AMR Action Plan in Japan and Activities of AMR Clinical Reference Center

Yoshiaki Gu, MD, MPH, PhD
Chief, Information and Education Division
AMR Clinical Reference Center
National Center for Global Health and Medicine Hospital
National Action Plan on Antimicrobial Resistance (AMR)

2016–2020

April 5, 2016
The Government of Japan
## Six Areas and Goals for Countermeasures on AMR

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### Numeral targets

<table>
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<tr>
<th>Proportion of resistant isolates of specific indicator microorganisms</th>
<th>2014</th>
<th>2020 (target)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of penicillin-resistance in <em>Streptococcus pneumoniae</em></td>
<td>48%</td>
<td>15% or less</td>
</tr>
<tr>
<td>Proportion of fluoroquinolone resistance in <em>Escherichia coli</em></td>
<td>45%</td>
<td>25% or less</td>
</tr>
<tr>
<td>Proportion of methicillin resistance in <em>Staphylococcus aureus</em></td>
<td>51%</td>
<td>20% or less</td>
</tr>
<tr>
<td>Proportion of carbapenem resistance in <em>Pseudomonas aeruginosa</em></td>
<td>17%</td>
<td>10% or less</td>
</tr>
<tr>
<td>Proportion of carbapenem resistance in <em>Escherichia coli/Klebsiella pneumoniae</em></td>
<td>0.1-0.2%</td>
<td>0.2% or less (same level as of 2014)</td>
</tr>
</tbody>
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## Numeral targets

### Antimicrobial Use for humans
(average amount of antimicrobials used per day per 1,000 population)

<table>
<thead>
<tr>
<th>Index</th>
<th>2014</th>
<th>2020 (target)</th>
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<tbody>
<tr>
<td>Total</td>
<td>15.8</td>
<td>Decreased by 33%</td>
</tr>
<tr>
<td>Oral cephalosporins, fluoroquinolones, macrolides</td>
<td>11.6</td>
<td>Decreased by 50%</td>
</tr>
<tr>
<td>Intravenous antimicrobials</td>
<td>1.2</td>
<td>Decreased by 20%</td>
</tr>
</tbody>
</table>

National Action Plan on Antimicrobial resistance (AMR) 2016-2020
Collaboration under One Health Approach

One Health Approach

Food
Aquaculture
Livestock
Agriculture
The Environment
Wild animals
Pets
Humans
• **AMR Clinical Reference Center (AMRCRC)**
  
  – Established in National Center for Global Health and Medicine Hospital in April 2017
  
  – Three divisions (Clinical Surveillance, Pharmacoepidemiology, Information and Education)

• **AMR Research Center (AMRRC)**
  
  – Established in National Institute of Infectious Diseases in April 2017
  
  – Eight divisions
## Six Areas and Goals for Countermeasures on AMR

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Various factors on AMR issue

- Antimicrobial usage
- Infection prevention and control etc.

Resistant bacteria

Infectious diseases due to resistant bacteria
Before Action Plan (2016)

National Surveillance in Japan

- Antimicrobial usage
- Infection prevention and control etc.

Resistant bacteria

Infectious diseases due to resistant bacteria

Japan Nosocomial Infections Surveillance (JANIS)
National Epidemiological Surveillance of Infectious Diseases (NESID)

National surveillance conducted by MHLW and NIID

MHLW: Ministry of Health, Labour and Welfare
NIID: National Institute of Infectious Diseases
Current situation

National Surveillance in Japan

- Antimicrobial usage
- Infection prevention and control etc.

Resistant bacteria

Infectious diseases due to resistant bacteria

AMU surveillance in Japan

Japan Nosocomial Infections Surveillance (JANIS)

National Epidemiological Surveillance of Infectious Diseases (NESID)

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AMRCRC: AMR Clinical Reference Center

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Current situation

Infectious diseases due to resistant bacteria

- Antimicrobial usage
- Infection prevention and control etc.

