriptions, the percentage of penicillin V prescriptions, and keeping track of other initiatives.

The implementation and application of diagnostic tests (point-of-care-tests) in general practice, as well as other decision support tools, could also assist physicians in making quick decisions on whether to prescribe antibiotics or not. However, diagnostic tests are not enough.

Antibiotics prescribed by dentists

General practitioners and private practice specialists are not the only professionals who prescribe antibiotics in the primary healthcare sector. According to the Danish National Prescription Registry, dentists in Denmark were responsible for around 7 % of antibiotic consumption in the primary healthcare sector in 2016. The number of prescriptions per 1000 inhabitants prescribed by dentists has been steadily increasing since 1999, but declined between 2015 and 2016. The Danish Health Authority's national clinical guidelines on the use of antibiotics in dental treatment, published in 2016, can assist healthcare professionals in determining the use of antibiotics in dental treatment.

Antibiotic public awareness campaigns

A broad, multifaceted campaign is considered essential for spreading information and changing public attitudes in regard to expectations of being treated with antibiotics.

Members of the public can receive information directly from a physician, or via information material in the waiting room which explains when antibiotic treatment is required. They can also receive information about antibiotic resistance from other sources. Municipal healthcare services, kindergartens and nursing homes play an important role in preventing the need for, and expectations of being treated with antibiotics.

National and local antibiotic awareness campaigns are launched each year to help ensure that members of the public receive knowledge about why antibiotics should only be prescribed when necessary. Previous national campaigns have focused on antibiotics for children, antibiotics for coughs, and antibiotics for urinary tract infections. These campaigns were aimed at both the general public and healthcare professionals, and may have helped to reduce the consumption of antibiotics. Campaign material can be found at www.antibiotikaellerej.dk, and physicians can order posters and brochures from the Danish Committee for Health Education. Several regions have initiated local public awareness initiatives, including Region Zealand (Sjælland) which has launched local public awareness campaigns entitled "Antibiotics? Only when necessary". This can be found on the region's website.

Municipal participation in the campaign initiative from the Danish Council for Better Hygiene, "Hygiene Week" can also help to raise awareness regarding the prevention of bacterial infections. Furthermore, a greater emphasis on cooperation with home nurses on communicating information to the public, such as parents of small children, about antibiotic resistance can also improve the dialogue between physicians and their patients regarding antibiotics.

Hygiene initiatives

Continual focus on systematic hygiene, including hand hygiene, in nursing homes, creches, preschools and schools can help to prevent the spread of infections – thereby helping to reduce the consumption of antibiotics in the primary healthcare sector.

Changes in hygiene routines at the Sofiegården Nursing Home in Aalborg and Gelsted Nursing Home in the municipality of Middelfart has shown positive results in reducing the number of urinary tract infections. Good advice on the prevention of urinary tract infections among elderly residents in nursing homes has been summarised in a leaflet at www.antibiotikaellerej.dk

Knowledge of, and emphasis on the implementation of the Danish Health Authority's "Guidelines on hygiene in daycare institutions" from 2004, as well as the Danish Health Authority's "Prevention package on hygiene" from 2012, can contribute to the prevention of infections, thereby reducing antibiotic consumption.

Good advice for the prevention of urinary tract infections among the elderly in nursing homes

Prevention
Good hygiene is an essential foundation for efforts to limit and prevent urinary tract infections. Frequent washing and hand disinfection helps to maintain good hand hygiene. This reduces the spread of bacteria.

Symptoms
Symptoms of urinary tract infections include fever above 38 degrees C., chills, and/or frequent urination. Should a resident present any of these symptoms, it could indicate a urinary tract infection. It is important to be alert and respond accordingly.

Diagnoses
Urinstix do not always provide correct results. A more precise result can be obtained by having a physician to do a microscopic analysis of a urine sample, or performing a urine culture. A correct diagnosis reduces the risk of overtreatment with antibiotics.

Treatment
Many nursing home residents have bacteria in their urine, and a urine culture, along with relevant symptoms, can determine whether they have a urinary tract infection.
If there are no pathogenic bacteria in the urine, treatment with antibiotics could lead to unnecessary adverse reactions – and at worst, resistance to antibiotics.

