Antibiotikabruk og resistensutvikling

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Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)
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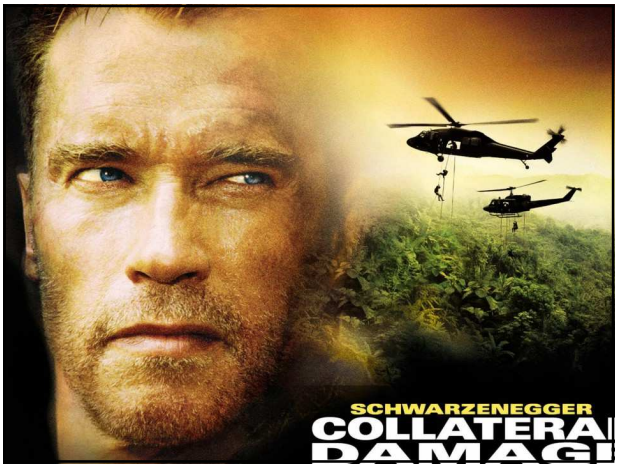

As soon as we use it, we lose it

"The greatest possibility of evil in self-medication is the use of too small doses so that instead of clearing up infection, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed to other individuals and from them to others until they reach someone who gets a septicemia or pneumonia which penicillin cannot save.

In such a case the thoughtless person playing with penicillin treatment is **morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism**. I hope this evil can be averted."

Alexander Fleming
New York Times 26. juni 1945

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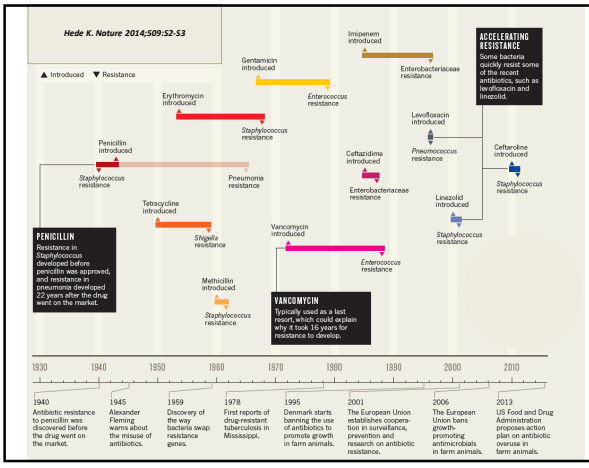

Konsekvenser av økt antibiotikaresistens

- Empirisk terapi svikter
- Adekvat terapi forsinkes

- Billige, smalspektrede midler ut
- Dyrere, bredspektrede midler inn

- Økte kostnader
- Økt resistens

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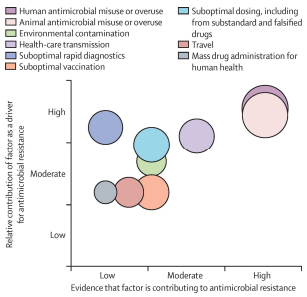
Hvilke faktorer bidrar til resistens?



Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Holmes AH et al. Lancet. 2016 Jan 9;387(10014):176-87

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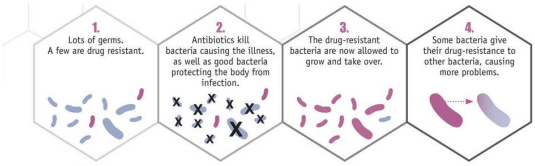
Seleksjonspress



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www.cdc.gov

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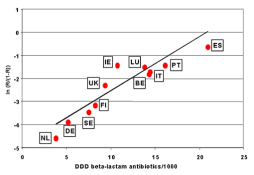
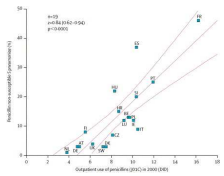


Bronzwaer et al. Emerg Infect Dis 2002;8:278-82



Goosens et al. Lancet 2005;365:579-87

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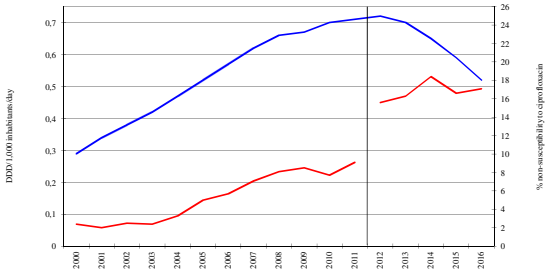

