WHO EML Antibiotic Working Group

Increasing AWARe-ness!

Professor Mike Sharland
On behalf of the EML Antibiotic Working Group
2017 WHO EML Expert Committee developed the **AWaRe** classification of Essential Antibiotics

**Access/ Watch/Reserve (Traffic light)**

**ACCESS** group: narrow spectrum affordable antibiotics widely available.

**WATCH** group: broader spectrum antibiotics used for specific and limited indications due to higher resistance and toxicity potential.

**RESERVE** group: last resort antibiotics that should be used only when other antibiotics have failed or for treatment of multi-resistant bacteria.

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**“EM List - WHAT TO USE”**

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- **2019 EML** committee expanded the **AWaRe** classification to around 200 antibiotics
- A new category of **Not recommended** was added – mainly inappropriate Fixed-Dose Combinations of multiple broad-spectrum antibiotics.
- WHO General Programme of Work (GPW) now includes a Target indicator that the proportion of **Access** antibiotics should be more than **60%** of total antibiotic use at country level
- [https://adoptaware.org/](https://adoptaware.org/)
Background - EML Antibiotic Working Group

- **WHO Mandate in 2016** to continuously *review and update the evidence for antibiotics listed on the EML* to optimize use of antimicrobials in human health (Objective 4 – AMR Global Action Plan).
  - Infection based (rather than drug based) approach to empiric treatment
  - *Reviews of systematic reviews and meta-analysis of all antibiotic RCTs and clinical guidelines for each infection between 1996-2016 was conducted by* McMaster University (WHO Collaborating Center).

- **Prevention** of the emergence of resistance
  - Focussing on optimising use of narrow spectrum antibiotics where appropriate

- **Parsimony**
  - Harmonising the use of essential antibiotics where appropriate

- **Benefits and harms**
  - Balancing efficacy and toxicity, selection of resistance

- **Practicality** – *pragmatic dosing schedules, considering formulation and implementation requirements*

- **Align with the WHO** list of Critically Important Antimicrobials for human medicine (where possible)

- **Align with existing WHO** guidelines (when available)
  - STIs, pediatric guidelines (e.g. pneumonia)
General principles of AWaRe

- **Goal of optimising use of narrow spectrum Access antibiotics**
- Provide guidance on **Symptomatic care** and **when to prescribe/not prescribe** using a risk-based approach (mild/severe symptoms; ill/not ill; underlying disease such as HIV/malnutrition/no underlying disease)
- Guidance regarding diagnostics was given where there was a **clear evidence base** for their added utility (choice of tests based on collaboration with the **WHO EDL**)
- Standardisation of guidance for drug/dose/duration across infections to simplify future implementation (and formulation development e.g. for children in collaboration with **WHO GAP-f**)

- Guidance varied based on different rates of AMR for common infections assessed using **GLASS data**.
- **RESERVE antibiotics** – criteria for selection and stewardship, short drug summaries and guidance on when to use specific drugs in relevant infections – clear linkage to **WHO AB Pipeline**
- Primary care focussed stewardship goals – closely aligned to **WHO ASP Toolkit** and **WHO Policy Guidance on Integrated Stewardship Activities**
- **Wide endorsement globally on AWaRe as a policy tool at Global level and individual countries** – rapid uptake
2021 - WHO EML Antibiotic Handbook

• To provide simple guidance on “HOW TO USE” the antibiotics on the EML to manage common infections
• Guidance for 36 infections; a strong focus on primary care also facility/hospital setting, children and adults.
  • acute bacterial infections (not TB/viral/fungal/parasitic infections)
  – Recommendations on empiric antibiotic treatment (i.e. presumptive diagnosis not requiring any laboratory diagnostic)
  – Includes guidance on making the clinical Diagnosis, the Decision if antibiotic needed, the choice of Drug, Dose, Duration
  – Short summaries of key features of microbiology, epidemiology, clinical presentation, diagnostics (in collaboration with EDL), prevention

  – Target audience: all health professionals giving antibiotics
Potential Primary Care Goals for optimising use of Access antibiotics (increasing use of narrow spectrum AB, reducing broad spectrum use)

- At least **80% of Antibiotic Prescribing in Primary Care** should be Access antibiotics

Potential Primary Care Goals for safely reducing inappropriate prescribing (reducing total AB use)

- 60% of 10 most common infections in primary care can be treated symptomatically/no AB for mild cases

- In some settings around half of patients attending a Primary Health Care facility receive an antibiotic (WHO goal of 30%).