The above information can be found in the article "Knowledge and advice on the prevention of urinary tract infections in the elderly", 2016, at: www.antibiotikaellerej.dk

Goal 2. Usually, ordinary penicillin is effective

Background for goal number 2
Antibiotics can be divided into two categories: narrow-spectrum and broad-spectrum antibiotics. Narrow-spectrum antibiotics are only effective against certain specific groups of bacteria, while broad-spectrum are effective against many different bacteria groups at once.

Broad-spectrum antibiotics are advantageous because they can be used to treat the patient before having identified the type of bacteria causing the infection. The disadvantage of these broad-spectrum antibiotics is that they often destroy useful and harmless bacteria, such as intestinal bacteria. This may lead to development of resistant bacteria.

Penicillin can typically be categorised in four groups, which can be used to treat different types of infections, such as throat infections, middle ear infections, or urinary tract infections. The consumption of penicillin V has decreased since 2007, while the consumption of the other three types of penicillin has remained stable or has increased during the same period. The decline in consumption of penicillin V gives cause for concern, as penicillin V has an excellent effect on many of the more common infections, particularly respiratory infections, which are among those most frequently seen in general practice. The use of penicillin V rarely leads to resistance, and should be the preferred penicillin for many infections.

Therefore, fewer broad-spectrum and more narrow-spectrum antibiotics should be used in the primary healthcare sector:

Goal 2

Narrow-spectrum antibiotics should be more frequently used in treatment. The use of Penicillin V should increase from 31 % in 2016 to compprise 36 % of the total antibiotic use in the primary healthcare sector in 2020, measured by the number of prescriptions per 1000 inhabitants.

Definition of the goal
The primary healthcare sector is defined here as general practitioners, private practice specialists, dentists and emergency physicians. Goal 2 does not include prescriptions by physicians in hospitals.

Penicillin V is a beta-lactam antibiotic (J01CE), which is a group of narrow-spectrum antibiotics that can be used in the treatment of respiratory infections, among others.

According to the statistics on antibiotics at esundhed.dk (Danish e-Health portal), penicillin V comprised 31.4 % of the total antibiotic consumption in the primary healthcare sector in 2016, measured by the number of prescriptions per patient. The percentage of goal 2 is determined as 36 %, as it must be assumed that goal 1 will lead to a decline in the number of “unnecessary” prescriptions, including prescriptions for penicillin V, wherefore it would be difficult to achieve a higher objective.

Initiatives to achieve the goal
Numerous national and local measures, that can facilitate the achievement of goal 1 have already been initiated. However, a single initiative would be insufficient on its own, as the reduction of antibiotic consumption requires a wide range of measures. At the same time, it will differ from region to region, which measures should be used.

Different examples of how to work with goal 2 is described below, keeping in mind that the decision on whether to prescribe antibiotics or not always must be based on a physician's assessment in each case.

Focus on the use of narrow-spectrum penicillin

The promotion of narrow-spectrum penicillin in the primary healthcare sector is recommended, while also reducing the use of more broad-spectrum antibiotics. Assessing patients for penicillin allergies and the use of diagnostic results are examples of initiatives that can support the prescribing physician in deciding the correct treatment. The percentage of narrow-spectrum penicillin is likely to increase due to monitoring and guidance on the use of antibiotics such as macrolides, ciprofloxacin and tetracyclines, which should all be used with caution, and only for specific indications.

Conveying knowledge of guidelines and strategies

The dissemination of knowledge for relevant guidelines on antibiotics can help to achieve goal 2.

The Danish Council for the Use of Expensive Hospital Medicine (now replaced by the Medicine Council) decided, in 2014, to establish a specialist committee to evaluate the rational use of antibiotics. This specialist committee will prepare a draft for background notes and obligatory treatment guidelines for the appropriate use of antibiotics in the primary healthcare sector and hospitals. This work will be based on the Danish Health Authority's "Guidelines for prescribing antibiotics" from 2012, antibiotic strategies outlined by the Institute for Rational Pharmacotherapy, as well as equivalent strategies from Norway. The Medicine Council's first treatment guidelines "Antibiotics and lower respiratory tract infections in general practice and hospitals", was presented in 2016, and reduced the number of treatment days from 7 to 5.