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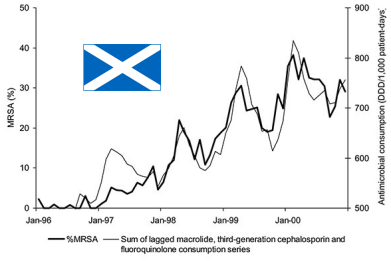

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Monnet DL et al. Emerg Infect Dis 2004;10:1432-41

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Antibiotikabruk og MRSA

	RR	95% CI	P
Alle antibiotika	1.8	1.7-1.9	<0.001
Kinoloner	3.0	2.5-3.5	
Glykopeptider	2.9	2.4-3.5	
Cefalosporiner	2.2	1.7-2.9	
Andre betalaktamer	1.9	1.7-2.2	

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Tacconelli et al. JAC 2008;61:26-38

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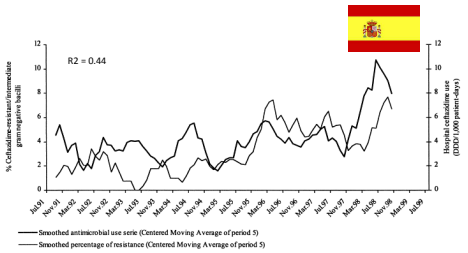

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

López-Lozano et al. Int J Antimicrob Agents 2000;14:21-31

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Antibiotikabruk og ESBL

TABLE 3. Multivariable Analysis of Antibiotic Use Among Patients Infected with Extended-Spectrum β-Lactamase–Producing *Escherichia coli* and *Klebsiella* Species (ESBL-EK)

Type of variable used to describe prior antibiotic use, variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	*P*
Categorical			
Use of 3rd-generation cephalosporin	16.0 (2.0-127.92)	7.44 (0.41-135.41)	.20
Use of vancomycin	7.15 (2.36-21.63)	7.85 (1.86-33.06)	.005
Length of stay in hospital before ESBL-EK infection	1.05 (1.02-1.09)	1.02 (0.99-1.06)	.18
Diabetes	2.46 (0.95-6.42)	4.44 (1.06-18.58)	.04
Continuous			
Use of 3rd-generation cephalosporin[a]	1.23 (1.02-1.47)	...	.03

NOTE. CI, confidence interval; OR, odds ratio.
[a] No other variables were confounders in the final multivariable analysis of antibiotic use as a continuous variable. The OR represents the odds associated with each increase of 1 day of use of a third-generation cephalosporin.

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Hyle EP et al. Infect Control Hosp Epidemiol 2007;28(6):647-54

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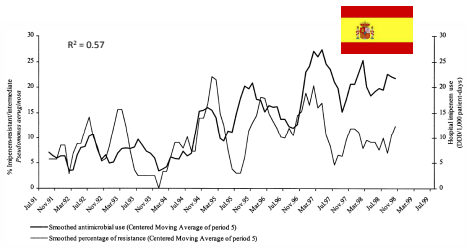
The more we use it, the more we lose it



Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

López-Lozano et al. Int J Antimicrob Agents 2000;14:21-31

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Antibiotikabruk og karbapenemresistente *P. aeruginosa*

TABLE 5 Conventional meta-analyses of the different risk factors for acquisition and transmission of carbapenem-resistant *P. aeruginosa*[a]

Risk factor	No. of factors	Pooled OR (random effects)	95% CI	Range of OR in individual studies	Risk of publication bias: Egger	*P* value	Kendall's tau	*P* value
Carbapenem use	16	7.09	5.43–9.25	3.6–76.0	1.39	0.02	0.47	0.01
Medical devices	19	5.11	3.55–7.37	2.1–64.3	2.30	<0.001	0.49	0.003
Other antibiotic use	19	3.56	2.52–5.03	0.3–43.7	1.49	0.06	0.38	0.02
ICU admission	8	3.02	1.62–5.61	1.1–13.3	2.96	0.002	0.07	0.90
Quinolone use	11	2.73	1.27–5.87	0.1–48.4	0.89	0.56	0.45	0.06
Underlying disease	13	2.44	1.23–4.84	0.1–25.0	1.34	0.06	−0.05	0.77
Vancomycin use	3	2.10	1.42–3.09	1.8–2.9	NC	NC	NC	NC
Patient characteristics	13	1.46	1.22–1.75	1.0–13.9	2.02	<0.001	0.56	0.007
Length of hospital stay	9	1.06	1.02–1.09	1.0–6.7	3.05	0.0003	0.56	0.04

[a] OR, odds ratio; CI, confidence interval; NC, not calculated because there were too few strata.

