Rapid Response

Tackling the Antibiotics Resistance Problem in Lebanon
A K2P Rapid Response responds to urgent requests from policymakers and stakeholders by summarizing research evidence drawn from systematic reviews and from single research studies. K2P Rapid Response services provide access to optimally packaged, relevant and high-quality research evidence for decision-making over short periods of time ranging between 3, 10 and 30-days.
Rapid Response

+ Included

Synthesis of evidence on a priority question or topic
Local context
International experiences
K2P Rapid Response

Tackling the Antibiotics Resistance Problem in Lebanon
A 10-day Rapid Response
Authors
Nadeen Hilal, Racha Fadlallah, Clara Abou Samra, Fadi El-Jardali*

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Merit Review

Citation
This K2P Rapid Response should be cited as

*senior author
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Key Messages
Key Messages

→ Antibiotics resistance constitutes a major health threat in Lebanon and around the world.
→ There is a striking incompatibility between the extent of the problem and the actions taken.
→ Antibiotic resistance has various causes including: lack of patient compliance, poor prescribing practices, and limited regulation.
→ Interventions to tackle antibiotic resistance have been identified at the patient, provider, organizational and system levels.

Recommendations
→ Educating patients can decrease unnecessary prescribing patterns.
→ Conducting interventions addressing physicians’ decision to treat, choice of antibiotics, and duration of treatment to reduce antimicrobial resistance and improve clinical outcomes.
→ Providing interactive and active education for physicians as an effective intervention in restricting overuse.
→ Using ancillary tests, particularly procalcitonin, as a tool to guide treatment decision as this was found to be associated with lower antibiotic exposure, treatment failure, and mortality.
→ Utilizing restrictive and persuasive control strategies can help achieve more favorable outcomes in terms of the decision, choice, or duration of treatment.
→ Adopting antimicrobial stewardship programs can reduce antimicrobial utilization, lower total antimicrobial costs, shorter average duration of antibiotic therapy, less inappropriate use, and reduce antibiotic adverse events.
Content
Problem and Causes

Problem Definition
Antimicrobial resistance is defined as the resistance of a microorganism to an antimicrobial drug that was originally effective for its treatment. Resistant microorganisms are able to withstand the antimicrobial drug’s attack. As a result, treatments become ineffective and infections persist, increasing the risk of complications and spread (WHO, 2014).

Context
Until the 1970s, many new antibacterial drugs were developed to which most common pathogens were initially fully susceptible. However, the most recent classes of antibacterial drugs were discovered during the 1980s. Thus, it is essential to preserve the efficacy of existing drugs through measures to minimize the development and spread of resistance (WHO, 2014).

Unfortunately, the pipeline for the development of new antibacterial drugs is currently virtually empty, particularly for the treatment of Gram-negative enteric bacteria. Furthermore, research in this field is still in its early stages. Consequently, the management of common conditions is at risk (WHO, 2014).

Underlying Causes
There are many causes for antimicrobial resistance, some of which include:

→ Poor prescribing practice, such as prescribing antimicrobial medicine when not required, incorrect choice of medication or incorrect dosage (IDSA, 2011; Spellberg et al, 2009; WHO, 2014).
→ Poor patient adherences to medication regimes (Borg et al, 2009)
→ Physicians fulfilling what they perceive as being patients’ expectations and fear of possible complications and spread (WHO, 2014).
complications (Lopez-Vazquez et al, 2012).

→ Pharmaceutical industry influence on physician’s prescribing behavior (Brennan et al, 2006).


→ Misuse and overuse in animal husbandry and agriculture (IDSA, 2011; Spellberg et al, 2004; WHO, 2014).

**Problem Consequences**

Multiple studies have shown that infections caused by antimicrobial-resistant microbes are associated with higher mortality, morbidity, costs, and prolonged hospital stay compared to infections caused by their drug-susceptible counterparts (Cosgrove et al, 2014; Sunenshine et al, 2007).

**What we found**

We conducted a thorough search for interventions aiming at reducing antimicrobial resistance. Our search excluded disease-specific reviews. Review of literature revealed 10 systematic reviews that presented elements for tackling the antibiotics resistance problem. Search findings are summarized below.

