Previous Efforts to Control Antimicrobial Resistance in Japan and their Direction in the Future

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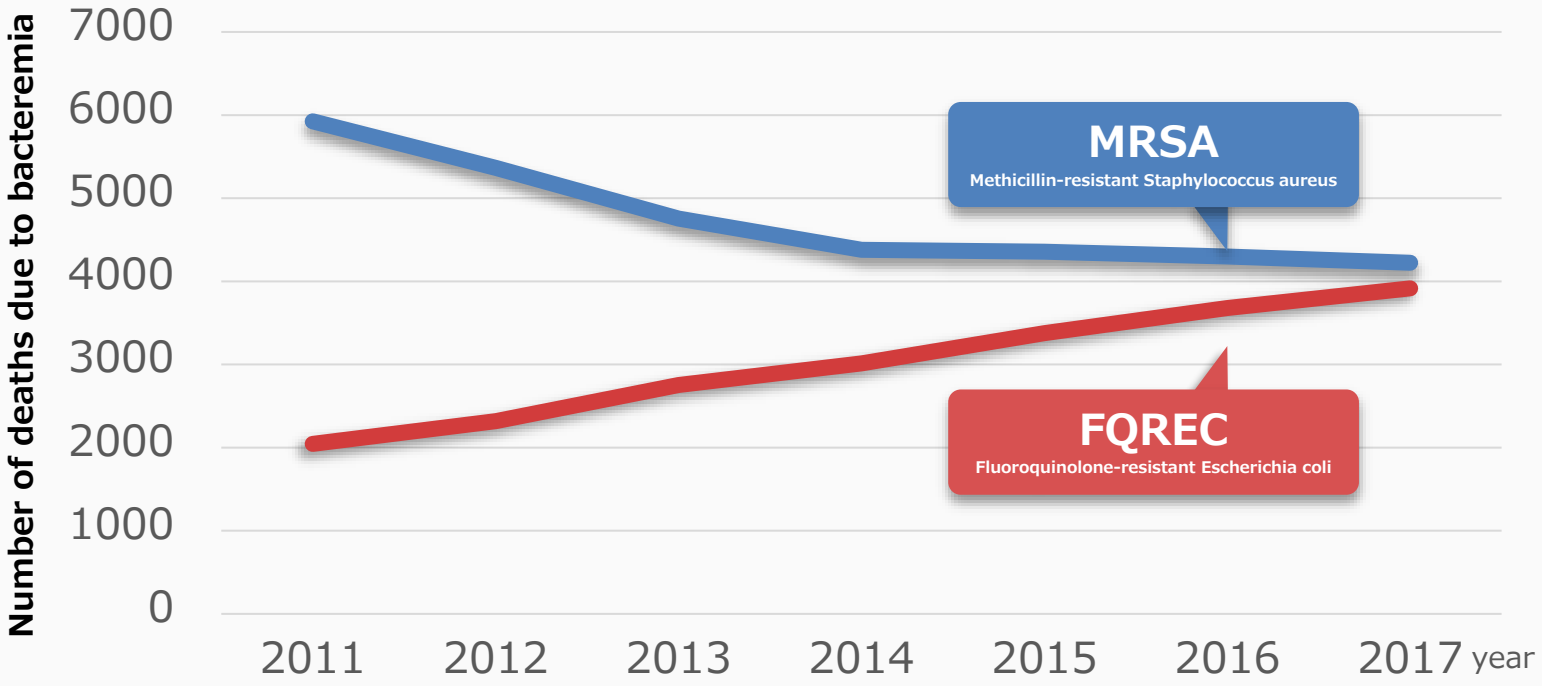
Clinical Reference Center

The number of deaths is increasing in Japan as well



Number of deaths due to traffic accidents 3,694 (2017)

Methicillin-resistant S. aureus bacteremia 4,224 deaths (Confidence interval: 2,769-5,994 deaths)

Fluoroquinolone-resistant E. coli bacteremia 3,915 deaths (Confidence interval: 3,629-4,189 deaths)

MRSA and third-generation cephalosporin-resistant E. coli are indices of SDGs

(As of 2017)

Tsuzuki, et al. JIC 2020

Where do drug-resistant microorganisms come from?

