

2. Introduction to DANMAP

2.1 The DANMAP surveillance system

DANMAP is a surveillance system with five key objectives:

- To establish the state-of-nation in regards to the use of antimicrobial agents in food-producing animals and humans
- To carry out surveillance of the occurrence of antimicrobial resistance in bacteria isolated from food-producing animals, food of animal origin (meat) and humans
- To identify areas for further research, e.g. antimicrobial resistance transmission or possible associations between antimicrobial consumption and antimicrobial resistance
- To deliver data to veterinarians, medical doctors and other health professionals for the development of antibiotic treatment guidelines
- To act as a knowledge base for authorities, academia and politicians when performing risk assessment and management, thus supporting decision making in the prevention and control of resistant bacterial infections

Since 2021, DANMAP also provides an integrated analysis of resistance in bacteria from humans and food animals.

The monitoring programme was initially developed in 1995 by researchers, based on frequent discussions and exchange of knowledge and results from research. Since then, DANMAP has evolved into a governmentally supported programme.

However, much of the design of the programme, including participation of the human laboratories and referral of strains is based on a voluntary principle.

DANMAP surveillance relies on four equally important components: well-established and well-functioning diagnostic systems, well-designed and representative surveys, reliable registers as well as mutual trust and openness between all collaborators.

A positive effect of the regular meetings and exchange between stakeholders is that these prove helpful in other aspects, for example, by contributing to a common knowledge pool regarding laboratory methods. This ensures and contributes to continuous improvements and harmonisation of the laboratory work. Meetings across sectors and between different stakeholders also contribute to a better mutual understanding, facilitating development and work towards mutual goals.

Surveillance is a complex undertaking and DANMAP encompasses many different surveillance components and covers resistance in different populations and contexts. Three categories of bacteria are always included in DANMAP:

- Human clinical isolates to reflect the antimicrobial resistance levels in the human population that seeks medical care
- Foodborne zoonotic bacteria along the whole farm-topatient chain to monitor the levels of antimicrobial resistance in shared pathogens
- Indicator bacteria from healthy food-producing animals to monitor status of antimicrobial resistance in the animal reservoirs

Surveillance resistance in pathogens from sick animals was included in DANMAP in 2022. The National Food Institute at the Technical University of Denmark, DTU and the National AMR reference laboratory at Statens Serum Institut (SSI) are responsible for data interpretation and output communication mainly via the annual DANMAP report. Interpretations are independent of policy, risk management and private industries.

The DANMAP programme is funded jointly by the Ministry of Health and the Ministry of Food, Agriculture and Fisheries. Support from the ministries has also helped build the databases and ensuring the registers, which the current surveillance system relies upon.

For further information on the development and history of DANMAP, please read chapter 2, "<u>DANMAP - A 20 year perspec-</u> <u>tive" in DANMAP 2015 and Chapter 1, "DANMAP - the begin-</u> <u>ning" in DANMAP 2020.</u>