→ At the patient level: interventions aiming at enhancing medication adherence such as counseling, use of a dose-dispenser, and augmented pharmacy services, have demonstrated equivocal results (Haynes et al, 2008).

→ At the physician level: education, guidance, audit, feedback, and use of ancillary testing (Procalcitonin), have proven to be effective in selecting the type of antibiotic, reducing treatment duration, and reducing deaths (Davey et al. 2013; Patel et al. 2007; Schuetz et al. 2013).

→ At multiple levels (patients and physicians): audit and feedback, as well as patients and physicians education have a positive impact on reducing unnecessary antibiotic prescriptions, improving selection of drugs, and reducing cost of treatment (Ranji et al. 2006, Arnold et al. 2005, Ranji et al. 2008).

→ At the organizational and system levels: ‘antimicrobial stewardship programs’ exert a positive impact by

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**Text Box 2: Context Issues**

**Lebanese Context**

**At the microbial level:**

Increasing rates of resistant isolates were noted Escherichia coli, Klebsiella pneumoniae, Salmonella, Shigella, Acinetobacter, and Pseudomonas aeruginosa (Arad et al, 2011).

**At the patients’ level:**

42% of population self-medicated with antibiotics.

There were many misperceptions surrounding the use of antibiotics (Cheaito et al, 2014).

**At the physicians’ level:**

Prescribed antibiotic was appropriate in only 61.5% of the studied cases.

Prescribed dose and the duration of the treatment were inaccurate in 52% and 64% of the cases, respectively (Saleh et al, 2015).

**Regional Context**

None of the countries of the Eastern Mediterranean Region reported having a national action plan.

No country had prepared a progress report in the previous 5 years.

Only about 38% of countries reported that they performed surveillance of resistant bacteria.

Only ten countries had a national regulatory authority.

Antimicrobial medicines were available without a prescription in nine countries.

Only three countries had conducted a public information campaign in the previous 2 years.

Only five countries had Infection Prevention and Control (IPC) strategies.

Only four reported that an IPC program was available in all tertiary hospitals. (data from WHO on 21 countries from EMR, WHO, 2015)
reducing unnecessary treatment decisions and duration, with no consequent increases in nosocomial infection rates, length of stay, or mortality. Study results are inconclusive in terms of selecting the appropriate treatment or effecting the rate antimicrobial resistance (Kaki et al. 2011, Filice et al. 2013, Drekonja et al. 2014)