National Surveillance in Japan

AMU surveillance in Japan

Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE)

Japan Nosocomial Infections Surveillance (JANIS)

National Epidemiological Surveillance of Infectious Diseases (NESID)

AMR-RC (NIID)

MHLW and NIID

Resistant bacteria

Infectious diseases due to resistant bacteria
Antibiotic consumption from 2013 to 2018 (sales data)

http://amrsrc.ncgm.go.jp/surveillance/020/20181128172618.html
Antibiotic use in 2016, prefectural level (reimbursement data)

http://amrcrc.ncgm.go.jp/surveillance/index.html
Current situation

National Surveillance in Japan

- Antimicrobial usage
- Infection prevention and control etc.

- Resistant bacteria

- Infectious diseases due to resistant bacteria

AMU surveillance in Japan

Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE)

AMR-RC (NIID)

Japan Nosocomial Infections Surveillance (JANIS)

National Epidemiological Surveillance of Infectious Diseases (NESID)

AMR-CRC (NCGM)
Approximately 2,100 hospitals are participating in Clinical Laboratory Division (AMR surveillance).

New participants are recruited every year.
<table>
<thead>
<tr>
<th>Date</th>
<th>Division</th>
<th>Reports Details</th>
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<tr>
<td>2017/09/27</td>
<td>Clinical Laboratory Division</td>
<td><strong>2016 Open Reports (CLSI2012 Version)</strong> was released</td>
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<tr>
<td>2017/04/04</td>
<td>Clinical Laboratory Division</td>
<td><strong>2015 Open Reports (CLSI2012 Version)</strong> was released</td>
</tr>
<tr>
<td>2016/03/31</td>
<td>Clinical Laboratory Division</td>
<td><strong>2014 Open Reports (CLSI2007 Version and CLSI2012 Trial Version)</strong> was released</td>
</tr>
<tr>
<td>2016/01/27</td>
<td>Clinical Laboratory Division</td>
<td><strong>2013 Open Report</strong> was released</td>
</tr>
<tr>
<td>2013/03/29</td>
<td>JANIS English website</td>
<td></td>
</tr>
</tbody>
</table>

Time course of antimicrobial resistance rates towards the targets

**S. aureus**

- **R (%)**
  - MRSA/S. aureus
  - Graph showing the resistance rate from 2011 to 2020.

**S. pneumoniae**

- **PCG resistance rate**
  - Graph showing the resistance rate from 2011 to 2020.
  - CSF specimens
  - Non-CFS specimens

**E. coli**

- **LVFX resistance rate**
  - Graph showing the resistance rate from 2011 to 2020.

**P. aeruginosa**

- **IPM resistance rate**
  - Graph showing the resistance rate from 2011 to 2020.

**K. pneumoniae**

- **Carbapenem resistance rate**
  - Graph showing the resistance rate from 2011 to 2020.
  - Imipenem
  - Meropenem

**E. coli**

- **Carbapenem resistance rate**
  - Graph showing the resistance rate from 2011 to 2020.
  - Imipenem
  - Meropenem

**Graphs**

- All graphs show the resistance rate for different antimicrobials (Imipenem, Meropenem) over the years 2011 to 2020, with different markers indicating the rate in CSF and non-CSF specimens.
Antimicrobial resistance (AMR) is resistance of a microorganism to an antimicrobial medicine to which it was originally sensitive. Also, AMR occur by use of antibiotics. This site is to disclose current status of antimicrobial resistance, antibiotic use and trends in Japan.

https://amr-onehealth.ncgm.go.jp/
Trends in the proportion (%) of antimicrobial-resistant *Escherichia coli*

Trends in the proportion (%) of antimicrobial-resistant *Acinetobacter*

Trends in the proportion (%) of CTX-resistant *E. coli* [the proportion of antimicrobial resistance in humans and animals]

Current situation

National Surveillance in Japan

- Antimicrobial usage
- Infection prevention and control etc.

