folkehelseinstituttet

Antibioitkaresistens – hva er trusselbildet

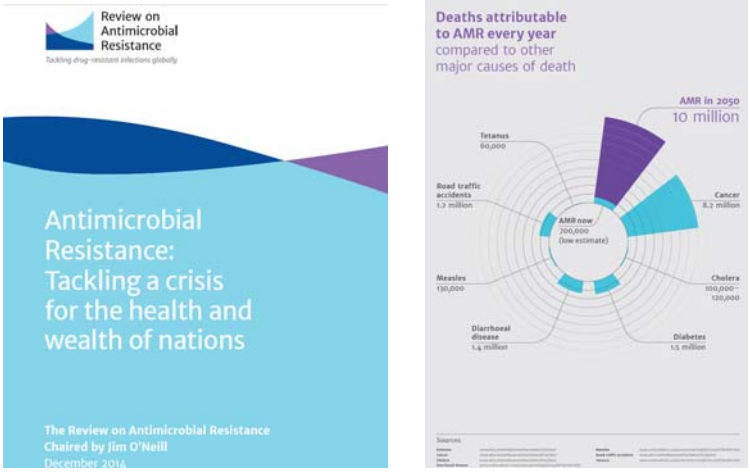
Martin Steinbakk, overlege
Folkehelseinstituttet

Noen fakta om antibiotika og antibiotikaresistens 2016

- Utvikling av nye antibiotika stoppet opp mot slutten av 1980-tallet
  - selv om noen nye midler er registrert til bruk etter år 2000 ble flere av disse utviklet tidligere
- Antibiotika er «societal drugs»
  - Bruk påvirker egen bakterieflora og denne floraen deles med omgivelser (både andre mennesker, dyr og øvrige miljø)
- Tradisjonell utvikling av antibiotika er lite (eller ikke) lønnsomt for industri
  - Så lite bruk som mulig, til så få pasienter som mulig
  - Nye initiativ på vei (offentlig og privat samarbeid, IMI og ND4BB m. fl.)
- Antibiotikaresistens øker både globalt og nasjonalt
  - Økende forståelse for at mulige kilder til smitte (reservoar) også finnes i mat og miljø og at kilde ikke bare er syke mennesker eller dyr
- Antibiotikaresistens påvirker mulighet for behandling av mange sykdommer
  - Moderne behandling svekker ofte infeksjonsforsvar og infeksjoner oppstår ofte i forløp av behandling av andre sykdommer som kreft, gikt-lidelser, kirurgi, intensiv-medisin (både nyfødte og voksne)

Europa: Ekstra antall dødsfall 25 000
USA: Ekstra antall dødsfall 23 000

The UK Prime Minister announced a Review on Antimicrobial Resistance in July, calling for ideas to bring this growing threat under control. This is the Review team's first paper, where we demonstrate that there could be profound health and macroeconomic consequences for the world, especially in emerging economies, if antimicrobial resistance (AMR) is not tackled.



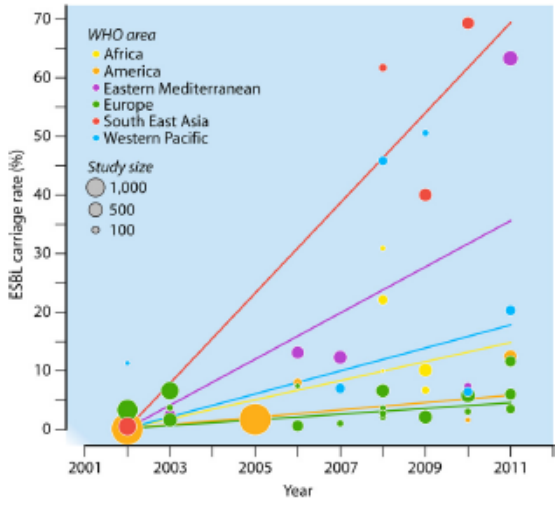
O'Neill-rapport 2014

Antibiotikaresistens – kunnskapshull, utfordringer og aktuelle tiltak
Ekspertgruppe-rapport av 18/8-14

- Formålet med ekspertgruppen er å utarbeide en rapport som
  1. Oppsummerer det som i dag er kjent kunnskap på området antibiotikaresistens, inkludert identifisering av kunnskapshull og mulige virkemidler, slik at vi kan bli best mulig rustet til å prioritere felles innsats mot antibiotikaresistens framover.
  2. Eventuelt foreslå relevante tiltak.

http://www.fhi.no/eway/default.aspx?pid=239&trg=Content_6496&Main_6157=6263:0:25,5785&MainContent_6263=6496:0:25,5793&Content_6496=6178:111438:25,5793:0:6562:1:::0:0

Forekomst av antibiotikaresistente bakterier i menneskers tarmflora øker



Ref: Woerther, P.L., Burdet, C., Chachaty, E., Andremont, A., 2013. Trends in human fecal carriage of extended-spectrum beta-lactamases in the community: toward the globalization of CTX-M. Clinical microbiology reviews 26, 744-758

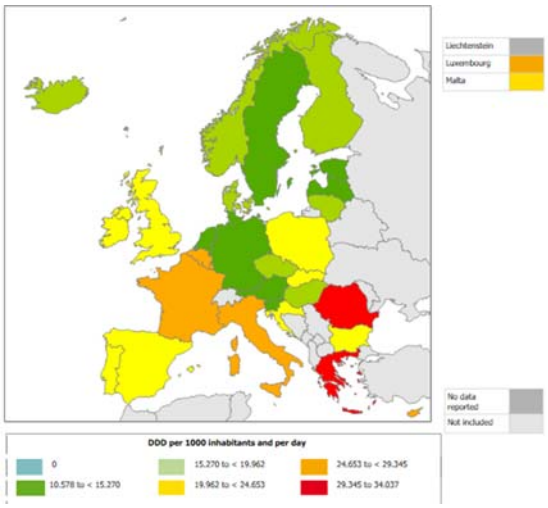
Overvåkning av antibiotika-bruk og -resistens i Norge og Europa