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Voor In 't Holt AF et al. Antimicrob Agents Chemother 2014;58:2626-37

Oslo universitetssykehus

Research Article

Statistics in Medicine

Received 6 June 2011, Accepted 5 September 2012 Published online 1 October 2012 in Wiley Online Library

(wileyonlinelibrary.com) DOI: 10.1002/sim.5636

Antibiotic resistance in hospitals: a ward-specific random effect model in a low antibiotic consumption environment

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Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

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Estimated relative change in stationary levels of incidence rates of *P. aeruginosa* and of proportions of *P. aeruginosa* resistant against meropenem following a relative change *S* in antibiotic consumption compared with the reference level from 2003 to 2006.

Relative change in antibiotic consumption *S*	Incidence rates	95% CI		Proportions	95% CI	
	Estimate	Lower	Upper	Estimate	Lower	Upper
0.5	0.93	0.89	0.97	0.83	0.74	0.93
0.7	0.95	-	-	0.89	-	-
0.9	0.98	-	-	0.97	-	-
1.5	1.07	-	-	1.22	-	-
2.0	1.15	1.06	1.31	1.42	1.18	1.65

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

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Antibiotikabehandling er risikofaktor for VRE

Table 3. The effect of antibiotic treatment as risk factor for vancomycin-resistant enterococci

	Cases (%)	Control (%)	Unadjusted effect		Adjusted for explanatory model[a]		Adjusted for model and other antibiotics[b]	
Antibiotic agent	(233)	(647)	OR	p value	OR (95% CI)	p value	OR (95% CI)	p value
Penicillins	67 (29)	134 (21)	1.5	0.04	.99 (.63 to 1.6)	0.97	1.0 (.64 to 1.7)	0.86
β-lactam-inhibitor combination	49 (21)	98 (15)	1.5	0.07	.94 (.6 to 1.5)	0.78		
Cephalosporins	104 (45)	248 (38)	1.2	0.28	1.5 (1.0 to 2.4)	0.048		
Third generation	66 (30)	97 (15)	2.6	0.001	5.8 (3.7 to 9.5)	<0.001	2.8 (1.7 to 4.8)	<0.001
Vancomycin (p.o.)	4 (1.7)	7 (1.1)	1.2	083	1.0 (.25 to 4.2)	0.96		
Vancomycin (i.v.)	67 (29)	121 (19)	1.7	0.016	1.4 (.89 to 2.3)	0.19	.99 (.57 to 1.7)	0.98
Metronidazole (p.o.)	13 (5.6)	23 (3.6)	1.5	0.29	1.0 (.42 to 2.5)	0.97		
Metronidazole (i.v.)	47 (20)	37 (6)	2.5	<0.001	2.3 (1.3 to 3.9)	0.003	2.1 (1.2 to 3.7)	0.008
Clindamycin	20 (8.6)	51 (7.9)	1	0.9	1.5 (.76 to 2.8)	0.26	1.1 (.55 to 2.3)	0.76
Quinolone[c]	48 (21)	68 (11)	2	0.005	1.6 (.94 to 2.6)	0.086	1.5 (.85 to 2.6)[c]	0.17[c]
Imipenem	19 (8.2)	27 (4.2)	1.7	0.12	1.3 (.61 to 2.9)	0.47	1.2 (.52 to 2.8)	0.66

[a]Adjusted for the explanatory model detailed in Table 2.
[b]When included as a continuous variable (number of days of treatment with quinolone) OR=1.03, p=0.05.
OR, odds ratio; p.o., orally; i.v., intravenously.