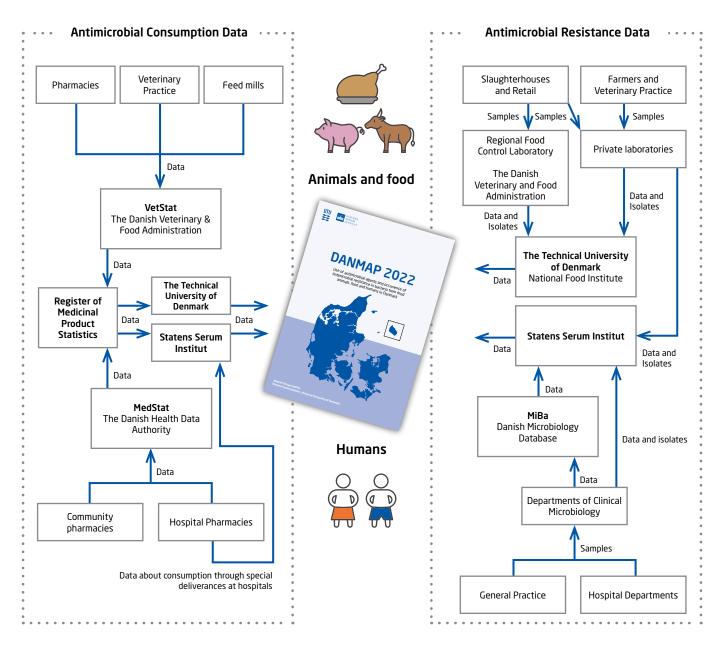
Organisation and data flow

Since 1995, a main purpose of DANMAP has been to monitor the entire chain from farm to fork to patient. The organisation and collection of DANMAP data and the interdisciplinary collaboration between sectors and organisations is presented in Figure 2.1.

The introduction of whole genome sequencing (WGS) has been a big step forward for surveillance purposes and in outbreak situations and has become routine standard in many clinical laboratories and most reference laboratories. However, phenotypical testing is still considered relevant, more feasible, cheaper and sometimes faster, especially in a clinical setting. Phenotypical testing also continues to be used in combination with WGS to describe and determine which resistance genes are relevant to look for when using molecular analysis. Furthermore, it complies with EU regulations in food and animal testing.

Figure 2.1 Organisation DANMAP regarding data and data flow

DANMAP 2022



Bacterial isolates from food, food animals and humans are submitted to the Regional Food Control Laboratory or occasionally the Technical University of Denmark and Statens Serum Institut, respectively, for further phenotypic and genotypic characterisation (Figure 2.1). The choice of the methods in surveying different bacteria and infections is described in more detail in the different chapters and sections of the report.

North Denmar Regior Central Denmark Region DCM Aarhus Capital Region of Denmark DCM Veile DCM Herley DCM Hvid CM Esbiera Region Zealand ion of Southe Denmark lagelse DCM Rea vkøbina

Figure 2.2 The five Danish healthcare regions and their respective population distributions. In addition, the ten DCMs are marked by black dots. The grey dot indicates the national reference laboratories (NRL) situated at Statens Serum Institut DANMAP 2022

North Denmark Region No. of inhabitants 591 740 No. of inhabitants/km² 75 No. of inhabitants/GP 1,785 **Central Denmark Region** No of inhabitants 1,341,856 No. of inhabitants/km² 103 No. of inhabitants/GP 1,636 **Capital Region of Denmark** No. of inhabitants 1,867,948 No of inhabitants/km² 729 No. of inhabitants/GP 1,699 **Region Zealand** 843,513 No. of inhabitants No. of inhabitants/km² 117 No. of inhabitants/GP 1,671 **Region of Southern Denmark** No. of inhabitants 1,228,362 No. of inhabitants/km² 100 No. of inhabitants/GP 1,527 GP = General Practioner DCM = Department of Clinical Microbiology NRL = National Reference Laboratories Data source: Statistics Denmark

Data source: Statistics Denmark [www.dst.dk] and the Danish Medical Association [www.laeger.dk]

2.2 Information on demographics and health care system

During the past 27 years, the human population in Denmark has increased from approximately 5.2 million inhabitants in 1995 to 5.9 million in 2022 [www.dst.dk]. Simultaneously, the average age has increased gradually. In 2022, the national average age was 44 years. The population and the respective regional distribution, in 2022, is presented in Figure 2.2, while regional differences and changes in age are presented in Figure 2.3.

In Denmark, microbiological analyses are carried out by ten hospital departments of clinical microbiology (DCMs) situated at the main regional hospitals, Figure 2.2. The analyses performed cover all samples from public hospitals and most samples from general practitioners (GPs). In addition, some GPs perform culturing of urinary samples from their patients. In the Capital Region of Denmark one private laboratory also performs additional analyses for the GPs. The activity in general practice during 2020-2022 differed from 2019. Figure 2.4 shows the number of consultations in general practice per thousand inhabitants from 2013-2022. The number of consultations per 1,000 inhabitants was 2.5% higher in 2022 compared to 2019.