Results are further detailed in Table 1 below.
<table>
<thead>
<tr>
<th>Study</th>
<th>Number of studies</th>
<th>Countries included</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Impact</th>
<th>Quality of Evidence</th>
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<tbody>
<tr>
<td><strong>Patient Level</strong></td>
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<tr>
<td>Interventions for enhancing medication adherence (Haynes et al, 2008)</td>
<td>9 (studies</td>
<td>USA, UK, Spain, Canada, Australia, the Netherlands, China, France, Mexico, Norway,</td>
<td>Provision of more detailed instructions to patients, Use of dose-dispensing, Counselling, Use of different medication formulations, Augmented pharmacy services</td>
<td>Medication adherence and patient outcomes</td>
<td>Equivocal results</td>
<td>Not available</td>
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<td>evaluating</td>
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<td>short-term</td>
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<td>treatments)</td>
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<td><strong>Physician Level</strong></td>
<td>89</td>
<td>USA, Netherlands, England, Canada, Scotland, France, Switzerland, Australia,</td>
<td>Persuasive interventions: Educational materials, Reminders, Audit and feedback, Educational outreach</td>
<td>84% of interventions targeted the choice of antibiotic prescribed, Remaining aimed to change exposure of patients to antibiotics by changing the decision to treat or the duration of treatment</td>
<td>Restrictive interventions had greater impact on prescribing outcomes at one month and on microbial outcomes at 6 months but there were no significant differences at 12 or 24 months.</td>
<td>AMSTAR 7/11</td>
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</table>
| A Review of Antimicrobial Control Strategies in Hospitalized and Ambulatory Pediatric Populations (Patel et al, 2007) | 28                | US, Europe, South America, Asia, Australia. | Physician Education  
Parent education  
Restrictive methods  
Ancillary tests | Antibiotic prescribing rates  
Prescribing errors  
Colonization and infection rates with resistant pathogens | 8 studies that used prescriber-focused education reported significant improvements in antimicrobial prescribing  
Antibiotic restriction policies did not result in reduction in antimicrobial resistance, hospital-acquired infections, or mortality  
Ancillary tests were associated with the greatest reductions in antibiotic use with up to 73% reduction in antibiotics use in neonates with suspected bacterial infection by utilizing C-reactive protein and interleukin (IL)-8 versus CRP and | Not available       |
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<tbody>
<tr>
<td>Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections (Schuetz et al, 2013)</td>
<td>14</td>
<td>Switzerland, Germany, China</td>
<td>Procalcitonin level as a tool for starting or stopping antibiotics over a large</td>
<td>All-cause mortality following randomization up to a follow-up time of 30 days.</td>
<td>Lower mortality in procalcitonin assigned group versus control (5.7 versus 6.3%)</td>
<td>Not available</td>
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<td>Setting-specific treatment failure.</td>
<td>Less treatment failure occurred in procalcitonin group patients compared to control patients (19.1 versus 21.9%).</td>
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<td>Total antibiotic exposure was significantly reduced overall across all clinical settings</td>
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<td>Multifaceted Interventions (patient physician)</td>
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</table>
| Closing the Quality Gap: A Critical Analysis of Quality Improvement Strategies (Ranji et al, 2006) | 54                | USA, Australia, Canada, UK, Norway, Sweden, Denmark, Netherlands, South Africa, Belgium, Cuba, Indonesia, Mexico, New Zealand, Sri Lanka | Clinician education  
Patient education  
Provision of delayed prescriptions  
Audit and feedback | Antibiotic treatment  
Antibiotic selection | Physician and patient education were effective at reducing prescribing, with an absolute reduction in antibiotic prescribing rates of 8.9% in intervention groups compared with | AMSTAR 6/11 |
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<tr>
<th>Study</th>
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<tbody>
<tr>
<td>Interventions to improve antibiotic prescribing practices in ambulatory care (Arnold et al, 2005)</td>
<td>39</td>
<td>USA, Canada, UK, Australia, Norway, Spain, Sweden, Finland, Indonesia, Mexico, Netherlands, New Zealand, South Africa, Sri Lanka</td>
<td>Clinician reminder systems&lt;br&gt;Financial or regulatory incentives for patients&lt;br&gt;Financial or regulatory incentives for clinicians</td>
<td>Improved the antibiotic selection decision, with a median absolute improvement of 10.6%</td>
<td>Clinician education, regulatory intervention, audit and feedback&lt;br&gt;Improved the antibiotic selection decision, with a median absolute improvement of 10.6%</td>
<td>AMSTAR 7/11</td>
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<tr>
<td>Interventions to reduce unnecessary antibiotic prescribing: A systematic review and quantitative analysis (Ranji et al, 2008)</td>
<td>43</td>
<td>USA, UK, Australia, Canada, Norway, Sweden, Belgium, Cuba, France, Indonesia, Mexico, Netherlands, New Zealand, South Africa, Sri Lanka, Switzerland, Zambia</td>
<td>Clinician education Patient education Audit and feedback Combined interventions of above</td>
<td>Antimicrobial resistance Antimicrobial use Patient satisfaction Cost</td>
<td>Multi-faceted interventions combining physician, patient and public education were the most successful in reducing antibiotic prescribing for inappropriate indications.</td>
<td>AMSTAR 6/11</td>
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<td>The median reduction in the proportion of subjects receiving antibiotics was 9.7% over 6 months median follow-up for all interventions combined No single intervention or combination of strategies was clearly superior. Active clinician education strategies trended toward greater effectiveness than passive strategies Compared with studies targeting specific conditions or patient</td>
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<tr>
<td>At the organizational and system level</td>
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<td>Antibiotic restriction or pre-approval</td>
<td>Antimicrobial utilization in the critical care setting.</td>
<td>Stewardship interventions were associated with reductions in antimicrobial utilization (11%–38% defined daily doses/1000 patient-days), lower total antimicrobial costs (US$ 5–10/ patient-day), shorter average duration of antibiotic therapy, less inappropriate use and fewer antibiotic adverse events. Stewardship interventions beyond 6 months were associated</td>
<td>Not available</td>
</tr>
<tr>
<td>Impact of antimicrobial stewardship in critical care: a systematic review (Kaki et al, 2011)</td>
<td>24</td>
<td>Not available</td>
<td>Antibiotic restriction or pre-approval</td>
<td>Antimicrobial utilization in the critical care setting.</td>
<td>Stewardship interventions were associated with reductions in antimicrobial utilization (11%–38% defined daily doses/1000 patient-days), lower total antimicrobial costs (US$ 5–10/ patient-day), shorter average duration of antibiotic therapy, less inappropriate use and fewer antibiotic adverse events. Stewardship interventions beyond 6 months were associated</td>
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</table>
| Antimicrobial Stewardship Programs in Inpatient Settings: A Systematic Review (Filice et al, 2013) | 35 | Not available | Audit and feedback  
Formulary Restriction and Preauthorization  
Guidelines  
Computerized Decision Support Protocols | Mortality  
Antibiotics utilization  
Appropriate use  
Duration of therapy  
Antibiotics resistance | Interventions to increase effective prescribing or decrease excessive prescribing had no effect on mortality  
Audit and feedback decreased use of targeted antibiotics and decreased excessive use  
Results for increasing appropriate use were mixed.  
Improvement in duration of therapy, antimicrobial selection  
Mixed results concerning decreased rates of | Not available | with reductions in antimicrobial resistance rates.  
Antibiotic stewardship was not associated with increases in nosocomial infection rates, length of stay or mortality. |
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</thead>
<tbody>
<tr>
<td>Antimicrobial Stewardship Programs in Outpatient Settings: A Systematic Review (Drekonja et al, 2014)</td>
<td>16</td>
<td>USA, Netherlands, Canada, Spain, UK, Denmark, Finland, France, Germany, Iran, Ireland, Japan, Norway, Poland, Sweden, Thailand</td>
<td>Provider or/and patient education Feedback, guidelines Delayed prescribing Communication skills Restriction Decision support Financial incentive Ancillary tests</td>
<td>Antibiotics utilization Antibiotics selection Number of visits, hospitalization, adverse events, satisfaction</td>
<td>Mixed results with education concerning decreased use or antibiotic selection Higher return visits per patient in 1 study during the month after the initial visit in the group receiving the education leaflet. No difference in hospitalizations, adverse events, or satisfaction</td>
<td>AMSTAR 7/10</td>
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Recommendations
Recommendations