Resistant bacteria

Infectious diseases due to resistant bacteria

AMU surveillance in Japan

Japan Nosocomial Infections Surveillance (JANIS)

National Epidemiological Surveillance of Infectious Diseases (NESID)

Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE)

AMR-RC (NIID)

MHLW and NIID

AMR-CRC (NCGM)
Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE)

“National Surveillance Platform”

Central Server

Data collection

Analysis Visualization

Hospital group

Large hospitals

Small and medium-sized hospitals

Regional Surveillance

Large hospitals

Small and medium-sized hospitals

Public Health Center

National Surveillance

Trends of AMR

A ntimicrobial Usage (AUD, DOT)

Indexes for HAI and clinical practice

feedback
## Components of J-SIPHE (Major components)

<table>
<thead>
<tr>
<th>Hospital outline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Quality indicators for infectious diseases (ID) management and ASP</td>
</tr>
<tr>
<td>2. Antimicrobial usage (AMU)</td>
</tr>
<tr>
<td>3. Quality indicators for infection control practices</td>
</tr>
<tr>
<td>4. Hospital-associated infection (HAI)</td>
</tr>
<tr>
<td>5. Microbiology including AMR bacteria</td>
</tr>
<tr>
<td>Number of major pathological bacteria and AMR bacteria</td>
</tr>
</tbody>
</table>

- Input is optional and multiple selections are possible
- Adopted items gained consensus by experts
Antimicrobial Use

- e.g. comparison of carbapenem use
Quality indicators for infection control practices

Antiseptic hand-rub usage of hand hygiene

Divided by patient-days

Each ward
The Group Making system
Antimicrobial Stewardship Team (AST)

ICT

Infection Control Team

Doctor

Pharmacist

medical technologist

Nurse

medical assistant

AST

Antimicrobial Stewardship Team
In outpatient care in Japan

• Antimicrobial drugs are administered to 60% of upper respiratory inflammation patients.
  – Third generation cephalosporin: 46%
  – Macrolide: 27%
  – Quinolone: 16%

※Upper respiratory inflammation: rheum, acute bronchitis, acute sinusitis, acute pharyngitis (except for those identified as bacterial), acute pharyngolaryngitis, and upper respiratory tract infection

Manual for Antimicrobial Stewardship by MHLW

Digest version

June 2017

http://amr.ncgm.go.jp/medics/2-7.html

English version

September 2017

February 2018

Flowchart of diagnosis and treatment of acute respiratory tract infection

Patient who visited a clinic or hospital and complained of a “cold”

- Consider a disease other than respiratory tract infection
  - No respiratory tract symptom
    - Respiratory tract symptom
      - Abnormal vital sign (tachypnea, altered mental status, or hypotension)
        - Sepsis
      - High fever, muscle pain, and/or joint pain during flu epidemic
        - Flu
    - Acute rhinosinusitis: Mainly severe nasal symptom
      - Mild
      - Moderate to serious
    - Acute pharyngitis: Mainly severe throat symptom
      - Red Flag:
        - Worst pain in life; cannot swallow saliva; trismus, hoarseness, or breathing difficulty
        - Consider peritonsillar abscess, acute epiglottitis, or retropharyngeal abscess
        - Sudden onset, vomiting, or scarce pharynx finding
        - Consider acute myocardial infarction, subarachnoid hemorrhage, carotid artery dissection, or vertebral artery dissection
      - No red flag
      - Red flag
        - GAS rapid antigen test or culture
          - Positive
            - Consider use of antibacterial agent
          - Negative
        - Complete examination
          - No above finding
          - Above finding
            - Work-up including chest X-ray image
    - Acute bronchitis: Mainly severe cough (within 3 weeks)
      - Finding to diagnose pneumonia:
        - Abnormal vital sign (One of temperature above 38°C, pulse of 100 beats/minute, and respiration rate of 24 breaths/minute) Or Abnormal finding in chest auscultation
      - No above finding
      - Above finding

No need of antibacterial agent
Financial incentive for antimicrobial stewardship under national health insurance system (April 2018 – )

- Inpatient
  - Antimicrobial Stewardship Team (1,000 JPY per patient)