Data on regional and national health care activity at hospitals in 2013 and 2022 are presented in Table 2.1. Denmark has a very high bed occupancy rate at hospitals and can reach maximum capacity during winter time for example due to high influenza activity. In 2022, the number of admissions at Danish somatic hospitals was registered to be 701.482 and the number of bed-days was registered to be 2,976,666. From 2013-2022, the number of bed-days decreased by 20%, the number of admissions decreased by 9% whereas the Danish population grew by 5%.

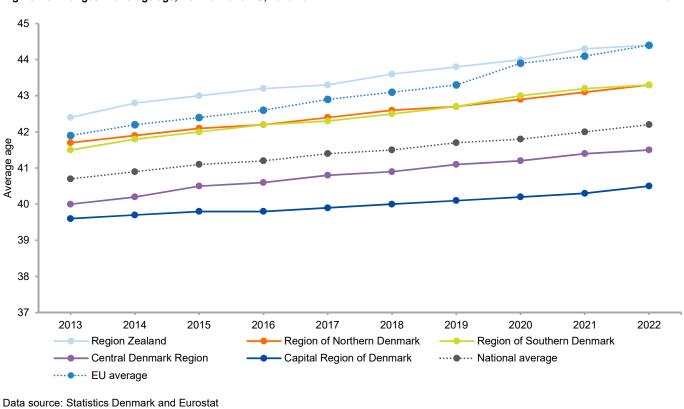


Figure 2.3 Changes in average age, Denmark and EU, 2013-2022

DANMAP 2022

DANMAP 2022

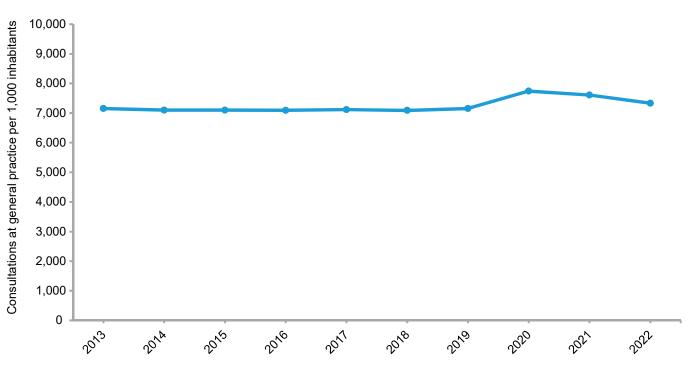


Figure 2.4 Number of consultations per 1,000 inhabitants in general practice, Denmark, 2013-2022

Data source: The National Health Insurance Service Registry and Register of Health Insurance Service Providers

Region	Number of bed-days in somatic hospitals		Number of admis hosp		Population	
	2013	2022	2013	2022	2013	2022
Capital Region of Denmark	1,306,920	970,169	255,073	230,629	1,732,068	1,867,948
Zealand Region	514,913	450,438	105,690	103,899	816,359	843,513
Region of Southern Denmark	760,382	606,951	163,450	145,567	1,201,419	1,228,362
Central Denmark Region	744,177	614,411	167,757	148,303	1,272,510	1,341,856
North Denmark Region	384,881	334,698	75,410	73,084	580,272	591,740
Denmark	3,711,273	2,976,666	767,380	701,482	5,602,628	5,873,420

Table 2.1 Activity at Danish hospitals, 2013 and 2022

DANMAP 2022

Data: Activity at somatic hospitals

Data source: The National Patient Register

2.3 Information on animal population and food production system

Denmark is an agricultural country, with more than half of its area managed by the agricultural sector. Livestock is of great importance and approximately 25% of the agricultural enterprises are specialised in the production of livestock, mainly pigs, cattle and chicken. The agricultural sector contributes around 24% of the Danish export earnings [Danish Agriculture and Food Council, 2019].

The production of food-producing animals as well as the production of meat and milk are presented in Table 2.2 and 2.3.