At the Patient Level

→ Patients should acquire a clear understanding of the emerging problem of antibiotics resistance with all its ramifications and consequences.

→ Patients should avoid self-medication and self-withholding of medications and should abide by the instructions of their caregivers concerning antibiotics intake.

At the Physician Level

→ Physicians should practice sound judgment regarding the decision to treat with antibiotics and follow guidelines and resistance patterns to decide on the choice and duration of treatment.

→ Physicians should make use of ancillary tests, particularly procalcitonin, to guide decision making.

At the Organizational Level

→ Comprehensive ‘antimicrobial stewardship culture’ should be implemented through:
  → Providing education for patients and health-providers;
  → Running restrictive or persuasive interventions for physicians;
  → Controlling pharmaceutical interference;
  → Setting standards for disease management and resistance measurement;
  → Encouraging surveillance; and
  → Facilitating research

At the System Level

→ Policies should be implemented that restrict the unauthorized dispersal of antibiotics at the pharmacies level.

→ Access of patients to primary healthcare should be further facilitated in an attempt to minimize the tradition of antibiotics self-treatment.

→ Regulation of antibiotics use in animal husbandry and agriculture should be introduced.

→ Application of ‘antimicrobial stewardship programs’ in organizations should be encouraged.

At the Research Level

→ Local studies are needed to provide assessment of the current status, answer questions, and evaluate interventions.
References


Knowledge to Policy Center draws on an unparalleled breadth of synthesized evidence and context-specific knowledge to impact policy agendas and action. K2P does not restrict itself to research evidence but draws on and integrates multiple types and levels of knowledge to inform policy including grey literature, opinions and expertise of stakeholders.