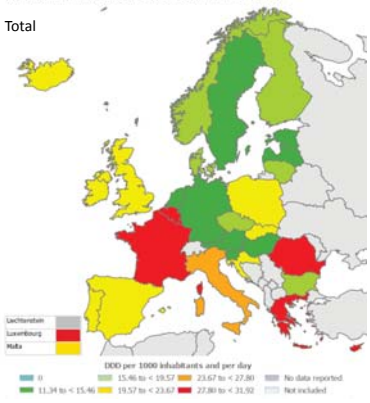
EARS-Net

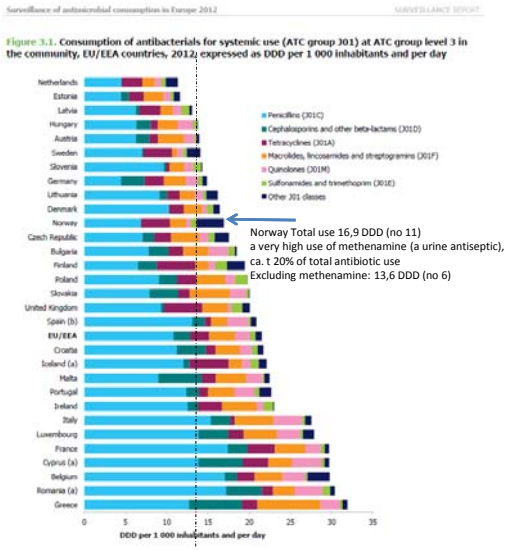
ESAC-Net

www.antibiotikaresistens.no

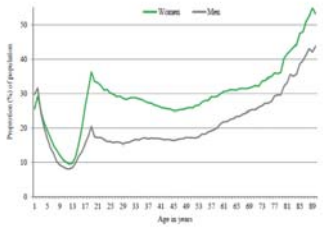
Consumption of Antibacterials For Systemic Use (ATC group J01) in the community (primary care sector) in Europe, reporting year 2014







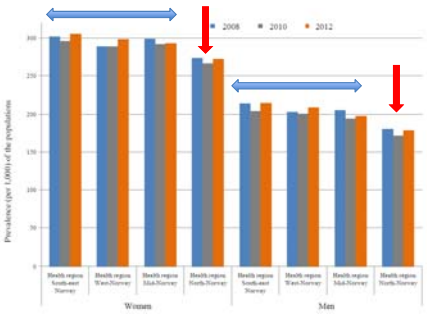
Antibiotikabruk/forskrivning ulik for kvinner og menn. Det brukes mindre antibiotika i nord enn i sør



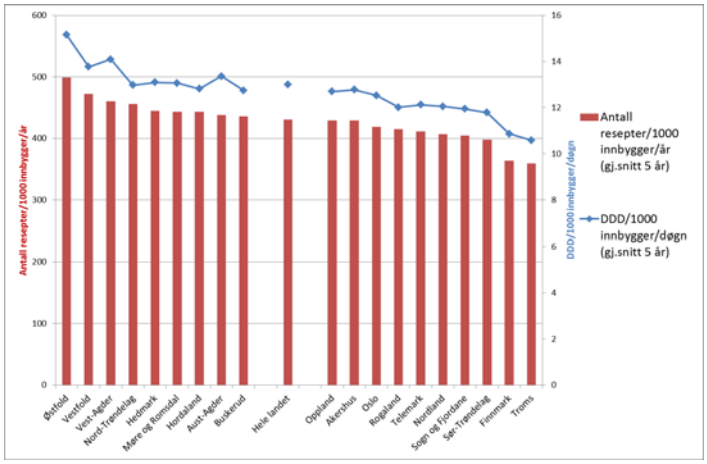
Kvinner bruker (mye) mer antibiotika enn menn

NORM/NORM-VET 2014

Befolkning i nord bruker 10-15% mindre antibiotika enn i sør

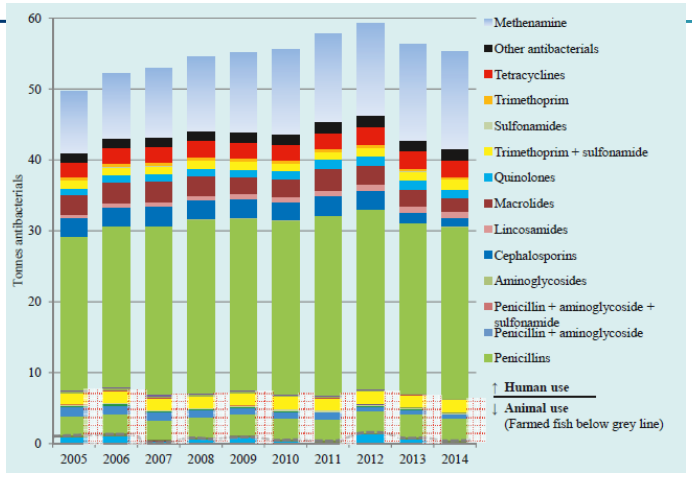


Figur 3. Gjennomsnittsbruk over siste 5 år av alle antibiotika i ATC gruppe J01 (systemiske antibakterielle midler) utenom metenamin i alle fylker. Antall resepter/1000 innbygger/år (røde kolonner) og DDD/1000innbygger/år (blå linje).



Det forskrives 40% flere resepter per 1000 innb/år i Østfold enn i Troms

Antibiotic use in humans an animals (by weight in tonnes)
NORM/NORM-Vet 2014



Antibiotikabruk i Norge 2014: 55 221 kg «total» forbruk
88% til mennesker, 11 % til landdyr og < 1% til fisk

NORM/NORM-VET 2014

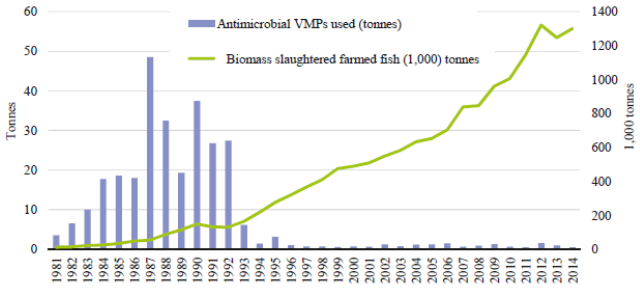
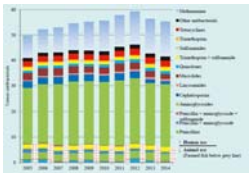


FIGURE 5. Total sales, in tonnes of active substance, of antimicrobial veterinary medicinal products (VMPs) for therapeutic use in farmed fish in Norway in the period 1981-2014 versus produced biomass (slaughtered) farmed fish.

TABLE 4. Total sales, in kilograms of active substance, of antimicrobial veterinary medicinal products (VMPs) for therapeutic use in farmed fish in Norway in the period 2004-2014.

