Swedish strategies and methods to combat antibiotic resistance

Stephan Stenmark
MD, PhD, County Medical Officer
Västerbotten County Council, Sweden
Head of Department for communicable disease control and prevention
Chairman of the Strama Programme Council, the Swedish strategic program against antibiotic resistance
General knowledge

Correlation between antibiotic use and resistance

Y-axis: PNSP (%)

Figure 6: Correlation between penicillin use and prevalence of penicillin non-susceptible S pneumoniae
AT, Austria; BE, Belgium; HR, Croatia; CZ, Czech Republic; DK, Denmark; FI, Finland; FR, France; DE, Germany; HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; NL, The Netherlands; PL, Poland; PT, Portugal; SI, Slovenia; ES, Spain; UK, England only.

By 2050, the death toll could be a staggering one person every three seconds if AMR is not tackled now.
THE IMPACT OF AMR BY 2050 WOULD BE WIDE-RANGING

28 MILLION PEOPLE
projected to fall into poverty because of AMR

UP TO 7.5% decline in global livestock production

UP TO 3.8% decline in global exports

UP TO 1 TRILLION US $
global increases in healthcare cost

www.worldbank.org/health
Antimicrobial Stewardship

= 

Strama in Sweden
The Swedish Strategic Programme against Antibiotic Resistance
The overall aim of Strama

• best available treatment to the patient
• to preserve the effectiveness of antibiotics and prevent the emergence and spread of resistant bacteria
Healthy individuals do not need antibiotics

- Reduce need
- Reduce spread
- Appropriate use - only when needed
Message from Strama (Primary Care): 
”Don´t use antibiotics if no or minor effect”

**No effect**
- Common cold
- Tonsillitis if neg Strep A rapid test
- Acute bronchitis

**Minor/no effect?**
- maxillary sinusitis
- sore throat (<3 centor) and pos Strep A
- acute otitis media (AOM) 1 - 12 years

**Reduce symptoms**
- lower UTI (not quinolones)
- tonsillitis (3 or 4 Centor) + pos Strep A

**Reduce complications**
- erytema migrans (Lyme/Borrelia)
- STI
- AOM < 1 year, > 12 years,
- AOM bilat, perfor., hearing deficit
- some skin and soft tissue infections

**Lifesaving**
- meningitis
- septicaemia
- pneumonia
- erysipelas, fasciitis
- pyelonephritis
Sweden: In the 1990ies:

- Increasing PNSP (Penicillin non susceptible pneumococci)
- Epidemic of PNSP in children in Southern Sweden
- Increasing antibiotic prescribing

Y-axis: Defined Daily Dosages* /1000 inhab/day

*The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults
The Strama enthusiasts
Swedish Agencies
Politics

Comittment

Time
All time high on the political agenda
New strategy from the government 2016

Swedish strategy to combat antibiotic resistance

Objective 1: Increased knowledge through enhanced surveillance
Objective 2: Continuous strong preventive measures
Objective 3: Responsible use of antibiotics
Objective 4: Increased knowledge for preventing and managing bacterial infections and antibiotic resistance with new methods
Objective 5: Improved awareness and understanding in society about antibiotic resistance and countermeasures
Objective 6: Supporting structures and systems
Objective 7: Leadership within the EU and at the international cooperation

http://www.government.se/information-material/2016/05/swedish-strategy-to-combat-antibiotic-resistance/
Lessons learned from our experiences

• Never give up
• Multiprofessional teams
  – National, regional and local level
• Strong commitment and engagement by the government and all relevant authorities
• Knowledge and acceptance among care-providers and professionals at all levels
• Important factors for change have been:
  – measurable national targets
  – quality indicators based on guidelines
  – feed-back of prescription profiles to the doctors
• Go public
Intersectoral Coordinating Mechanism

23 agencies and organisations within different sectors led by the Public Health Agency and the Swedish Board of Agriculture

Ministry of Health and Social Affairs

Swedish Association of Local Authorities and Regions

Strama Programme Council

Expert groups:
- Veterinary
- Strama
- Pharmacist
- Strama
- Dental care
- Strama