National guidelines and strategies

The Medicine Council's treatment guidelines "Antibiotics and lower respiratory tract infections in general practice and hospitals", 2016.

The Danish College of General Practitioners' guidelines "respiratory infections in general practice", 2014.

The Danish Health Authority's "Guidelines for prescribing antibiotics" from 2012.

For more information, see the chapter on Inspiration for antibiotic initiatives.

The Danish College of General Practitioners (DSAM) presented their guidelines "Respiratory tract infections – diagnosis and treatment" in 2014. According to DSAM's guidelines, approx. 90 % of all antibiotic prescriptions come from general practice, and two-thirds of these are given to patients with respiratory tract infections. DSAM's guidelines state that acute middle ear infections (otitis media) are one of the most frequently occurring infections among children, and approx. 80 % of all children have had at least one acute middle ear infection by the age of 3. This disease usually occurs between the ages of 0 to 5, and comprises 10 % of all clinical contact in general practice. For acute middle ear infections requiring antibiotics, the initial treatment is primarily aimed at pneumococcal and Group A streptococcus infections, which are the most frequent and most serious causes of infections. DSAM's guidelines "Respiratory tract infections – diagnosis and treatment" recommend penicillin V as the first-line antibiotic. Broad-spectrum antibiotics have not been found to be more effective than penicillin V.

The Danish Health Authority's "Guidelines for prescribing antibiotics" from 2012 emphasise greater caution regarding the use of antibiotics. The Danish Health Authority aims at restricting indications for use of antibiotics , and in increasing the use of antibiotics that are less likely to lead to the development of resistance (narrow-spectrum antibiotics).

The Institute of Rational Pharmacotherapy (IRF), under the Danish Health Authority, works to promote rational pharmacotherapy in general practice, and to improve inexpedient prescription practices through the provision of balanced information on treatment with medicinal products that give the best effect and fewest and least serious adverse effect at the lowest possible treatment cost. The IRF is preparing recommendations for the rational use of antibiotics, including those for the treatment of urinary tract infections in older women.

Cooperation with regional pharmaceutical consultants

As mentioned in goal 1, cooperation between physicians and regional pharmaceutical consultants regarding a rational use of antibiotics, with an emphasis on reducing antibiotic consumption among specific target groups, can contribute towards a more rational consumption of antibiotics. Focus on a rational antibiotic consumption may also involve the increased use of penicillin V.

Goal 3. Use critically important antibiotics with care

Background for goal number 3
Approx. 10 % of the total antibiotic consumption in Denmark takes place in hospitals.

The transmission of (multi)resistant bacteria is especially serious in hospitals, as elderly patients and patients with weakened immune systems have a higher risk of developing serious infections. The spread of bacteria can be prevented by proper hygiene in hospitals – including thorough hand hygiene.

The Danish Health Authority's "Guidelines for prescribing antibiotics" from 2012 present a a general set of rules for antibiotic prescription, as well as rules applying to three specific critically important antibiotics, which the Danish Health Authority aims to target, and if possible, restrict the use of. These three critically important antibiotics are carbapenems, fluoroquinolones and cephalosporins.

Although the use of both fluoroquinolones and cephalosporins has declined over the past few years, fluoroquinolones comprised 8 % of antibiotic use in hospitals in 2016, while cephalosporins comprised 10 %. Carbapenems comprised 4 % of the total use in hospitals, and this percentage has remained unchanged since 2011. It is of great concern that the use of critically important antibiotics has not had a greater decline over the past few years. A rise in consumption may be leading to bacterial resistance in hospitals – a situation that can have very serious consequences for each individual patient as well as for more vulnerable patients in hospitals. Cooperative efforts are needed to combat the development of resistant bacteria, for instance, through a rational and prudent antibiotic policy in hospitals.

Based on the Danish Health Authority's "Guidelines for prescribing antibiotics" from 2012, there should be a decline in the use of certain types of antibiotics which are critically important for the treatment of infections in humans:

Goal 3

The consumption of critically important antibiotics should be reduced by 10 % by 2020 measured by DDD/100 bed-days for hospitalised patients, as compared with consumption in 2016.