Group of substances/active substance		2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Tetracyclines:	Oxytetracycline	9	8	0	19	23	40	10	1	1	0	0
Amphenicols:	Florfenicol	111	202	302	139	166	303	275	336	191	300	403
Quinolones:	Flumequine	4	28	7	18	1	1	0	0	0	0	0
	Oxolinic acid	1,035	977	1,119	406	681	926	308	212	1,399	672	108
Combinations:	Spectinomycin + lincomycin (2+1)	0	0	50	66	70	43	57	0	0	0	0
Total		1,159	1,215	1,478	648	941	1,313	649	549	1,591	972	511

Sales, in kg of active substance, of human and veterinary antibacterials and coccidiostats according to formulation 2014



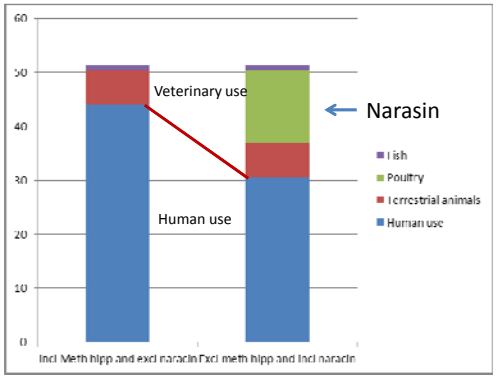
Formulation	Humans	Terrestrial animals	Aquaculture	Poultry	All species
Dermal	105	11			116
Oral	42 785	2 250	511	13 722	59 268
Parenteral	5 783	3 249			9 032
Eye/Ear	34	12			46
Intramammary		322			322
Others	54	105			159
Total	48 761	5 949	511	13 722	68 943
% of all	70,7 %	8,6 %	0,7 %	19,9 %	100,0 %

Total antimicrobial use in humans and animals 2014 (tonnes) (including/excluding methenamine hippurate and coccidiostats)

Forbruk i Norge i 1000 kg

Human use including methenamine

Veterinary use excluding naracin



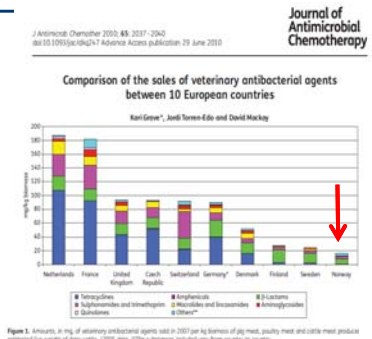
Human use excluding methenamine

Veterinary use including naracin

Naracin > 90% of all ionophore coccidiostats

Data from NORM/NOR-VET 2014

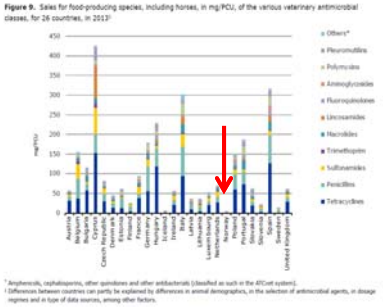
Antibiotic usage in animal husbandry varies enormous between countries
Norway: humans 88%, terrestrial animals 11%, fish 1%
(NORM/NORM-VET 2014)



2009 Norway 20 mg/kg biomass
Denmark 50 mg/kg biomass (2,5x↑)
Holland 180 mg/kg biomass (9x↑)
Fish not included for Norway 2009

2013 Norway 3,7 mg/PCU
Denmark 44,9 mg/PCU
Holland 69,9 mg/PCU

Data for Norway includes fish where almost no antibiotics are used



EMA, 5th ESVAC report. Sales of veterinary antimicrobial agents in 26 EU/EEA countries in 2013

E. coli blood culture isolates
ciprofloxacin: use and resistance level

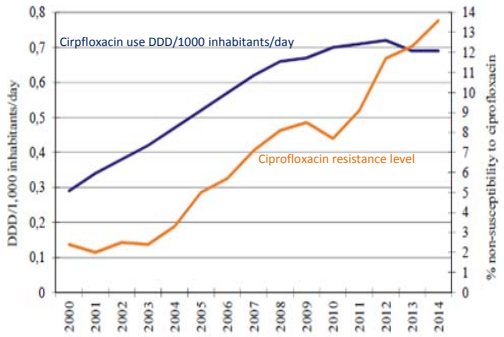


FIGURE 44. Usage of ciprofloxacin (blue) and prevalence of ciprofloxacin non-susceptibility in *Escherichia coli* blood culture isolates as defined by the 2015 breakpoints (orange) 2000-2014.

NORM/NORM-VET 2014

Effect of azithromycin and clarithromycin therapy on pharyngeal carriage of macrolide-resistant streptococci in healthy volunteers: a randomised, double-blind, placebocontrolled study

Surbhi Malhotra-Kumar, Christine Lammens, Samuel Coenen, Koen Van Herck, Herman Goossens
***Lancet* 2007; 369: 482–490**

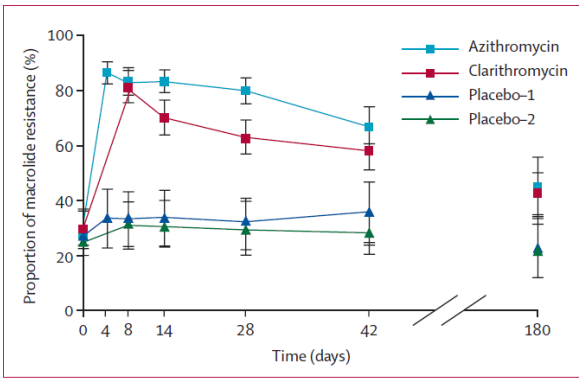
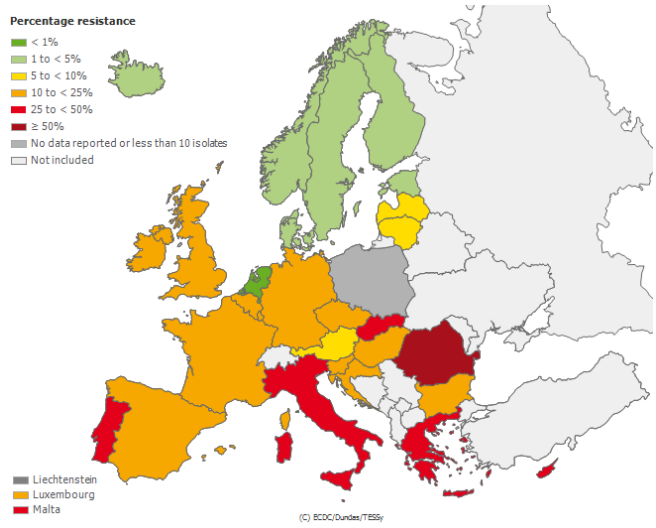


Figure 2: **Temporal changes in the proportion of macrolide-resistant streptococci after azithromycin and clarithromycin use**
Data shown are for all 204 volunteers followed through to day 42, and for 99 volunteers followed through to day 180. Error bars are 95% CI.