Specialist associations:
- Infectious diseases
- Microbiology
- Infection Control
- General Practitioners
- Pediatrics
- Surgery
- ENT

Public Health Agency

21 local Strama groups

- network
Members of a local Strama group

- General practitioner
- Infectious diseases specialist
- Microbiologist
- Infection control/hospital hygiene
- County medical officer
- Pharmacist
- ENT, paediatrics, geriatrics…
Strama 1995-2015

• the number of prescriptions in out-patient care per 1000 inhabitants / year decreased by 40 percent
  – most prominently among children aged 0-4 years where the reduction was 71 percent.
• adherence to guidelines have gradually increased and sales of all antibiotics used for respiratory tract infections decreased, especially of macrolides and cephalosporins.
• for urinary tract infections, there was a major shift to narrow spectrum antibiotics and a decrease in fluoroquinolones and trimethoprim use.
• In hospital care, the use of cephalosporins in community acquired pneumonia as well as fluoroquinolones in female cystitis decreased significantly.
Prescriptions/1000 inhabitants and year

Start of Strama campaigns

0-4 year: >70 % reduction

Källa: Folkhälsomyndigheten 2015
2010: 4-års patientförsvarskampanj för att belöna länscow som uppnår mål för att minska antibiotikaanvändning.

All age groups: Decreased prescription 2010-2014!
Long term goal is 250 prescriptions/1000 inhabitants/year for all age groups.
The county of Västerbotten have reached the 250 goal

Antibiotika på recept i Västerbotten

År

recept/1000 inv

0 50 100 150 200 250 300 350 400 450

Strama 20 years
Campaigns with multifaceted approach

- **Workshops** to produce treatment guidelines
- **Education** - multiple target groups
- **National and regional meetings** to catalyze multisectoral collaboration
- **Campaigns** to improve prescribing
- **Studies** e.g. on diagnosis-prescribing
- **Local implementation** of treatment guidelines
- **Monitoring** the international scientific literature and media
- **Increasing awareness** among professionals politicians and the public
- **Regular information** to Swedish media
National Guidelines
"common infections in out patients"
by
Swedish Medical Product Agency
Strama
Public Health Agency

- AOM
- Tonsillitis
- Sinusitis
- Lower UTI
- Lower RTI
- Skin infections
- Early warning signs of serious infections in children
Strama 20 years
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10 most common diagnosis of prescription in Primary Care = 85% of all prescriptions (2009 and 2013)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>2009</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystitis</td>
<td>22%</td>
<td>27%</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>15%</td>
<td>13%</td>
</tr>
<tr>
<td>AOM</td>
<td>14%</td>
<td>10%</td>
</tr>
<tr>
<td>Rhinosinusitis</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Skin infections NUD</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Common cold</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3%</td>
<td>6%</td>
</tr>
<tr>
<td>Impetigo</td>
<td>3%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Source: Primary Care Registry (6-800 000 inhabitants), Unpublished data. Prof. S. Mölstad
The safety aspects of respiratory infections
Hospital admissions for acute mastoiditis, peritonsillar abscess, and acute rhinosinusitis in children were stable or decreased 1987-2004

Data from the national registry of diagnosis in hospital care (National Board of Health and Welfare)

Lancet Infect Dis 2008; 8: 125–32
Many challenges in Swedish hospitals

- Increasing use of antibiotics
- Low no of hospital beds
- Many patients with:
  - Old age
  - Comorbidities
  - Immunosuppression
  - Catheters
  - Multiple riskfactors

Increasing no of AMR

Antibiotika (301 exkl. metenamin) på slutetavårdsreviskvisjon 1 per län/region och för riket, DDD/1000 invånare och dag, 12-månadersperioder
Källa: Infekt, ekhioloomenyheten samt statistik från Region Västerbottens län

Sverige har lägst andel vårdplatser i EU

3.5.1 Hospital beds per 1000 population, 2010 and change between 2000 and 2010

<table>
<thead>
<tr>
<th>Country</th>
<th>2010 (or nearest year)</th>
<th>Change 1999-00 (or nearest year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Austria</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Iceland</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Norway</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Finland</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>53</td>
<td></td>
</tr>
</tbody>
</table>