2.4 Registered antimicrobial agents

Table 2.4 shows the antimicrobial agents registered to treat bacterial infections in humans and animals. Some of these are listed on the highest priority list of critically important antimicrobial agents for the treatment of bacterial infections in humans, according to definitions made by a working group under the World Health Organization [AGISAR, 6.revision, WHO 2019]. In order to be considered critically important, an antimicrobial must meet two criteria; 1) be the only - or one of a limited number of compounds available to treat serious human disease and 2) be used to treat infections caused by bacteria that are either possibly transmitted from non-human sources, or carry resistance genes from non-human sources. In the newest revision from 2019, five drug classes were considered critically important and of highest priority: fluoroquinolones, 3rd, 4th and 5th generation cephalosporins, macrolides, glycopeptides and polymyxins. In addition, in Europe carbapenems are not allowed to be used in food production. In Denmark, the use of these drug classes (except macrolides) in food-producing animals has generally been low or reduced through either voluntary or legislative restrictions. See Chapter 4 for more information.

Furthermore, other antimicrobials may also be restricted due to national risk mitigation. For trends and preferred therapeutic choices in the antimicrobial treatment of humans, see Chapter 5.

Growth promoters are no longer used for animals in Denmark and are shown in parentheses in Table 2.4. Most of these influenced Gram-positive bacteria. Since 1995, the indicator enterococci from animals and meat have been used to monitor resistance towards former growth promoters.

Table 2.2 Production (1,000 heads) of food animals, Denmark

DANMAP 2022

DANMAP 2022

	Pigs		Cattle		Poultry	
Year	Total	Exported (a)	Slaughter cattle	Dairy cows	Broilers	Turkeys ^(b)
2013	28996	9864	551	582	117315	692
2014	30002	11120	556	563	115497	595
2015	30874	12133	511	561	114238	598
2016	31660	13280	540	572	120685	834
2017	31662	14173	509	570	117602	601
2018	32571	14449	533	575	122268	642
2019	31694	14897	518	567	123976	661
2020	32018	14736	500	567	120508	684
2021	32646	14092	506	564	118431	467
2022	31669	13856	493	557	114698	427

Source: Statistics Denmark (www.dst.dk). Export data for poultry from Statistics Denmark (personal communication)

a) Export of live pigs. These are included in total number of heads

b) Since 2006, more than 99% of the turkeys have been exported for slaughter

Table 2.3 Production (mill kg) of meat, milk and fish, Denmark

						Farm	Farmed fish (c)	
Year	Pork	Beef	Broiler meat (a)	Turkey meat	Milk ^(b)	Land based	Marine net ponds	
2013	1903	140	177	8	5507	33	15	
2014	1944	143	174	9	5592	32	14	
2015	1954	135	172	9	5744	36	16	
2016	1943	142	182	10	5892	36	12	
2017	1896	135	178	7	6088	37	14	
2018	1967	142	185	10	6305	38	14	
2019	1864	137	187	8	6323	41	14	
2020	1952	133	195	8	6394	36	11	
2021	2079	134	144	6	6390	37	12	
2022	1956	128	200	6	6392	-	-	

Source: Statistics Denmark (www.dst.dk). Export data for poultry and average weight after slaughter from Statistics Denmark (personal communication). Production data for farmed fish from the Danish Aquaculture Producer Organisation (personal communication) a) In 2022, a final slaughtered weight of 1.74 kg per broiler produced and 12.93 kg per turkey produced was estimated b) conventional and organic

c) The numbers for 2022 are not final. Data are based on accounts statistics for aquaculture. The production of farmed fish includes fish transferred from one production facility to another

 Table 2.4 Antimicrobial agents registered for systemic and veterinary intramammary therapeutic use in animals and humans,

