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UMCG Antimicrobial Stewardship Program

Day 2 bundle: implementation and first results




Disclosures:
 - Joint projects: Copan, Pathogenica/Life Technologies
 - Travel support IDweek (co-funding): Wyeth/Pfizer

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Empiric therapy (severe infections)



**Time is critical:
Get it right from the beginning!**

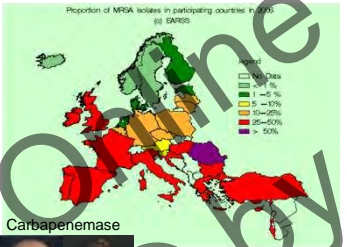
=> Predict clinical success based on expert knowledge and data

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Consumption and resistance:


country	Antibiotic consumption
Netherlands	8,9
Denmark	11,3
Sweden	13,5
Germany	13,6
Belgium	26,7
Portugal	28,8
Spain	32,4
France	36,5

ESAC data 2004
 DDD (1000 inhabitant days)
 (European Surveillance of Antimicrobial Consumption)



Proportion of MRSA isolates in participating countries in 2005 (n= 54722)

Carbapenemase

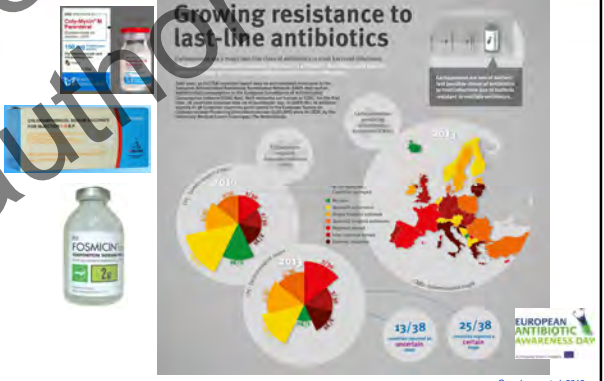


Glasner, Grundmann et al. 2013

EUROPEAN ANTIBIOTIC AWARENESS DAY

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Growing resistance to last-line antibiotics



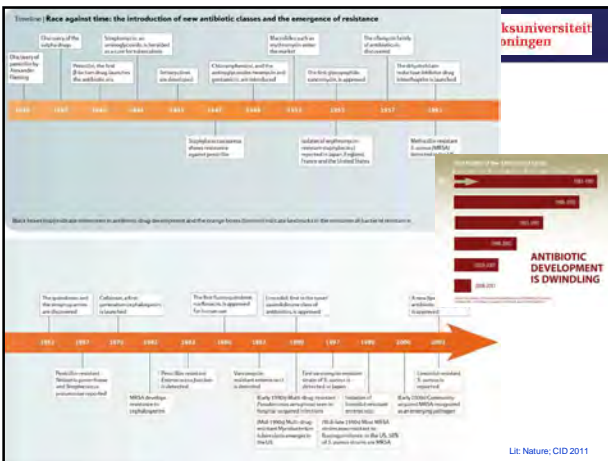
13/38 countries with antibiotic resistance awareness day

25/38 countries with antibiotic awareness day

EUROPEAN ANTIBIOTIC AWARENESS DAY

Grundmann et al. 2013

Timeline | Race against time: the introduction of new antibiotic classes and the emergence of resistance



ANTIBIOTIC DEVELOPMENT IS DWINDLING

Lit: Nature, CID 2011

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Global deaths from infections: Time for action!



Deaths attributable to AMR every year compared to other major causes of death

AMR in 2016: 10 million

All infections (currently): ≈ 9 mio

Not mentioned:
 Pneumonia: 3.1 mio
 HIV/AIDS: 1.5 mio
 Malaria: 0.8 mio
 TB: 1.3 mio (data for 2012)

Tackling drug-resistant infections globally: final report and recommendations (May 2016)
 Tackling a crisis for the health and wealth of nations (Dec 2014)
 The Review on Antimicrobial Resistance (Chair: J. O'Neill)

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The solution?