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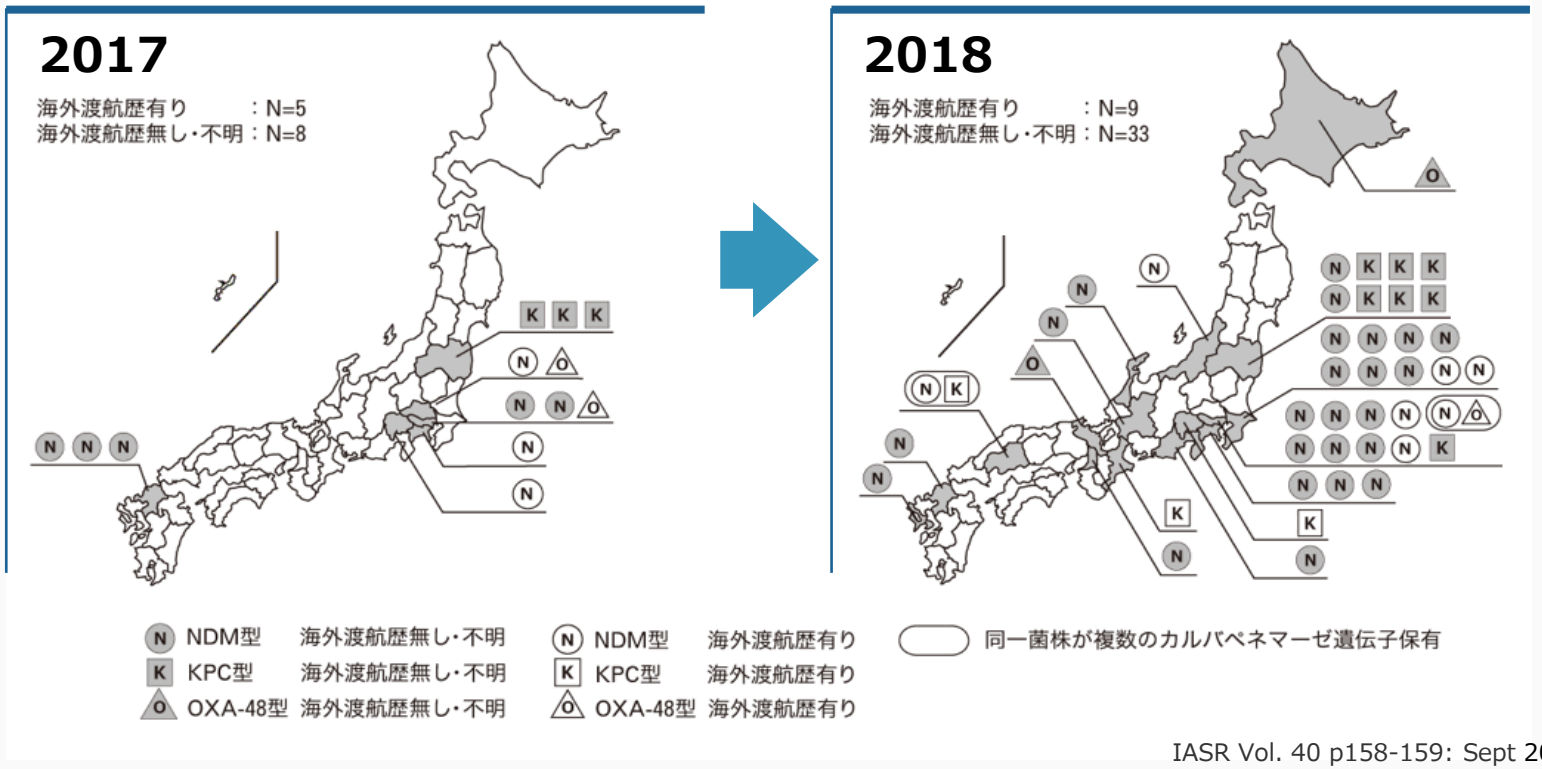
Reports of infections due to patients in whom carbapenemases of foreign origin were detected are increasing each year

Areas where detection of carbapenemases of foreign origin was reported



IASR Vol. 40 p158-159: Sept 2019.
https://www.niid.go.jp/niid/ja/cre-m/cre-iasrd/9125-475d02.html

Prefectures and major metropolitan areas where vancomycin-resistant enterococcal infections have been detected are increasing