- Outpatient
  - Explanation for not prescribing antibiotics for respiratory symptom and diarrhea among children (800 JPY per patient)
Action plan published
Establishment of AMR clinical reference center
Manual by MHLW published
Manal (digest ver.) published
Financial incentive for antimicrobial stewardship started
Education for health-care professionals

• Seminars (2018)
  – Medical doctors and health-care workers: 10 cities
  – Dentists: 1 city
  – Public health officials: 5 cities

• e-learning system
Development and efficacy of a clinician-targeted refresher course for treating nonpneumonia respiratory tract infections

Shungo Yamamoto MD, DTM&H, DrPH1,2 | Yoshiaki Gu MD, MPH, PhD3 |
Yumiko Fujitomo MD3 | Nobuyuki Kanai MD4,5 | Yoshihiro Yamahata MD6 |
Hiroyuki Saito MD, MBA7 | Tadayuki Hashimoto MD8 | Norio Ohmagari MD, MSc, PhD3,9

**TABLE 2** Prescription of antibiotics in response to six acute respiratory tract infection vignettes before and after the refresher course

<table>
<thead>
<tr>
<th>Vignette</th>
<th>Prescribed antibiotics prequestionnaire (%)</th>
<th>Prescribed antibiotics postquestionnaire (%)</th>
<th>Difference (95% confidence interval), P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Common cold</td>
<td>0</td>
<td>2.8</td>
<td>2.8% (-5.4 to 10.9), P = 1.0</td>
</tr>
<tr>
<td>2. Acute bronchitis</td>
<td>58.3</td>
<td>11.1</td>
<td>-47.2% (-66.3 to -28.1), P &lt; .001</td>
</tr>
<tr>
<td>3. Common cold</td>
<td>18.9</td>
<td>2.7</td>
<td>-16.2% (-30.8 to -1.6), P = .03</td>
</tr>
<tr>
<td>4. Acute pharyngitis</td>
<td>70.3</td>
<td>43.2</td>
<td>-27.0% (-49.0 to -5.0), P = .02</td>
</tr>
<tr>
<td>5. Acute rhinosinusitis</td>
<td>50.0</td>
<td>16.7</td>
<td>-33.3% (-53.3 to -13.3), P = .002</td>
</tr>
<tr>
<td>6. Acute bronchitis</td>
<td>5.6</td>
<td>2.8</td>
<td>-2.8% (-14.9 to 9.4), P = 1.0</td>
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E-learning system for health-care professionals

Five courses, more than 50 lectures

https://amrlearning.ncgm.go.jp/
Public awareness about antibiotics in Japan
(internet survey, Mar 2017)

Antibiotics kill viruses
- Yes: 46.8%
- No: 21.9%
- Don't know: 31.3%

Antibiotics are effective against common cold and influenza
- Yes: 40.6%
- No: 24.6%
- Don't know: 34.8%

Public awareness campaign

• AMR clinical reference center has developed campaigns to raise public awareness on AMR through internet websites, SNS, newspapers, public events, seminars etc.

• Media attention is a key.
Activities in schools

Special lectures regarding AMR and antimicrobials at elementary schools

Are antibiotics effective against common cold?

- Effective: 34, Not effective: 33, Don’t know: 10

Do you know what is AMR?

- Know well: 42, Ever heard but don’t know well: 23, Don’t know or never heard: 13
Senryu contest

Senryu (川柳) is a Japanese form of short poem which is similar to haiku in construction.

The first-place in 2017

“Just in case” is a trigger for increasing resistant bacteria.
Educational materials published by AMRCRC

P: Poster, L: Leaflet, B: Booklet
http://amr.ncgm.go.jp/materials/
Page Views of AMR information website

http://amr.ncgm.go.jp (in Japanese)
Poster for awareness month (November) this year
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Strategies to promote research on AMR

Basic
- Research on the emergence and transmission of antimicrobial resistance
- Preclinical development of novel methods for prevention, diagnosis and treatment

Clinical
- Research on surveillance and risk assessment
- Optimization of existing methods for prevention, diagnosis and treatment
- Clinical development of novel methods for prevention, diagnosis and treatment