Blood culture isolates (N=12 237) NORM 2014

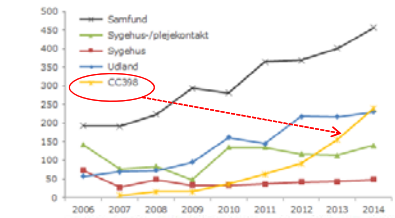
	Excludin skin flora skin	%
Staphylococcus aureus	1693	13,8 %
Streptococcus pneumoniae	550	4,5 %
Viridans strept	705	5,8 %
E nterococcus faecalis	589	4,8 %
Enterococcus faecium	251	2,1 %
Other G+ aerobic	1128	9,2 %
Sum G+ cocci	4916	40,2 %
E. coli	3739	30,6 %
Klebsiella	1075	8,8 %
Other Enterobacteriaceae	878	7,2 %
Pseudomonas	278	2,3 %
Other G- aerobes	308	2,5 %
Sum G- rods/cocci	6278	51,3 %
Bacteroides	346	2,8 %
Other anaerobes	475	3,9 %
Sum Anaerobes	821	6,7 %
Yeasts	222	1,8 %
Sum G+/G-/Ana/yeast	12237	100,0 %

EARS-Net data from 2014 MRSA



MRSA i Danmark 2006-2014 (Epi-Nytt uge 23 2015)
Eurosurveillance September 2015

Figur 2. Fordeling af kliniske MRSA-infektioner efter klassifikation, 2006-2014



Tabel 1. Epidemiologisk klassifikation af anmeldte MRSA-tilfælde 2014 samt antal (%) med klinisk infektion

Klassifikation	I alt	Klin. inf.	(%)
Erhvervet i udlandet	411	230	(56)
Erhvervet på sygehus	95	38	(40)
Samfundserhvervede med kontakt til sygehus/plejehjem (12 måneder)			
-Kendt eksposition på sygehus/plejehjem	34	13	(38)
-Kontakt til sygehus/plejehjem	153	125	(82)
-Erhverv på sygehus/plejehjem	30	13	(26)
Samfund			
- Eksponerede	478	86	(18)
- Ikke eksponerede	468	370	(79)
CC398	1.276	240	(19)
I alt	2.965	1.115	(38)

RESEARCH ARTICLE

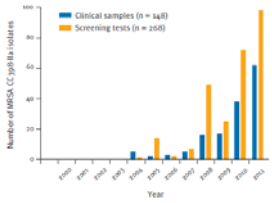
Meticillin-resistant *Staphylococcus aureus* CC398 is an increasing cause of disease in people with no livestock contact in Denmark, 1999 to 2011

I Larsen[1], A Petersen[2], M Sørum[3], M Stegger[4], L van Alphen[5], P Valentiner-Branth[6], LK Knudsen[6], LS Larsen[1], B Feingold[5], LB Price[1,5], PS Andersen[1], AR Larsen[1], RL Skov[1]
1. Microbiology and Infection Control, Statens Serum Institut, Copenhagen, Denmark
2. Infectious Disease Epidemiology, Statens Serum Institut, Copenhagen, Denmark
3. National Food Institute, Technical University of Denmark, Søborg, Denmark
4. Department of Environmental Health Sciences, University at Albany, State University of New York, School of Public Health, Rensselaer, NY, United States
5. Center for Food Microbiology and Environmental Health, Translational Genomics Research Institute, Flagstaff, AZ, United States
6. Milken Institute School of Public Health, George Washington University, Washington, DC, United States
Correspondence: Jesper Larsen (JRL@ssi.dk)

Citation style for this article:
Larsen I, Petersen A, Sørum M, Stegger M, van Alphen L, Valentiner-Branth P, Knudsen LK, Larsen LS, Feingold B, Price LB, Andersen PS, Larsen AR, Skov RL. Meticillin-resistant Staphylococcus aureus CC398 is an increasing cause of disease in people with no livestock contact in Denmark, 1999 to 2011. Euro Surveill. 2015;20(37):pii=30021. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2015.20.37.30021
Article submitted on 15 November 2014 / accepted on 12 March 2015 / published on 17 September 2015

FIGURE 1

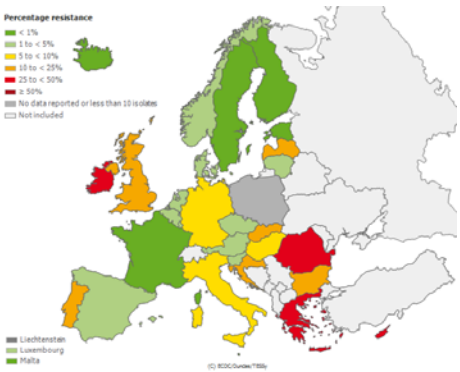
Annual number of meticillin-resistant *Staphylococcus aureus* (MRSA) CC398-IIa isolates, from each newly identified MRSA-positive person, Denmark, 1999–2011 (n = 416)



EARS-Net data from 2014 VRE

E. faecalis Vanco R

E. faecium Vanco R



Forekomst av VRE i Norge 1996-2013 (Kilde: NORM/NORM-VET 2013)

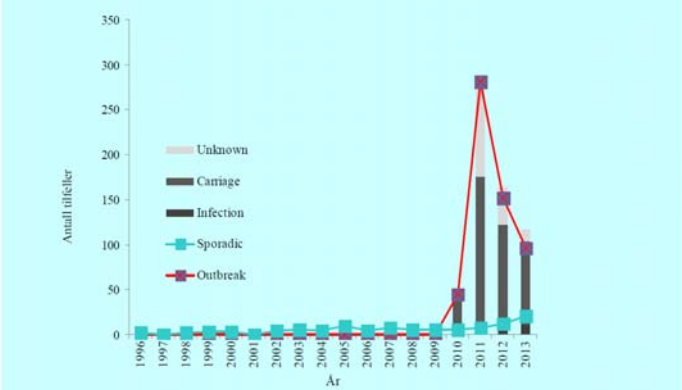
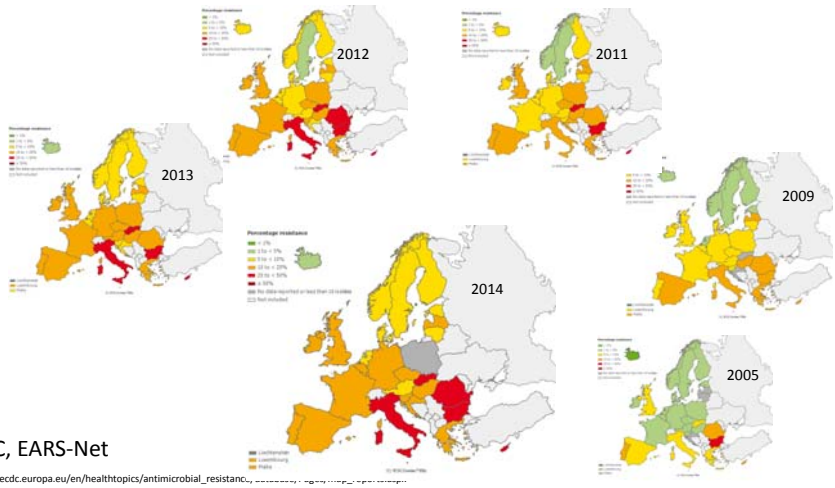