Antimicrobial Stewardship Program (ASP)

Prudent and rational use of antimicrobials
(= Good clinical care)

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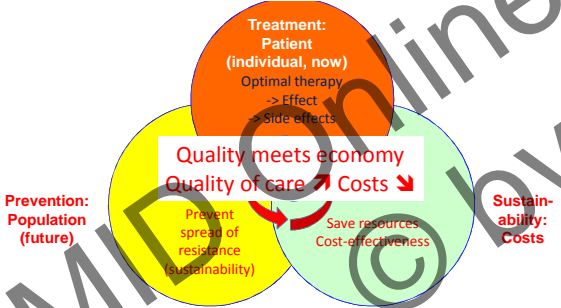
Major goals of an ASP

- Optimize therapy (clinical outcome)
 - Indication, drug, dose, schedule, route, duration
 - Adherence to guidelines, rational choice
 - Use of last line antimicrobials
- Reduce collateral damage
 - Toxicity
 - Selection of pathogenic organisms (e.g. *C. difficile*)
 - Emergence of resistance

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Different aspects in health care:

Good clinical practice




Treatment: Patient (individual, now)
Optimal therapy
-> Effect
-> Side effects

Prevention: Population (future)
Prevent spread of resistance (sustainability)

Sustainability: Costs
Save resources
Cost-effectiveness

Quality meets economy
Quality of care → Costs

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Two aspects


- Empiric/calculated therapy
 - Local/regional epidemiologic data required (microbiology)
 - Supported by local antimicrobial guidelines
 - Clinical consults (infectious diseases, clinical microbiology)
- Directed therapy
 - Appropriate and timely diagnostics required (microbiology, clinical chemistry, imaging, pathology, etc.)
 - Bedside consults (Antimicrobial Stewardship Team, "A-team")

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How to implement?



What to do?
Where to start?

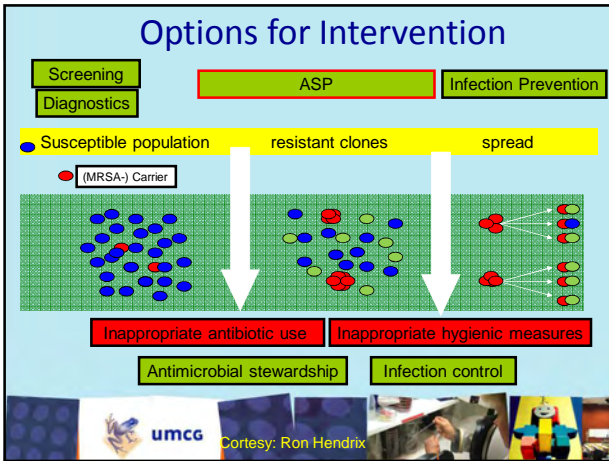
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Setting UMCG

- Tertiary care
 - Approx. 1,300 beds
 - Large regional catchment area (> 150 km radius)
 - Largest outpatient clinic (specialties)
- Transplantations
 - Largest center in NL
 - All solid organs and hematology
- Tuberculosis
 - Largest center in NL (32 beds)

NL: ASP compulsory since 1 Jan 2014

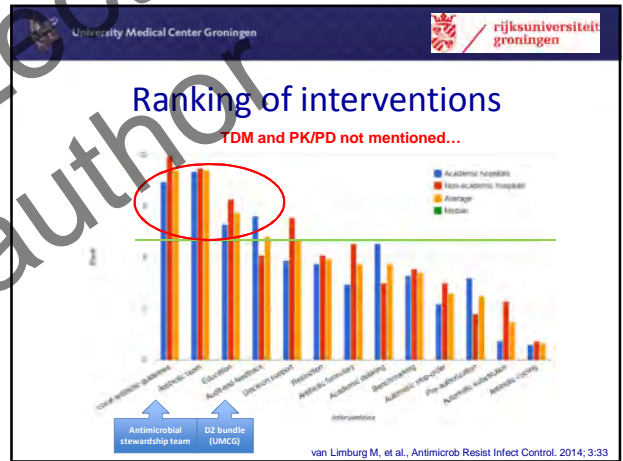


Pilot ASP UMCG

Day 2 bundle
(consensus-based)

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Setting up local guidelines translation national -> local setting

Web-based, publicly available!

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Gram-negative rods: 2013 (7-11)

Gevocht op, zie verspreid tabel **

Micro-organismen	Jaar	IPM	AMOX	AMCL	PITA	CFOT	GENT	TOBR	CIPR	TRIM	TRK	NITR	POLY	MERO
Enterobacteriaceae	2013	53												
Enterobacter aerogenes	2013	40												
Enterobacter cloacae	2013	31												
Enterobacter coli	2013	23												
Enterobacter sp.	2013	17												
Enterobacteriaceae	2013	241												
Morganella morganii	2013	49												
Proteus mirabilis	2013	281												
Providencia stuartii	2013	355												
Serratia marcescens	2013	81												

** - data niet weergegeven wegens relatief kleine aantallen.

Cross resistance E. coli-ESBL (up to 2011)

(Patients: 261)

ESBL	CIPR	GENT	TOBR	MERO	PITA	SULF	TRIM	TRSU	Patterns	%
	59% R	34% R	40% R	1% R	21% R	% R	72% R	68% R	391	100

(Patients: 335)