- Critical importance of maintaining/enhancing “Access to Access” antibiotics in most vulnerable populations, but also “Access to Reserve”

<table>
<thead>
<tr>
<th>Common Primary Care Infections</th>
<th>Recommended AWaRe antibiotic</th>
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<tbody>
<tr>
<td>Bronchitis</td>
<td>None</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Access</td>
</tr>
<tr>
<td>Otitis Media</td>
<td>Access</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Access</td>
</tr>
<tr>
<td>CAP (mild)</td>
<td>Access</td>
</tr>
<tr>
<td>COPD exacerbations</td>
<td>Access</td>
</tr>
<tr>
<td>UTI Lower</td>
<td>Access</td>
</tr>
<tr>
<td>Dental</td>
<td>Access</td>
</tr>
<tr>
<td>SSTI</td>
<td>Access</td>
</tr>
<tr>
<td>Acute Bacterial Diarrhoea</td>
<td>Watch</td>
</tr>
</tbody>
</table>

**DRAFT Recommendations**
Variation of antibiotic use by countries/regions

The proportion of countries where 60% of total oral antibiotic use was of Access antibiotics was 59/75 (78.7%), but only 14/75 (18.7%) reached 80% of oral Access antibiotic use (Table 1, Figure 5).

<table>
<thead>
<tr>
<th>Access antibiotics accounted for</th>
<th>60% of total oral antibiotic use</th>
<th>70% of total oral antibiotic use</th>
<th>80% of total oral antibiotic use</th>
<th>90% of total oral antibiotic use</th>
</tr>
</thead>
<tbody>
<tr>
<td>HICs, n/39 (%)</td>
<td>31 (79.5)</td>
<td>21 (53.8)</td>
<td>7 (17.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>LMICs, n/36 (%)</td>
<td>28 (77.8)</td>
<td>23 (63.9)</td>
<td>7 (19.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total, n/75 (%)</td>
<td>59 (78.7)</td>
<td>44 (58.7)</td>
<td>14 (18.7)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

HICs, high-income countries/regions; LMICs, low-middle-income countries/regions

The proportion of oral Watch antibiotics for each country varied between 12.1% to 81.5% of total use (median 34.9% in HICs and 38.2% in LMICs) (Figure 5). The use of Not-Recommended antibiotics was higher in LMICs (6.2% of total) compared to HICs (0.7%). The use of oral Reserve antibiotics was very low with the highest proportions in Japan, Egypt, and India (1.2%, 0.7%, and 0.4%, respectively).
The AWaRe system

• Continuous re-evaluation of *which are the essential* antibiotics on the EML, the drug, indication, dose and formulation – generic and new agents
• Handbook provides a platform to build *future implementation programs on improving the use of antibiotics*
• Working with GARDP, GLASS, CIA, AMR teams to develop a coherent evidence-based quality improvement program around the optimal use of antimicrobials
• Continuous update of the AWaRe categorisation of antibiotics and improving the evidence base for these groups
• More formal evaluation of RESERVE antibiotics and assisting with a program of enhanced access – defining unmet public health needs
• Better RCT evidence for future policy interventions, country level adoption and implementation
MANY THANKS

• ALL MEMBERS OF EML SECRETARIAT AND ANTIBIOTIC WG (Veronica Zanichelli-!).
• GLASS: participated in meetings and exchanged ideas on how AMR surveillance data could be used (including for future updates)
• AMR/AMS group: participated in meetings and exchanged ideas for possible future implementation of the Handbook and linkage with Toolkit.
• MCA: harmonising with IMCI and Pocket book
• EDL: informed the choice of laboratory tests to include
• NICE: assisted meetings based on their summaries of the evidence (particularly on symptomatic care)
• McMaster University (WHO Collaborating Center): reviewed the evidence for the EML application, updated the reviews and conducted new reviews.
• SPECTRUM (mobile platform for infectious diseases): developed infographics based on the content of the chapters