FIGURE 58. Annual number of cases of vancomycin resistant enterococci reported to the Norwegian Surveillance System for Communicable Diseases (MSIS) during 1996-2013. The bars indicate whether cases represent infection, carriage only or unknown clinical status. Coloured lines classify number of cases as sporadic (blue) and outbreak related (red).

Proportion of 3rd generation cephalosporins (R+I) resistant *Escherichia coli* isolates in participating countries in 2005 - 2014



ECDC, EARS-Net

http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistanc...

Prevalence of ESBL-positive E. coli and Klebsiella spp i Norway (NORM/NORM-VET 2014)

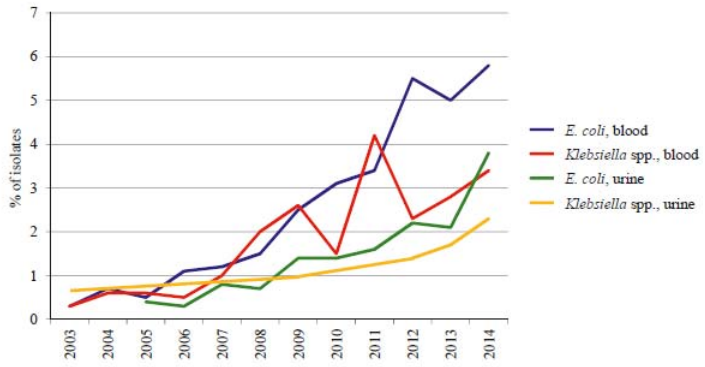
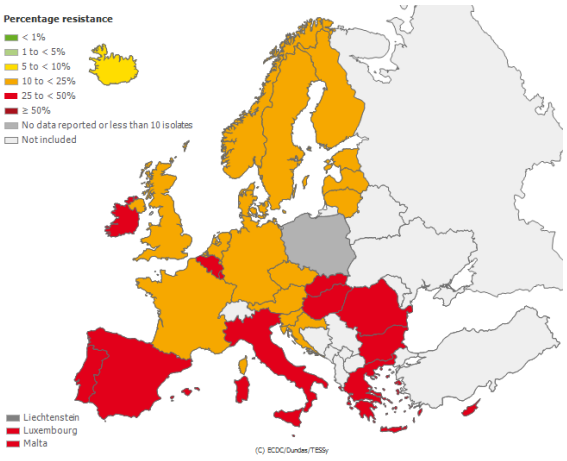


FIGURE 46. Prevalence of ESBL production among *Escherichia coli* and *Klebsiella* spp. isolates from blood and urine 2003-2014.

E. coli Fluroquinolone R+I (EARS-Net 2014)



Resistens hos E. coli i blodkultur

Gentamicin

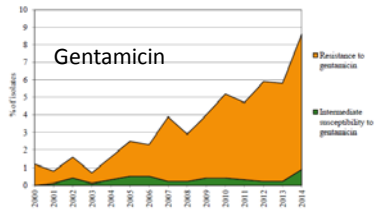


FIGURE 43. Prevalence of intermediate susceptibility and resistance to gentamicin in *Escherichia coli* blood culture isolates 2000-2014.

Ciprofloxacin

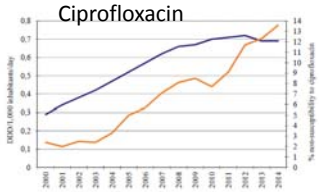


FIGURE 44. Usage of ciprofloxacin (blue) and prevalence of ciprofloxacin non-susceptibility in *Escherichia coli* blood culture isolates as defined by the 2015 breakpoints (orange) 2000-2014.

ESBL-positive E. coli og Klebsiella

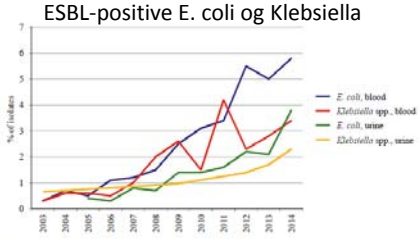


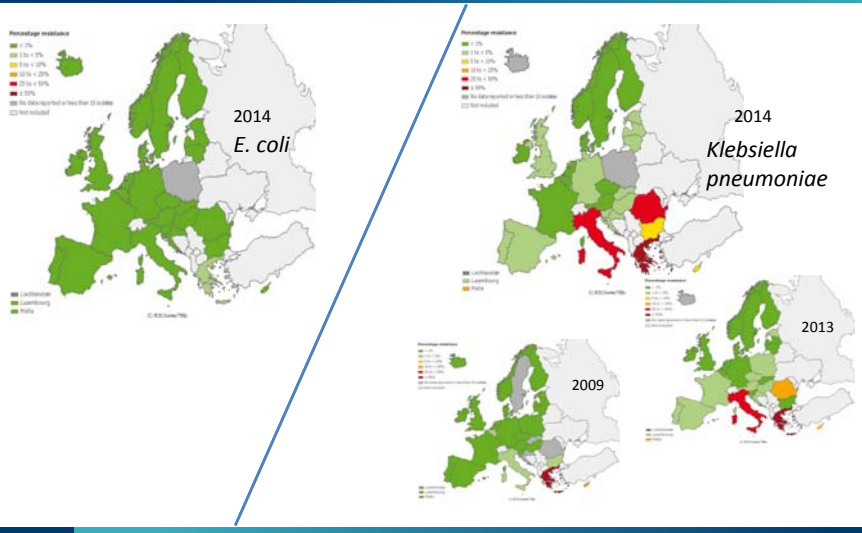
FIGURE 46. Prevalence of ESBL production among *Escherichia coli* and *Klebsiella* spp. isolates from blood and urine 2003-2014.