CFOT	CFOT	CIPR	GENT	TOBR	MERO	PITA	SULF	TRIM	TRSU	Patterns	%
11% R	11% R	22% R	10% R	10% R	0% R	10% R	% R	42% R	39% R	4208	100

Data: Jan Arends UMCG

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UMCG guidelines (www.umcg.swabid.nl)

Via button **AB** **AB** **Poliplus** (=UMCG EPD)

Sources with link to protocols

TDM with link to "bepalingenwijzer"

Drugs with link to Index

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Education: symposia

- 1.) Regionaal Microbiologisch Infectiologisch Symposium (REMIS) 10 x / year (contribution by A-Team)
- 2.) International Symposium 2014
- 3.) Workshop 2015 Biennial (focused)

136 registered participants (~ 25% international)

56 registered participants (~ 20% international)

<http://www.eursafety.eu/symposium/program.html>

http://www.umcg.nl/NL/UMCG/Afdelingen/Wenkebaan/Instituut/Artsen/cursus/A-Drug_for_Every_Euro/PK-PD-of-Antibiotics-17388.aspx

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Antimicrobial stewardship team workflow

Day 0: Empiric therapy, Diagnostics

Day 2: E-mail alert, A-Team consult

Day 2: Microbiology results available

Day 30: Evaluation

Consensus model (interdisciplinary)

Modified from Lo-Ten-Foo JR, et al. Ned Tijdschr Geneeskd. 2014;158:A6795

Antibiotic Stewardship TEAM UMCG

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Flow: Patient enters hospital → Receives antibiotics → Alert after 48 hrs → Bed-side consultation

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Automatic E-mail alert

Coverage: > 75% of prescriptions

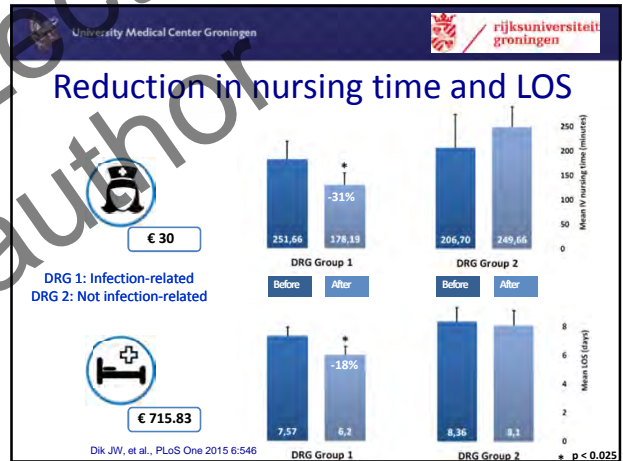
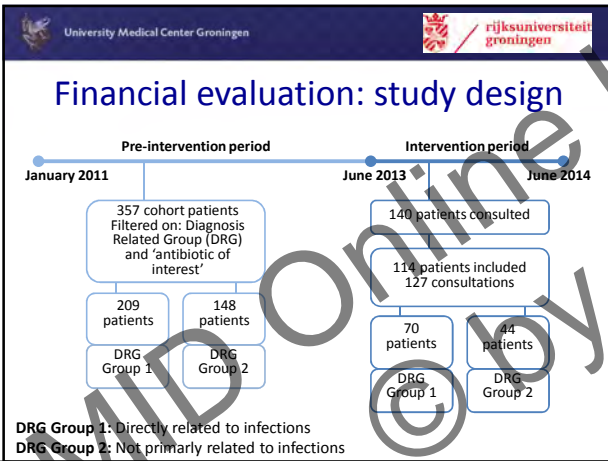
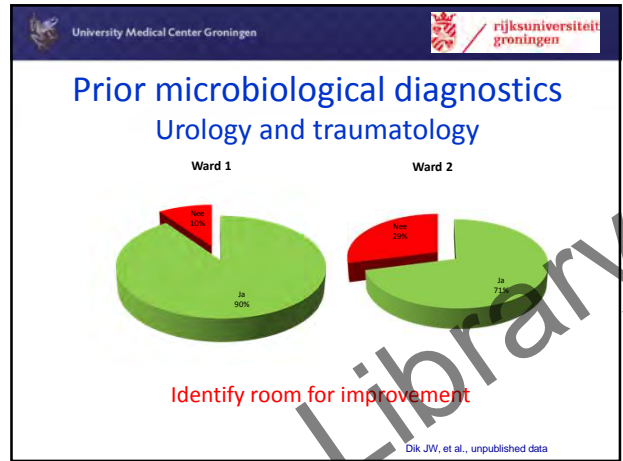
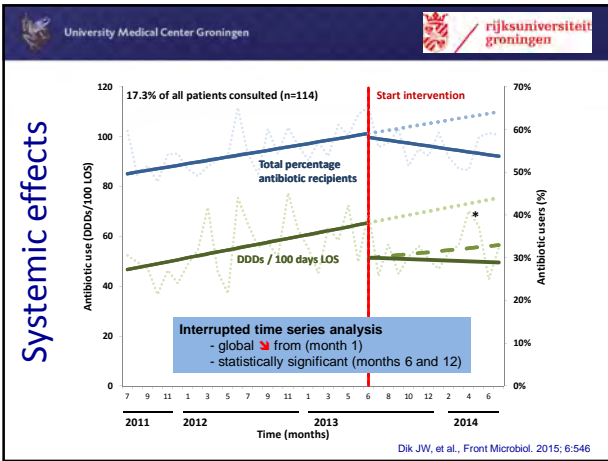
Prashant Nannan Panday