 Denmark
 DANMAP 2022

ATC / ATCvet codes (a)	Therapeutic group	Antimicrobial agents within the therapeutic groups			
		Animals	Humans		
J01AA / QJ01AA,QJ51AA	Tetracyclines	Chlortetracycline, doxycycline, oxytetracycline	Doxycycline, lymecycline, tetracycline, tigecycline, eravacyclin		
QJ01BA	Amphenicols	Florfenicol			
J01CA / QJ01CA	Penicillins with extended spectrum	Ampicillin, amoxicillin	Ampicillin, pivampicillin, amoxicillin, pivmecillinam, mecillinam		
J01CE / QJ01CE	Beta-lactamase sensitive penicillins	Benzylpenicillin, phenoxymethylpenicillin, procaine penicillin, penethamate hydroiodide	Benzylpenicillin, phenoxymethylpenicillin		
J01CF / QJ51CF	Beta-lactamase resistant penicillins	Cloxacillin, nafcillin	Dicloxacillin, cloxacillin, flucloxacillin		
J01CR / QJ01CR	Comb. of penicillins and beta- lactamase inhibitors	Amoxicillin/clavulanate	Amoxicillin/clavulanic acid, piperacillin/tazobactam		
J01DB / QJ01DB,QJ51DB	First-generation cephalosporins	Cefalexin, cefadroxil, cefapirin	Cefalexin, cefazolin		
J01DC	Second-generation cephalosporins		Cefuroxime		
J01DD / QJ01DD,QJ51DD	Third-generation cephalosporins incl. comb. with beta-lactamase inhibitors	Cefoperazone, ceftiofur, cefovecin	Cefotaxime, ceftazidime, ceftriaxone, ceftazidime/avibactam		
J01DE / QJ51DE	Fourth-generation cephalosporins	Cefquinome	Cefepime		
J01DF	Monobactams		Aztreonam		
J01DH	Carbapenems		Meropenem, ertapenem, imipenem and cilastatin		
J01DI	Fifth-generation cephalosporins incl. comb. with beta-lactamase inhibitors		Ceftaroline fasamil, ceftolozan/ tazobactam, ceftobiprol		
J01EA	Trimethoprim and derivatives		Trimethoprim		
J01EB / QJ01EQ	Short-acting sulfonamides	Sulfadimidine	Sulfamethizole		
J01EE / QJ01EW	Comb.of sulfonamides and trimethoprim, incl. derivatives	Sulfadiazine/trimethoprim, sulfadoxine/trimethoprim, sulfamethoxasol/trimethoprim	Sulfamethoxazole/trimethoprim		
J01FA / QJ01FA	Macrolides	Spiramycin, tylosin, tilmicosin, tylvalosintartrat, tulathromycin, gamithromycin, tildiprocin	Erythromycine, roxithromycine, clarithromycine, azithromycine		
J01FF / QJ01FF	Lincosamides	Clindamycin, lincomycin	Clindamycin		
QJ01XX ^(b)	Streptogramins	(Virginiamycin)			
J01GB / QJ01RA,QA07AA	Aminoglycosides	Streptomycin, dihydrostreptomycin, gentamicin, neomycin, apramycin	Tobramycin, gentamicin, amikacin		
J01MA / QJ01MA	Fluoroquinolones	Enrofloxacin, marbofloxacin, difloxacin, ibafloxacin, pradofloxacin	Ciprofloxacin, levofloxacin, moxifloxacin		
QJ01MB	Other quinolones	Oxolinic acid			
QJ01MQ ^(b)	Quinoxalines	(Carbadox, olaquindox)			
J01XA,A07AA / Not in ATCvet ^(b,c)	Glycopeptides	(Avoparcin)	Vancomycin, teicoplanin, dalbavancin		
J01XB / QA07AA ^(b)	Polypeptides (incl. polymyxins)	Colistin, bacitracin	Colistin		
J01XC	Steroid antibacterials		Fusidic acid		
J01XD,P01AB (c)	Imidazole derivatives		Metronidazole		
J01XE	Nitrofurane derivatives		Nitrofurantoin		
J01XX / QJ01FF	Other antibacterials	Spectinomycin	Methenamine, linezolid, daptomycin fosfomycin		
QJ01XQ	Pleuromutilins	Tiamulin, valnemulin	,		
QP51AG04	Antiprotozoals, sulfonamides	Sulfaclozine			
Not in ATCvet ^(b)	Oligosaccharides	(Avilamycin)			
Not in ATCvet ^(b)	Flavofosfolipols	(Flavomycin)			

a) ATCvet codes start with a Q

b) Animal growth promoters used before 1999 are listed in parentheses

c) Intestinal antiinfectives (A07AA) and imidazole derivatives for protozoal diseases (P01AB) were, for the first time, included in DANMAP 2014, since their widespread use in the treatment of *Clostridium difficile* infections makes them belong to the most used antibiotics in human infections in Denmark