Når bakteriene er resistente mot cefalosporiner, hva kan vi så bruke?

- Karbapenemer
  - Meropenem, (imipenem, doripenem og ertapenem)
- Polymyxiner
  - Colistin

CRE – Carbapenamase producing Enterobacteriaceae

Carbapenem-resistance (R+I) in E. coli (left) and Klebsiella pneumoniae (right) 2014



ESBL-CARBA producing Enterobacteriaceae in Norway

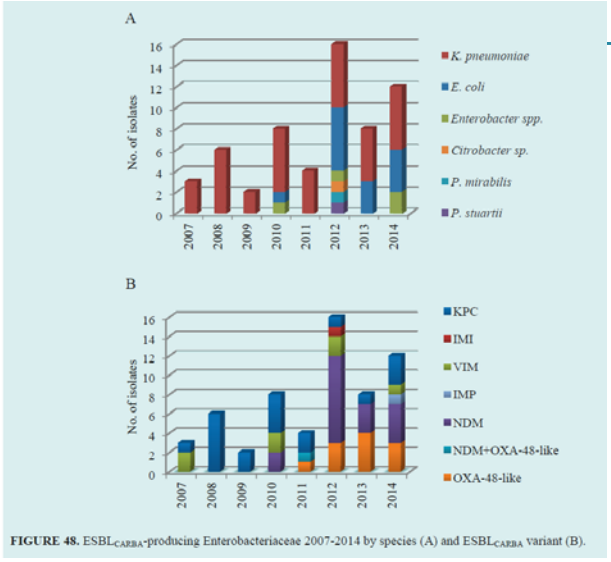
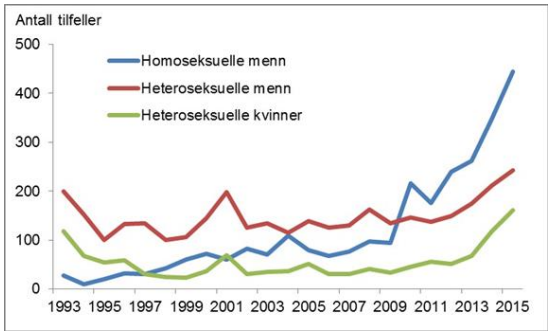
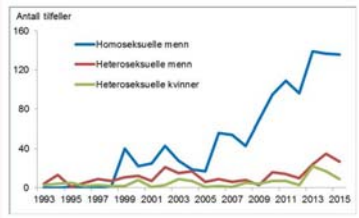


FIGURE 48. ESBL$_{CARBA}$-producing Enterobacteriaceae 2007-2014 by species (A) and ESBL$_{CARBA}$ variant (B).

Forekomst av gonore og syfilis i Norge 2005-2015 (MSIS)

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Gonore	278	236	238	301	269	411	370	444	506	682	851
Syfilis	24	67	61	56	76	118	130	109	185	189	172





Figur 2. Tilfeller av syfilis (primær, sekundær og tidlig latent syfilis) i Norge meldt MSIS 1993-2015 etter diagnoseår, smittemåte og kjønn.

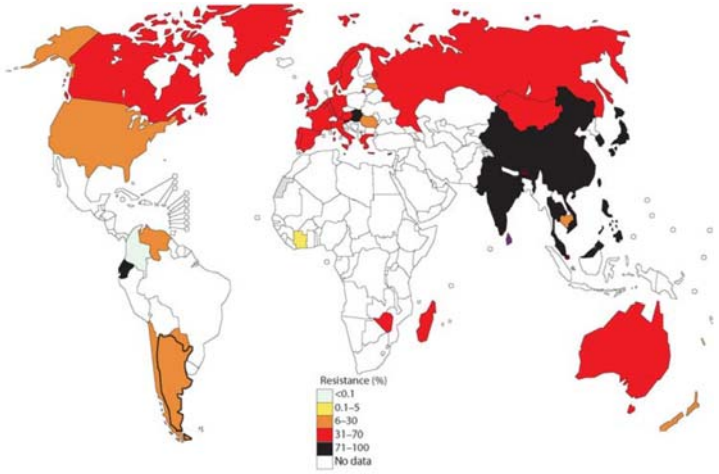
Figur 1. Tilfeller av gonore i Norge meldt MSIS 1993-2015 etter diagnoseår, smittemåte og kjønn

Neisseria gonorrhoeae

TABLE 47. *Neisseria gonorrhoeae* from all specimen types in 2014 (n=255). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	Susceptible	Resistant	Susceptible	Intermediately susceptible	Resistant
Penicillin G	≤ 0.06	> 1	3.9	49.4	46.7
Ceftriaxone	≤ 0.125	> 0.125	98.8	-	1.2 ←
Cefixime	≤ 0.125	> 0.125	96.1	-	3.9
Azithromycin	≤ 0.25	> 0.5	62.8	29.0	8.2
Ciprofloxacin	≤ 0.03	> 0.06	24.3	0.4	75.3 ←
Tetracycline	≤ 0.5	> 1	22.4	22.4	55.2
Spectinomycin	≤ 64	> 64	100.0	-	0.0
Beta-lactamase	Negative	Positive	69.4	-	30.6

Quinolone resistant *Neisseria gonorrhoeae* – GASP 2012



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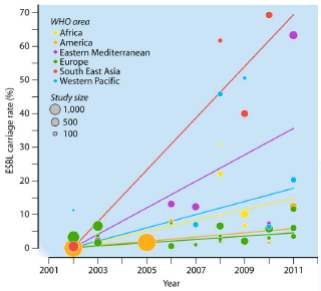
Forekomst av antibiotikaresistente bakterier i menneskers tarmflora øker



Ref: Woerther, P.L., Burdet, C., Chachaty, E., Andremont, A., 2013. Trends in human fecal carriage of extended-spectrum beta-lactamases in the community: toward the globalization of CTX-M. Clinical microbiology reviews 26, 744-758

Endring i trusselbildet

INVITED ARTICLE FOOD SAFETY

Patricia M. Griffin, Section Editor

Do Human Extraintestinal *Escherichia coli* Infections Resistant to Expanded-Spectrum Cephalosporins Originate From Food-Producing Animals? A Systematic Review

Benjamin Lazarus,[1] David L. Paterson,[1] Jeanne L. Mollinger,[2] and Benjamin A. Rogers[1,3]

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To find out whether food-producing animals (FPAs) are a source of extraintestinal expanded-spectrum cephalosporin-resistant *Escherichia coli* (ESCR-EC) infections in humans, Medline, Embase, and the Cochrane Database of Systematic Reviews were systematically reviewed. Thirty-four original, peer-reviewed publications were identified for inclusion. Six molecular epidemiology studies supported the transfer of resistance via whole bacterium transmission (WBT), which was best characterized among poultry in the Netherlands. Thirteen molecular epidemiology studies supported transmission of resistance via mobile genetic elements, which demonstrated greater diversity of geography and host FPA. Seventeen molecular epidemiology studies did not support WBT and two did not support mobile genetic element–mediated transmission. Four observational epidemiology studies were consistent with zoonotic transmission. Overall, there is evidence that a proportion of human extraintestinal ESCR-EC infections originate from FPAs. Poultry, in particular, is probably a source, but the quantitative and geographical extent of the problem is unclear and requires further investigation.