Definition of the goal
This goal emphasises the reduction of critically important antibiotic consumption in hospitals.

Critically important antibiotics include three types of antibiotics defined in the Danish Health Authority's "Guidelines for prescribing antibiotics": these are carbapenems, fluoroquinolones and cephalosporins.

The baseline for goal 3 is the 2016 consumption level of critically important antibiotics.

It is a precondition for goal 3, that there must be no increase in the consumption of each of the antibiotics, but that a reduction of all three types of these antibiotics is achieved.

Goal 3 utilises DDD (Defined Daily Dose), since this unit of measurement offers the opportunity to compare consumption with other countries.

Furthermore, this is a unit of measurement that can be monitored through existing surveillance systems. DDD indicates the standard dose estimated for each antibiotic group for treatment of its primary indication (such as a standard dose for treatment of pneumonia with penicillin V). DDD is determined by WHO, and as such an international standard. DDD does

not take national or local treatment traditions into account. The dose normally used in Denmark for treatment of a specific infection may therefore deviate from the DDD. Since this goal does not focus on the change between different antibiotic categories, or between narrow-spectrum and broad-spectrum antibiotics, but rather on a decline in the total level of these three critically important antibiotics over time, it is considered appropriate to use the DDD unit of measurement in goal 3. DDD will in this case be adjusted for hospital activity, by estimating consumption per 100 bed-days.

Goal 3 is intended to supplement and support the objective regarding critically important antibiotics defined by the National Learning and Quality Team for the rational use of antibiotics.

Initiatives to achieve the goal

Numerous initiatives may assist in achieving goal 3. However, a single initiative would be insufficient on its own, as the reduction of antibiotic consumption requires a wide range of measures. At the same time, it will differ from region to region, which measures should be used to achieve goal 3.

Different examples of how to work with goal 3 is described below, keeping in mind that the decision on whether to prescribe antibiotics or not always must be based on a physician's assessment in each case.

The Danish Health Authority's "Guidelines for prescribing antibiotics"

Goal 3 can be achieved by using the Danish Health Authority's guidelines for prescribing antibiotics, drafted with input from the National Antibiotics Council. These guidelines are used by the Danish regions,among others, to support the work carried out by the new National Learning and Quality Team for Antibiotics, where one of the objectives is to reduce the use of critically important antibiotics.

Establishing local antibiotic committees at all hospitals (wherever these are not yet in place) and providing continuous monitoring of antibiotic consumption at all hospitals can also contribute to the reduction of antibiotic consumption. Regions may also be inspired by measures initiated in other regions, such as the Task Force Group for the Prevention of Hospital Infections, established by the Capital Region.

Learning and Quality Team for Antibiotics

A total of 35 million DKK was earmarked for the establishment of national Learning and Quality Team from 2015 to 2018, as part of the new National Quality Programme. This includes a new national Learning and Quality Team devoted to the rational use of antibiotics in hospitals. The Learning and Quality Team for Antibiotics has its primary focus on hospitals.

The new Learning and Quality Team for Antibiotics aims to ensure that knowledge and research results about what works best will be communicated as quickly as possible to all regions.

The national Learning and Quality Team for Antibiotics have an overall objective of "A decline in the use of antibiotics that carry a high risk of resistance". This objective will be achieved through four specific initiatives:

1) Indications for the use of antibiotics
2) Choice of antibiotics
3) Reassessment of treatment
4) Duration of treatment

Learning and Quality Team

The new Learning and Quality Team for Antibiotics will ensure the acquisition of knowledge across regions.

Based on the overall objectives, participating units formulate concrete local goals (by %) to reduce the use of antibiotics, but which take patient composition into account. These goals must be ambitious, but realistic.

A description of the Learning and Quality Team on the rational use of antibiotics, March 2017.

The project is intended to support the implementation of the Danish Health Authority's Guidelines for the prescription of antibiotics from 2012, by focusing on changing the direction of prescription patterns and practices to make them more rational, including fewer cases of unnecessary antibiotic consumption. Finally, the national Learning and Quality Team for Antibiotics will be supported by regional and local goals in hospitals and their departments.