2013 2014 2015

Antal fall per år

2011 2012 2013 2014 2015

MRSA ESBL VRE PNSP
### Increased use of antibiotics in Swedish hospitals

**DDD*/100 patient-days in somatic medical care in Swedish acute care hospitals 2010-2014.** *The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults*

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracyclines (J01AA)</td>
<td>4.6</td>
<td>5.0</td>
<td>5.3</td>
<td>5.4</td>
<td>5.4</td>
</tr>
<tr>
<td>Penicillins with extended spectrum (J01CA)</td>
<td>6.0</td>
<td>6.5</td>
<td>6.9</td>
<td>7.5</td>
<td>7.7</td>
</tr>
<tr>
<td>Betalactamase sensitive penicillins (J01CE)</td>
<td>6.7</td>
<td>7.2</td>
<td>7.6</td>
<td>7.6</td>
<td>7.5</td>
</tr>
<tr>
<td>Betalactamase resistant penicillins (J01CF)</td>
<td>10.9</td>
<td>11.3</td>
<td>12.0</td>
<td>13.1</td>
<td>13.5</td>
</tr>
<tr>
<td>Combinations of penicillins (J01CR)</td>
<td>3.3</td>
<td>3.8</td>
<td>4.4</td>
<td>5.5</td>
<td>5.9</td>
</tr>
<tr>
<td>Cephalosporins (J01DB-DE)</td>
<td>7.1</td>
<td>6.8</td>
<td>6.7</td>
<td>7.1</td>
<td>6.8</td>
</tr>
<tr>
<td>Carbapenems (J01DH)**</td>
<td>2.5</td>
<td>2.6</td>
<td>2.7</td>
<td>3.0</td>
<td>3.1</td>
</tr>
<tr>
<td>Trimethoprim (J01EA)</td>
<td>0.9</td>
<td>0.8</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Trimethoprim with sulphonamides (J01EE)</td>
<td>2.1</td>
<td>2.3</td>
<td>2.3</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Macrolides (J01FA)</td>
<td>0.9</td>
<td>1.1</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Lincosamides (J01FF)</td>
<td>1.7</td>
<td>1.7</td>
<td>1.9</td>
<td>2.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Aminoglycosides (J01GB)</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>Fluoroquinolones (J01MA)</td>
<td>6.1</td>
<td>6.2</td>
<td>6.3</td>
<td>6.6</td>
<td>6.9</td>
</tr>
<tr>
<td>Glycopeptides (J01XA)</td>
<td>0.8</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Imidazole derivatives (J01XD)</td>
<td>1.3</td>
<td>1.2</td>
<td>1.1</td>
<td>1.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Nitrofurantoin (J01XE)</td>
<td>0.4</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Methenamine (J01XX05)</td>
<td>0.6</td>
<td>0.5</td>
<td>0.5</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Linezolid (J01XX08)</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>All agents (J01)</strong></td>
<td><strong>57.4</strong></td>
<td><strong>59.8</strong></td>
<td><strong>62.9</strong></td>
<td><strong>67.2</strong></td>
<td><strong>68.2</strong></td>
</tr>
</tbody>
</table>

*Denominator data from 2013.
** Includes all sales on requisition

Källa: Folkhälsomyndigheten 2015
Increasing numbers of antibiotic resistance

![Bar chart showing increasing numbers of antibiotic resistance from 2010 to 2016. The chart includes data for PNSP, VRE, MRSA, ESBL, and ESBL carba.](chart.png)
Number of cases and types of $\text{ESBL}_{\text{CARBA}}$ in Enterobacteriaceae in Sweden 2007-2015
EARS-Net 2010-13; MRSA in blood isolates
Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use

Full guideline

Methods, evidence and recommendations

August 2015

National Institute for Health and Care Excellence

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

ECDC DRAFT TECHNICAL REPORT

Proposals for draft EU guidelines on the prudent use of antimicrobials in human medicine

An Audit-Based, Infectious Disease Specialist-Guided Antimicrobial Stewardship Program Profoundly Reduced Antibiotic Use Without Negatively Affecting Patient Outcomes

Cochrane Library

Interventions to improve antibiotic prescribing practices for hospital inpatients (Review)

Cochrane Database of Systematic Reviews

What is Antimicrobial Stewardship (AMS)?