Social
- Research on infection prevention/control and antimicrobial stewardship
- Evaluation of impact on public awareness, education and socioeconomics
Every year, Antimicrobial Resistance (AMR) kills approximately 700,000 people globally. The magnitude of this issue drove the WHO to adopt a Global Action Plan on AMR during its May 2015 World Health Assembly. That action plan called upon member states to reinforce measures against AMR and draw up their own national action plans. In addition to those efforts, many countries have been working to establish alliances on this issue. Such momentum for international collaboration must be sustained. It is hoped that measures against AMR will be included in the agenda of the upcoming G20 Osaka Summit to be held in June 2019.

In Japan, AMR has become a major challenge for many medical facilities, with cases of community-acquired drug-resistant infections on the rise nationally. Japan enacted its National Action Plan on Antimicrobial Resistance in April 2016. Sensing the growing concern about AMR domestically and abroad, HGPI has taken the initiative to host three expert meetings on this subject since 2016. The 1st expert meeting, “Japan’s Role in Addressing Global Antimicrobial Resistance” brought together actors from the Government, academia, and industry for a debate on policy. The 2nd meeting produced “Seven Recommendations for Promoting Measures Against AMR.” The 3rd meeting coincided with World Antibiotic Awareness Week, and again brought together stakeholders from the Government, academia, and industry for a discussion on Japan’s national action plan, concrete obstacles to its implementation, and measures to overcome those obstacles. In September 2018, HGPI convened the AMR Alliance Japan Kick-off Meeting to discuss the vision for AMR Alliance Japan and further promote policies on AMR based on the conversations in the previous three expert meetings.

https://hgpi.org/en/events/amr-2.html
概要
2011年、世界保健機関（WHO）が薬剤耐性（AMR）に対する取組の必要性を国際社会に訴えてから6年が経ちました。ワンヘルス・アプローチに基づいてAMR対策を推進するには誰に何をすることを求められるのか？国、医療従事者、学会や関係団体、製薬企業、一般市民はどのように連携できるか？AMR問題に取り組む世界的リーダー達が、最新の情報と今後の対策の方向性について語るシンポジウムです。

日時
平成29年11月14日（火）13:00～17:00
Tuesday, November 14, 2017 Time: 13:00-17:00

会場
笹川記念会館 2階 国際会議場
The SASAKAWA HALL 2F
〒100-0073 東京都港区三田3-12-12
3-12-12 Minato, Tokyo, Japan

主催
厚生労働省
Ministry of Health, Labour and Welfare

定員
400名まで（お足数になり次第、締め切らせていただきます。）
400名 at the end (applications will be closed as soon as the number of participants reaches the limit)

言語
日英両言語通訳
Simultaneous interpretation service will be available for Japanese and English

プログラム

<table>
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<tr>
<th>時間</th>
<th>内容</th>
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<tr>
<td>13:00</td>
<td>開催挨拶 Opening Remarks</td>
</tr>
<tr>
<td>13:00～14:00</td>
<td>セッション1 基調講演：サリー・ディビス卿 英政府首席医務官 Session 1 Keynote Lecture: Professor Dame Sally Davies</td>
</tr>
<tr>
<td>14:00～15:00</td>
<td>セッション2 抗生物薬の適正使用： 大塚 英大 国立国際医療研究センター AMR臨床リファレンスセンター長 他2名 Session 2 Antimicrobial Stewardship：</td>
</tr>
<tr>
<td>15:15～15:30</td>
<td>休憩 Break</td>
</tr>
<tr>
<td>15:30～17:00</td>
<td>セッション3 抗生物薬適正使用のためのワンヘルス・サービスライン： 保田 惠吾 国立感染症研究所 総合第二部長 他2名 Session 3 One Health Surveillance for Antimicrobial Stewardship</td>
</tr>
<tr>
<td>17:00</td>
<td>閉会挨拶 Closing Remarks</td>
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お申し込みは、
For an application, visit:
http://www.tokyo-amr2017.jp

Nov 2017
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Thank you