Strategies for infection hygiene

Systematic cleaning and good (hand) hygiene are considered essential factors in the prevention of hospital-acquired infections. The Statens Serum Institute's national guidelines for infection control, which are continuously updated, should be followed in the implementation of good hygiene in hospitals.

Digital and monitoring systems

In recent years, there has been greater digitisation in the field of microbiology, where systems such MiBa (Microbiology dataBAse) and HAIBA (Hospital Acquired Infection dataBAse) have enabled greater knowledge of microbiological findings and hospital-acquired infections in real time. The hope is that these systems will in time, through a smart use of existing health data, be utilised, to a greater extent, to support patient treatment during outbreaks, spread of infections and rational consumption.

Antibiotics are monitored through antibiotic statistics from medstat.dk, as well as through esundhed.dk (Danish Health Data).

Antibiotics and pooled funds

A total of 17 million DKK was allocated for pooled funds in the 2014 Budget Act, for measures to reduce hospitals-acquired infections. These funds were allocated to specific projects in the regions in 2014 and 2016, The 2016 Budget Act allocated 7,5 million DKK to pooled funds to reduce antibiotic use and resistance, and to prevent infections in primary and hospital health care sectors.

By the end of 2016, the Ministry of Health allocated funding to 14 specific antibiotic projects in various regions and municipalities. These projects received approx. 16.6 million DKK from the two antibiotic pooled funds. The projects focused on reducing the consumption of antibiotics and on resistance in hospitals, nursing homes and in general practice. At the end of 2014, the Ministry of Health allocated funding for seven specific projects aimed at the prevention of hospital-acquired infections. These projects received a total of 7.9 million DKK from the Ministry of Health's pooled funds for the prevention of hospital-acquired infections.

A working group, set up by the National Antibiotic Council, assisted the Ministry of Health in prioritising projects that would receive funding from the antibiotic pooled funds. The results of these projects will contribute to the creation of new ideas and methods to be used across municipalities and regions, and will contribute towards the reduction of antibiotic resistance and consumption.

The One Health National Antibiotic Council

Members of the National Antibiotic Council support national and international initiatives for the prevention of antibiotic resistance and consumption, contribute towards solutions to specific national tasks in the field of antibiotics, and assist by conveying and ensuring local implementation of initiatives and proposals for solutions, discussed by the Council.

The structure of the National Antibiotic Council was strengthened in 2017, as defined in the Council's new mandate. The Council received additional members and representatives from municipalities, patient groups and consumers.

The Ministry of Health holds the chairmanship and hosts the secretariat administration of the One Health National Antibiotic Council.

Conference on Antibiotics in 2018

As stated in the 2017 – 2019 mandate for the National Antibiotic Council, a conference will be held in 2018, aimed at gaining greater knowledge of the prevention and reduction of antibiotic resistance in humans and animals. This conference will provide a platform for the communication of knowledge from projects that have received funding from the Ministry of Health's pooled funds. Furthermore, the conference will focus on sharing experiences from initiatives that can contribute towards achieving the national measurable goals for antibiotic consumption in humans.

The conference will be organised with input from the National Antibiotic Council, which will contribute by providing topics and speakers for the conference, as well as planning potential workshops for discussion and sharing of knowledge across sectors, regions and municipalities.

National Quality Programme and national goals for the healthcare system

In the 2016 Financial Agreement, the Venstre (Left) Cabinet party and the Danish Regions reached an agreement to introduce a new National Quality Programme.

The new Quality Programme includes national goals with accompanying indicators. One of these goals involve a higher survival rate and improved patient safety. This goal emphasises the following two indicators for the reduction of hospital-acquired infections:

1. Bacteraemia, number per 10,000 risk days
2. Clostridium difficile, number per 100,000 inhabitants

The two above-mentioned indicators are monitored using the monitoring tool, HAIBA. A "traffic light" with red, yellow or green colours indicate whether there is a positive or negative development in the overall plan, and whether the level of risk is above or below the national average. National goals and indicators are followed up on an annual basis. Current efforts will also enable greater focus on the reduction of hospital-acquired infections, including the consumption of critically important antibiotics.