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Carmeli et al. Emerg Infect Dis 2002;8;802-7

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Potensiell seleksjonsrisiko

	MRSA	VRE	ESBL	MDR PA	*C. difficile*
Carbapenems					
Piperacillin-tazobactam					
3rd generation cephalosporins					
Fluoroquinolones					

Clear evidence of selection risk; No clinical activity; potential to select; Borderline clinical activity and/or selection risk

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Wilcox et al. Int J Antimicrob Agents 2009;34:S6-10

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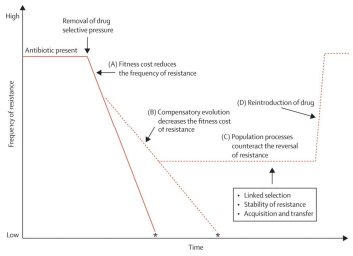
«Easy to get – hard to lose»



Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

Johnsen P et al. Lancet Infect Dis 2009;9(6):357-64

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Status 2017

- Påvist ervervet resistens mot alle registrerte antibiotika hos alle klinisk viktige bakterier
- Antibiotika med nye virkningsmekanismer mangelvare

Arbeidsgruppen for antibiotikaspørsmål og metoder for resistensbestemmelse (AFA)

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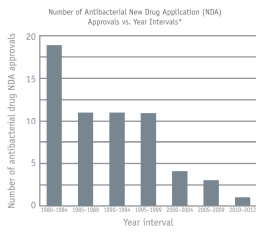
The antibiotic pipeline – running dry?

The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.



*Intervals from 1980–2009 are 5-year intervals; 2010–2012 is a 3-year interval. Drugs are limited to systemic agents.
Data courtesy of FDA's Center for Drug Evaluation and Research (CDER).

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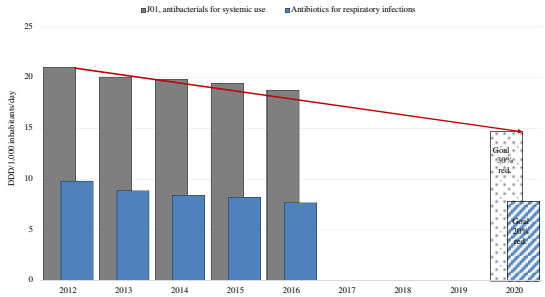
30% reduksjon innen 2020



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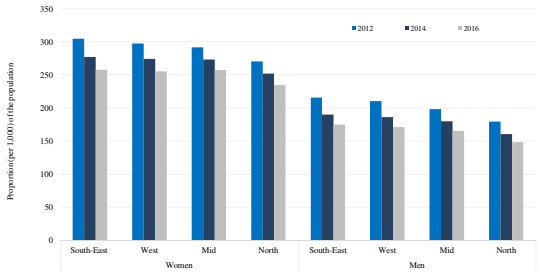
Antibiotikabruk i allmennpraksis 2012-2016



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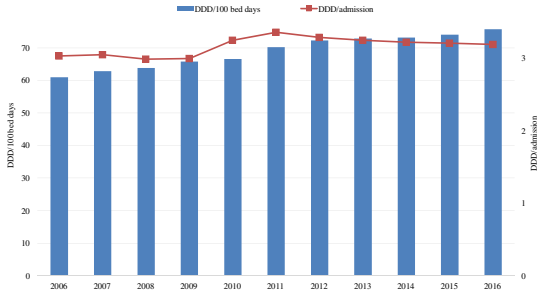
Antibiotikaforbruk i sykehus 2006-2016



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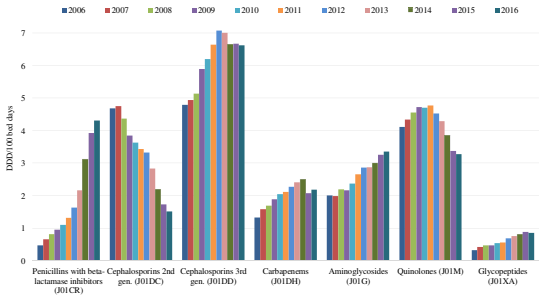

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«The big battle» – eller mange små?

- Riktig bruk av antibiotika
  - På riktig indikasjon
  - Riktig dosering og varighet
- Smittevern
  - Håndhygiene
  - Screening og isolering
- Mikrobiologiske laboratorier
  - Rask og korrekt identifikasjon og resistensbestemmelse
  - Selektiv rapportering av resistens?
- Overvåkning
- Forskning og utvikling

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Takk for oppmerksomheten!

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

MacCallum CJ (2007) PLoS Biol 5(4): e112. doi:10.1371/journal.pbio.0050112