Figure 1. The 4Ds of antimicrobial therapy: the right Drug, Dose, Duration and De-Escalation.

4 Ds of AMS
Start smart
- initiate effectively antibiotic a.s.a.p. for serious infections
- send appropriate specimens prior to starting treatment
- use local and national guidance
- document in notes
- shortest course
- choose narrow spectrum with least ecological damage
- TDM when relevant to reduce toxicity e.g. aminoglycosides
- single dose for surgical prophylaxis
- consult local infection experts in difficult cases

Then Focus
- at 48-72 hours review
- stop if no infection
- streamline according to micro results
- iv to oral switch

Take Home Message: Right drug, right time, right dose & right duration
Establish and provide the necessary funding for antimicrobial stewardship programmes in all healthcare facilities [11-14].

For hospitals, the elements of such programmes should include:

i. An antimicrobial committee or similar formal organisational structure.

ii. An antimicrobial stewardship team including at least a clinician (iii) and a pharmacist (iv).

iii. A clinician with expertise in the management of infections to be responsible for the antimicrobial stewardship team.

iv. A pharmacist responsible for antimicrobial use.

v. Salary support and dedicated time for antimicrobial stewardship activities. Example: 0.5–1.5 full-time equivalents (FTEs) per 250 acute care beds [15,16]. Example of indicator: number of FTEs for antimicrobial stewardship activities.

vi. IT support for antimicrobial stewardship activities.
Summary

• All agree on that antimicrobial resistance is a major threat to public health
• In Sweden we have had some success in increased adherence to guidelines reduced prescription in out-patient care
• We still have a long way to go with stewardship and structured evaluation of treatment in hospitals
• We must continue to implement strategies to active action
Välkommen till Stramas webbplats

Kunskapsstyrning är ett centralt utvecklingsområde för att skapa en bättre hälso- och sjukvård.

NYHETER

POLITIK 2016/09/22
Möte om antibiotikaresistens i FN:s generalförsamling 21 sept

REMISS 2016/07/27
EU-riktlinjer för korrekt och ansvarfull antibiotikaanvändning

FÖRSKRIVNING 2016/07/18
Fortsett sjunkande antibiotikaföreskrivning på recept

UTbildningar / möten

UTbildning 2016/08/26
Kostnadsfri onlinekurs om antibiotikaresistens. Start 3 oktober

Workshop 2016/06/08
Antibiotikaronder på sjukhus. Fyra regionala workshops i höst v 47 och 49

SE ALLA
Skydda antibiotikan

I filmen kan du se hur det kan gå till när antibiotika räddar liv inom världen.

Se och dela berättelsen här. Antibiotika är ett av de mest värdefulla läkemedel vi har. Vi har länge tagit för givet att vi kan använda antibiotika för att behandla infektioner orsakade av bakterier, men resistensen mot antibiotika ökar.

Alla kan bidra till att antibiotika ska fungera även i framtiden och när det verkligen gäller. Det gör du genom att göra kloka val i din vardag:

- Prata med din läkare eller veterinär om när antibiotika gör nytta.
- Använd inte överbliven antibiotika utan lämna in den på apoteket.
- Förebygg infektioner och smittspridning när det går, till exempel genom att tvätta händerna och följa vaccinationsprogram.

23 samhällskontätor som arbetar mot antibiotikaresistens står bakom råden. Här kan du läsa mer och dela kunskapen.

Människor får mer antibiotika än djur

År 2015 använde människor i Sverige ca 60 ton antibiotika, medan ca 10 ton gavs till våra djur. Läs mer och dela fakta om hur vi använder antibiotika...

Detta kan du göra

Små val i vardagen gör skillnad när det gäller antibiotikaresistens. Läs mer om kloka val här...
Antibiotic resistance is the next great global challenge - we must act now: [link](https://wef.ch/2dJS6lK)
Samverkan mot antibiotikaresisten