Follow-up on national goals

In order for the goals to have a positive effect, it is essential to ensure awareness of, and compliance with these goals.

A working group established by the Ministry of Health will follow up and facilitate awareness of the national measurable goals for antibiotics in humans. The working group will be comprised of members of the National Antibiotic Council, and will therefore have a broad composition of actors. Members of the working group should contribute to the local implementation of initiatives to support the goals, and will also raise awareness of the goals among relevant local actors.

The working group for the follow-up of the national goals will meet biannually, and initiatives will be monitored annually in order to follow the progress in achieving the goals. The working group will also follow the development of the total disease burden, to ensure that there is no increase in disease as a result of reduced antibiotic consumption.

Just as the national goals will be followed up and monitored, an overall evaluation of the goals will be performed, with input from the National Antibiotic Council. There may also be discussions on other potential goals, based on experiences gained from the three 2017 goals.

Summary of antibiotic initiatives

The three national goals should be achieved within the current financial framework by 2020.

Initiative	Description	Funding
The One Health National Antibiotic Council.	The Council was established in 2010 and the chairmanship and secretariat administration is overseen by the Ministry of Health. The Council received a new mandate from 2017, and its structure was strengthened. The Council shall contribute to the improved sharing of knowledge and implementation of national goals.	Financed within the current financial framework.
National antibiotic public awareness campaigns.	Each year since 2012, the Ministry of Health has carried out national antibiotic awareness campaigns together with members of the National Antibiotic Council.	Financed within the current financial framework.
Pooled funds for the prevention of hospital-acquired infections.	A total of 17 million DKK was earmarked for pooled funds in the 2014 Budget Act. The pooled funds have been utilised and will help to ensure a more appropriate use of antibiotics in hospitals, and reduce the number of infections.	Financed within the current financial framework.
Pooled funds directed at antibiotic consumption and resistance, and prevention of infections in primary and secondary healthcare sectors.	A total of 7.5 million DKK was earmarked for pooled funds in the 2016 Budget Act. The pooled funds have been utilised and will help to ensure a more appropriate use of antibiotics in hospitals, and reduce the number of infections.	Financed within the current financial framework.
DANMAP.	In 1995, Denmark was the first country in the world to establish a One Health Network for monitoring antibiotic resistance and consumption in humans and animals.	Financed within the current financial framework.

Initiative	Description	Funding
National digital surveillance.	In recent years, there has been greater digitisation in the field of microbiology, where systems such MiBa (Microbiology dataBAse) and HAIBA (Hospital Acquired Infection dataBAse) have enabled greater knowledge of microbiological findings and hospital-acquired infections in real time. The hope is that these systems will in time, through a smart use of existing health data, be utilised, to a greater extent, to support patient treatment during outbreaks, contagions and rational consumption. Antibiotics are monitored through antibiotic statistics from medstat.dk, as well as through esundhed.dk (Danish Health Data).	Financed within the current financial framework.
Learning and Quality Team for Antibiotics.	As part of the new National Quality Programme, a total of 35 million DKK was allocated for the establishment of National Learning and Quality Teams from 2015 to 2018. This includes new National Learning and Quality Team devoted to the rational use of antibiotics in hospitals.	Financed within the current financial framework.
New Quality Programme and new national goals for the healthcare system.	In the 2016 Financial Agreement, the Venstre (Left) Cabinet party and the Danish Regions reached an agreement to introduce a new National Quality Programme, and to set up 8 national goals. One of these goals involve a higher survival rate and improved patient safety. This goal focuses on the reduction of hospital-acquired infections.	Financed within the current financial framework.
Continuous updates of the national guidelines for antibiotics and hygiene.	The Danish Health Authority and Statens Serum Institute work together to draft and continuously update national guidelines for antibiotics and hygiene. The Institute of Rational Pharmacotherapy provides recommendations for the rational use of antibiotics.	Financed within the current financial framework.

Initiative	Description	Funding
Continuous follow-up of physicians' use of specific indication codes for antibiotic prescriptions.	The Danish Health Data Authority follows the development of physicians' use of specific indication codes for antibiotic prescriptions.	Financed within the current financial framework.
Updates of the monitoring system for physicians' prescriptions of antibiotics (Ordiprax).		Financed within the current financial framework.