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Alteration for 3 out of 4 patients*

Alteration	Percentage
Continue;	26%
Intervened;	74%
- 9% Deescalate	9%
- 16% Change duration	16%
- 4% Optimize dosage	4%
- 22% Switch AB	22%
- 24% Switch IV-PO	24%
- 24% Stop	24%

* N consulted patients: 114; N total patients: 809 Dik JW, et al., Front Microbiol. 2015; 6:546



One consultation saved € 475

€ 80.26 * 127 cons = - € 10,193

€ 30 * $\frac{73.74}{60}$ hr * 52 ptx = + € 1910


€ 715.83 * 1.37 d * 70 ptx = + € 68,648

Savings for this study per year (Urology unit) **€ 60,365**

Return on investment: 5.9


Dik JW, et al., PLoS One 2015 6:546

- Conclusions I**
- Even in low use setting improvement possible
-> Analyse local situation, go for easy targets to start with
 - Show added value of your activity
-> Carefully select success parameters: e.g. patients on antimicrobials, total antimicrobial consumption, LOS, epidemiology
-> Avoid: one fits all approach (most likely to fail!)
 - Emphasize persuasive approach
-> Advantage: no bypassing effect; acceptance
Common practice: selective reporting of results, drug formulary

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Conclusions II

- **To start: Be realistic, but creative**
 - > Start with a pilot project (where you are welcome)
 - > Support your colleagues (no "antibiotic police")
 - > Build networks (UMCG: "Link Docs", pyramid model)
- **Readjust and develop as appropriate**
 - > What does work, what should be improved?
 - > Tackle increasingly more difficult goals
 - > Word of mouth helps to expand your success
- **Structural support does help**
 - > Decreases effort to maximise effect (e.g. prescription trigger where possible)

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Caveats

- **Direct costs of antimicrobials**
 - > Reduced purchase price: "success"
 - > Reducing dose (e.g. Ciprofloxacin, Meropenem, Flucloxacillin, Fluconazole): "success"
 - > Relative marginal contribution to budget
- **Other costs much more substantial**
 - > Quality of care ↗, LOS ↘, complication rate ↘
- **Microbial resistance**
 - > Delay to effect; import into institution (patient networks)
- **Clinical outcome difficult to monitor**
 - > Data lacking, high effort, not real time

University Medical Center Groningen **People** 

- **UMCG**
 - Kasper Wilting
 - Jerome Lo Ten Foe
 - Yanka Kyuchukova
 - Marleen van Oosten
 - Loredana Piri
 - Eveline Kloetze
 - Sander van Assen
 - Rik Winter
 - Mathieu Bolhuis
 - Jan-Willem Dik (cand. PhD)
 - Prashant Nannan Panday
 - Piet Rijpaard/Johan de Jong
 - Bhanu Sinha
 - Alex Friedrich
- **UMCG (ctd)**
 - Link Docs; Annemarie Leliveld
 - Anja Roters
 - Bert Meijeringh (Controlling)
 - Igor van der Weide (Controlling)
- **RUG**
 - Maarten Postma (Pharm. Econ.)
- **Lvl/Certe**
 - Ron Hendrix
- **U Twente**
 - Maarten v. Limburg
 - Jobke Wenzel
 - Nienke de Jong
 - Lisette Gemert v. Pijnen



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Thank you! Questions?

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Funding and institutions




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AID Stewardship Model

Antimicrobial Stewardship Program
Infection Prevention Stewardship Program
Diagnostic Stewardship Program



ASP No. patients and staff DSP No. patients and staff

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Dik JW, et al., Future Microbiology, 2016; 11:93-102

Patient enters hospital Receives antibiotics Alert after 48 hrs Bed-side consultation

Antibiotic Stewardship TEAM UMCG

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