Keywords. zoonosis; ESBL; *E. coli*; ST131; urinary tract; poultry.

The global spread, rapidly rising incidence, and increased mortality of expanded-spectrum cephalosporin-resistant Escherichia coli (ESCR-EC) infections over the past decade have made it one of the biggest threats to human health worldwide [1, 2].

In many regions, this rising incidence has coincided with a shift in the epidemiology of human infection, from healthcare associated to community acquired [1].

Discovering the origins of this shift may reveal new targets for public health intervention [3].

Highly similar cephalosporin resistant *Escherichia coli* and AmpC resistance plasmids found in both patients and poultry meat in Norway

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1) Department of Foodborne Infections, Norwegian Institute of Public Health, Oslo, Norway. 2) Department of Diagnostic services, Norwegian Veterinary Institute, Oslo, Norway. 3) Department of Bacteriology and Immunology, Norwegian Institute of Public Health, Oslo, Norway. 4) Norwegian National Advisory Unit on Detection of Antimicrobial Resistance, Department of Microbiology and Infection Control, University Hospital of North Norway, Tromsø, Norway. 5) Research group for Host-Microbe Interactions, Faculty of Health Sciences, University of Tromsø – The Arctic University of Norway, Tromsø, Norway. 6) Department of Medical Microbiology, Stavanger University Hospital, Stavanger, Norway. 7) Akershus University Hospital, Department of Clinical Microbiology and Infection Control, Lørenskog, Norway

Introduction:

Like the situation in many other countries, the broiler production chain in Norway has a relatively high prevalence of *E. coli* resistant to 3rd generation cephalosporins. The bla_{CMY-2} gene encoding a plasmid mediated AmpC β-lactamase is responsible for cephalosporin resistance, except for a small proportion of isolates with up-regulated chromosomal ampC (Mo, 2014a)[1]. Resistant bacteria in food may have an impact on resistance development in human bacterial populations.

The aim of this study was to compare cephalosporin resistant *E. coli* isolates and resistance plasmids from poultry with human clinical isolates by whole genome sequencing (WGS) in order to investigate a possible overlap between the two reservoirs.

Materail and methods:

Broiler isolates: A total of 10 bla_{CMY-2} positive *E. coli* from chicken meat (n=7) and chicken faecal samples (n=3) were included. These isolates were chosen for comparison as they represented a common genotype occurring in chicken meat (Mo, 2014b). The isolates carried the bla_{CMY-2} gene on conjugative IncK plasmids. The isolates were collected during 2011-2014.

Human clinical isolates: A total of 257 *E. coli* isolates with AmpC phenotype were forwarded from Norwegian clinical microbiology laboratories. The isolates originated mainly from cases of urinary tract infection or blood stream infection and were isolated during 2010 to 2014.

Molecular characterization: All isolates were tested by PCR for presence of bla_{CMY-2} and IncK sequences. Isolates positive for both bla_{CMY-2} and IncK were subjected to 10-loci multi-locus variable-number tandem repeat analysis (MLVA) and WGS.

DNA for WGS was purified either by use of the manual Wizard® Genomic DNA Purification Kit (Promega) or automated in a MagNA Pure LC using the Total Nucleic Acid Isolation Kit (Roche). WGS was performed on an Illumina HiSeq 2500 platform (BGI Hong Kong) and analysed by software available from Center for Genomic Epidemiology, Technical University of Denmark, (https://cge.cbs.dtu.dk/services/) for *in silico* typing and phylogeny.

Results:

PCR screening showed that 21 human *E. coli* isolates were positive for both bla_{CMY-2} and IncK replicon sequences. The majority of the human isolates were genetically diverse but six clustered in the SNP analysis (CSI Phylogeny) together with the isolates from poultry (Fig. 1). These 16 isolates grouped within the multi locus sequence type 38 (ST38), and most of them contained the O7 antigen and shared two unique and nearly identical MLVA profiles. Phylogeny (NDtree) on 14 of these genome sequences revealed very few SNP differences as shown in figure 2, whereas the last two were more distantly related.

WGS analysis of plasmid sequences with all human and poultry isolates showed that highly similar bla_{CMY-2} containing IncK plasmids were present in both the closely related as well as in the more distantly related isolates. This indicates that closely related bla_{CMY-2} containing plasmids may circulate within the *E. coli* populations

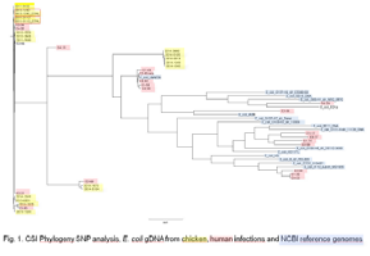

Fig. 1. CSI Phylogeny SNP analysis. *E. coli* gDNA from chicken, human infections and NCBI reference genomes

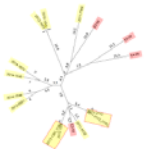

Fig. 2. NDtree Phylogeny SNP analysis of the closely related *E. coli* from chicken and human infections

Conclusion:

Highly similar *E. coli* isolates carrying bla_{CMY-2} were found in both poultry and from humans with infections. Furthermore, these isolates carried closely related IncK plasmids with bla_{CMY-2} that also were detected in genetically unrelated human clinical *E. coli* isolates. These findings indicate that *E. coli* from poultry may represent a source of resistance plasmids and resistant *E. coli* infecting humans.