Inspiration for antibiotic initiatives

National initiatives
The National Antibiotic Council, Ministry of Health, www.sum.dk

"National One Health Strategy for Prevention of Antibiotic Resistance in Humans and Animals", Ministry of Health and Ministry of Environment and Food, 2017

"National One Health Antibiotic and Resistance Action Plan", Ministry of the Interior and Health, and the Ministry of Food, Agriculture and Fisheries, 2010

National Learning and Quality Team for Antibiotics, at the Danish Regions' website:
http://www.regioner.dk/kvalitetsteams

National Goals for the Healthcare System, Danish Health Authority website:
http://www.sum.dk/Temaer/Nationale-maal-for-sundhedsvaesenet.aspx

Projection description for the National Learning and Quality Team regarding the rational use of antibiotics, March 2017

Guidelines and strategies on antibiotics and hygiene
"Guidelines for the prescription of antibiotics", Danish Health Authority (Sundhedsstyrelsen), 2012

"Guidelines on respiratory tract infections", Danish Organisation of General Practitioners (DSAM), 2014

"Antibiotics – lower respiratory tract infections in general practice and in hospitals", Council for the use of Expensive Hospital Medicines (RADS), 2016

"National Clinical Strategies for the Use of Antibiotics in Dental Treatment", Danish Health Authority, 2016

"National Infection Hygiene Strategies", Statens Serum Institute (SSI)

Recommendations for Antibiotics, Institute of Rational Pharmacotherapy
"Guidelines on hygiene in day institutions", Danish Health Authority, 2004

"Prevention package for hygiene", Danish Health Authority, 2012.

Campaigns
National antibiotic campaigns, www.antibiotikaellerej.dk
Hygiene Week, Council for Better Hygiene

National surveillance and monitoring systems
DANMAP,
HAIBA
Miba
Ordiprax
Medstat.dk
Antibiotic statistics at www.esundhed.dk

Other initiatives
Antibiotic Package – Task Force for Prevention of Hospital Infections, Capital Region, 2016

Facts about antibiotics

"Children, infections and antibiotics", Strama, 2009. www.regionhalland.se/vard-halsa/for-vardgivare/smittskydd/strama/strama-bvc/

"Guidelines for diagnostics and treatment of respiratory tract infections in general practice", Happy audit, 2008. www.happyaudit.org

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"Delayed antibiotics for respiratory infections", Spurling GK, Del Mar CB, Dooley L, Foxlee R, Farley R. Cochrane Database Syst Rev 2013; 4:CD004417.

"Which treatment strategy for women with symptoms of urinary tract infection?" Bjerrum L, Lindbæk M: BMJ 2015, 351(December):h6888.

"The natural course of uncomplicated lower urinary tract infection in women illustrated by a randomized placebo controlled study", Ferry S a., Holm SE, Stenlund H, Lundholm R, Monsen TJ:. Scand J Infect Dis 2004, 36:296–301.

"Does this woman have an acute uncomplicated urinary tract infection?", Bent S, Nallamothu B, Simel D: JAMA 2002, 287:2701–2710.

"Point of care susceptibility testing in primary care - does it lead to a more appropriate prescription of antibiotics in patients with uncomplicated urinary tract infections?", Protocol for a randomized controlled trial.Holm A, Cordoba G, Sørensen TM, Jessen LR, Siersma V, Bjerrum L: BMC Fam Pract 2015, 16:106.

Stamm W, Counts G: Diagnosis of coliform infection in acutely dysuric women. N Engl J Med 1982:463–8.

Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD: Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010, 340:c2096.

Ferry S, Holm S, Stenlund H, Lundholm R, Monsen TJ: Clinical and bacteriological outcome of different doses and duration of pivmecillinam compared with placebo therapy of uncomplicated lower urinary tract infection in women: the LUTIW project. Scand J Prim Health Care 2007, 25:49–57

Spurling GK, Del Mar CB, Dooley L, Foxlee R, Farley R. Delayed antibiotics for respiratory infections. Cochrane Database Syst Rev 2013; 4:CD004417.

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