References

1) Mo SS, et al. 2014a. Emergence of AmpC-producing *Escherichia coli* in the broiler production chain in a country with a low antimicrobial usage profile. Vet Microbiol 171, 315-20

2) Mo SS, et al. 2014b. Characterization of AmpC- producing *Escherichia coli* isolated from broilers and retail chicken meat in Norway. Poster, ESVAC-MVM meeting, July 2014, Brighton, UK

***Lancet Infect Dis* 2016; 16:**
Commentary p 132-133 , Article p 161–68

Colistin resistance: a major breach in our last line of defence

In hospital practice, clinicians have been buoyed by the recent development of new antibiotics active against multidrug resistant Gram-negative bacilli. However, recently approved antibiotics like ceftazidime-avibactam or ceftolozane-tazobactam do not provide activity against all Gram-negative bacilli, with notable gaps in their coverage, including the notorious New Delhi metallo-β-lactamase 1-producing organisms and many strains of carbapenem resistant *Acinetobacter baumannii*. For this reason, the polymyxins (colistin and polymyxin B) remain the last line of defence against many Gram-negative bacilli. Colistin-resistant and even pan-drug-resistant Gram-negative bacilli have

Liu and colleagues[4] present data from China showing that *E coli* from pigs at slaughter and from retail chicken and pork have high rates of plasmid-mediated colistin resistance. The same mechanism was found in *E coli* and *K pneumoniae* isolates from Chinese patients in hospital. These findings suggest that the links between agricultural use of colistin, colistin resistance in slaughtered animals, colistin resistance in food, and colistin resistance in human beings are now complete. One of the few solutions to uncoupling these connections is limitation or cessation of colistin use in agriculture. This will require substantial political will and we call upon Chinese leaders to act rapidly and decisively.

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See Articles page 161

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu, Yang Wang*, Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Danxia Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhong Shen*

Summary

Background Until now, polymyxin resistance has involved chromosomal mutations but has never been reported via horizontal gene transfer. During a routine surveillance project on antimicrobial resistance in commensal *Escherichia coli* from food animals in China, a major increase of colistin resistance was observed. When an *E coli* strain, SHP45, possessing colistin resistance that could be transferred to another strain, was isolated from a pig, we conducted further analysis of possible plasmid-mediated polymyxin resistance. Herein, we report the emergence of the first plasmid-mediated polymyxin resistance mechanism, MCR-1, in Enterobacteriaceae.

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Published Online November 18, 2015 http://dx.doi.org/10.1016/S1473-3099(15)00424-7
See Comment page 132

ExPEC Extraintestinal Pathogenic E. coli

USA ca. 80% av antibiotika brukes til dyr/landbruk
Norge ca. 10% av antibiotika brukes til dyr

Resistens – hvor kommer den fra (og hvor går den hen?)

- Mikrobiota
  - Mennesker
    - Kliniske isolat (bakterier fra syke individer)
    - Normalflora hos oss alle
  - Produksjonsdyr
    - Tarmflora (Fjørfe!)
  - Mat
    - Kylling, kalkun, importert mat (sjømat fra østen)
  - Miljø
    - Enkelte områder i verden

«Alt» henger sammen

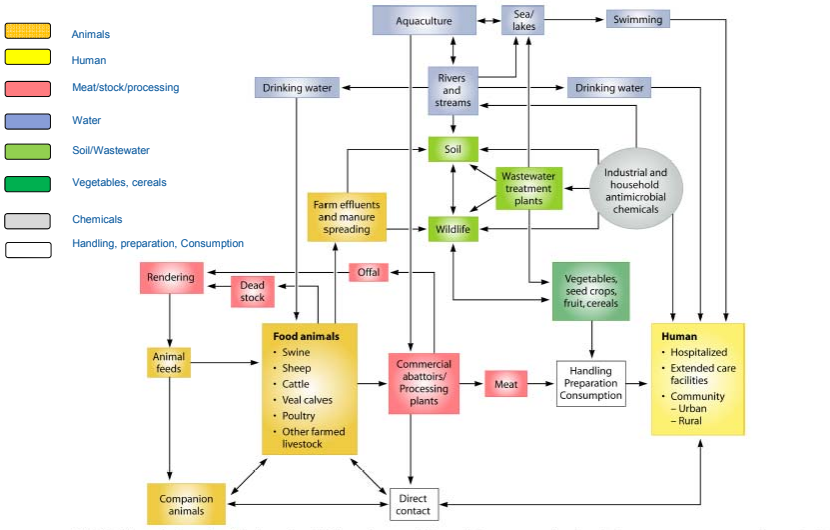

FIG. 4. Dissemination of antibiotics and antibiotic resistance within agriculture, community, hospital, wastewater treatment, and associated environments. (Adapted from reference 49 and reference 83a with permission of the publishers.)

Davis J and Davis D. Origins and evolution of Antibiotic resistance MMBR 2010 74 417-433

Antimicrobials: access and sustainable effectiveness 2

Understanding the mechanisms and drivers of antimicrobial resistance

Lancet online, November 18 2015

Alison H Holmes, Luke S P Moore, Arnfinn Sundsfjord, Martin Steinbakk, Sadie Regmi, Abhilasha Karkey, Philippe J Guerin, Laura J V Piddock

To combat the threat to human health and biosecurity from antimicrobial resistance, an understanding of its mechanisms and drivers is needed. Emergence of antimicrobial resistance in microorganisms is a natural phenomenon, yet antimicrobial resistance selection has been driven by antimicrobial exposure in health care, agriculture, and the environment. Onward transmission is affected by standards of infection control, sanitation, access to clean water, access to assured quality antimicrobials and diagnostics, travel, and migration. Strategies to reduce antimicrobial resistance by removing antimicrobial selective pressure alone rely upon resistance imparting a fitness cost, an effect not always apparent. Minimising resistance should therefore be considered comprehensively, by

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This is the second in a Series of five papers about access to and sustainable effectiveness of antimicrobials

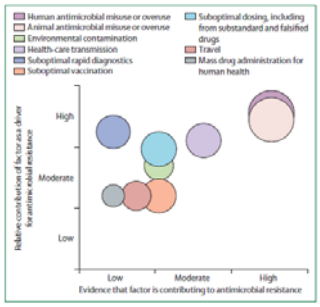

Figure 3: Role of modifiable drivers for antimicrobial resistance: a conceptual framework

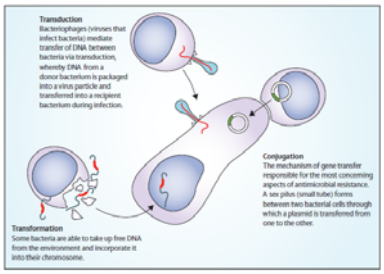

Figure 1: Transmission of genetic material between microorganisms

http://www.thelancet.com/series/antimicrobials-access-and-sustainable-effectiveness

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- Takk for oppmerksomheten!

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