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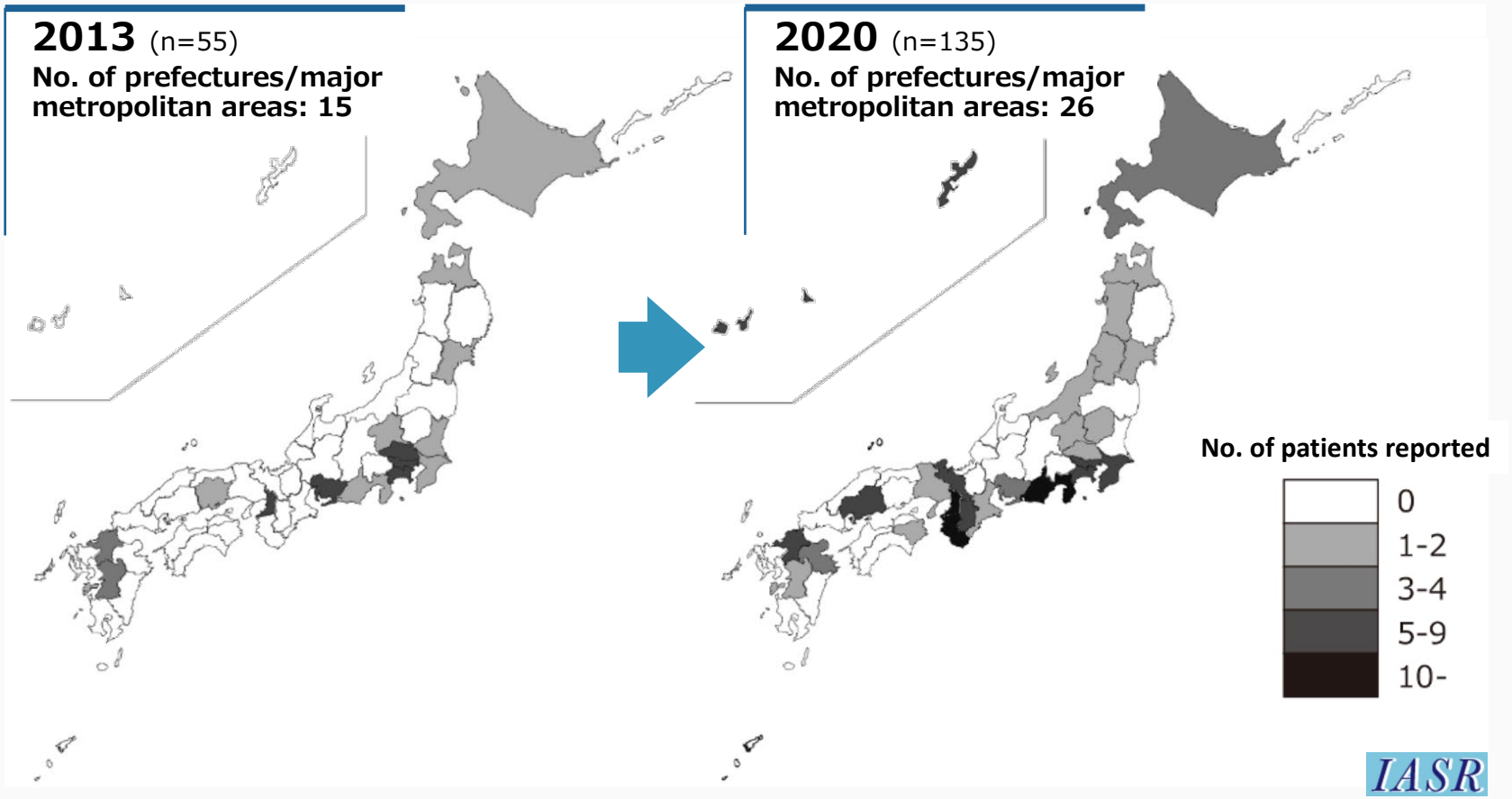
Vancomycin-resistant enterococcal infections according to the National Epidemiological Surveillance of Infectious Diseases

No. patients reported by prefecture/major metropolitan area (as of January 25, 2021)



IASR

https://www.niid.go.jp/niid/images/iasr/2021/5/495p01f02.gif

The current status of and issues with education and educational campaigns

Knowledge and awareness of antimicrobial resistance and behavior when feeling unwell

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Survey SUMMARY

A low percentage of people with accurate knowledge about antimicrobials/antibiotics

"Antimicrobials/antibiotics are ineffective against viruses"
18.0% of people had accurate knowledge

An insufficient awareness of controlling antimicrobial resistance

About 80% of people responded that they had been or might have been infected with a drug-resistant microorganism, but about 60% of those people responded that they had taken no steps to control resistance

A change in behavior with regard to infection control was evident

50.6% of people "will take time off" when feeling unwell,
a 13.5% increase from 2019
Still, 49.5% "cannot or will not take time off"

Sample: General public Nationwide 700 respondents
30 males in their teens, 73 men in their 20s, 62 in their 30s, 70 in their 40s, 64 in their 50s, and 51 age 60 or over
20 females in their teens, 74 women in their 20s, 64 in their 30s, 64 in their 40s, 64 in their 50s, and 64 age 60 or over
Survey methodology: Online survey Survey period: August 2021

http://amr.ncgm.go.jp/pdf/20211004_report_press.pdf

The healthcare-seeking behavior of citizens has changed

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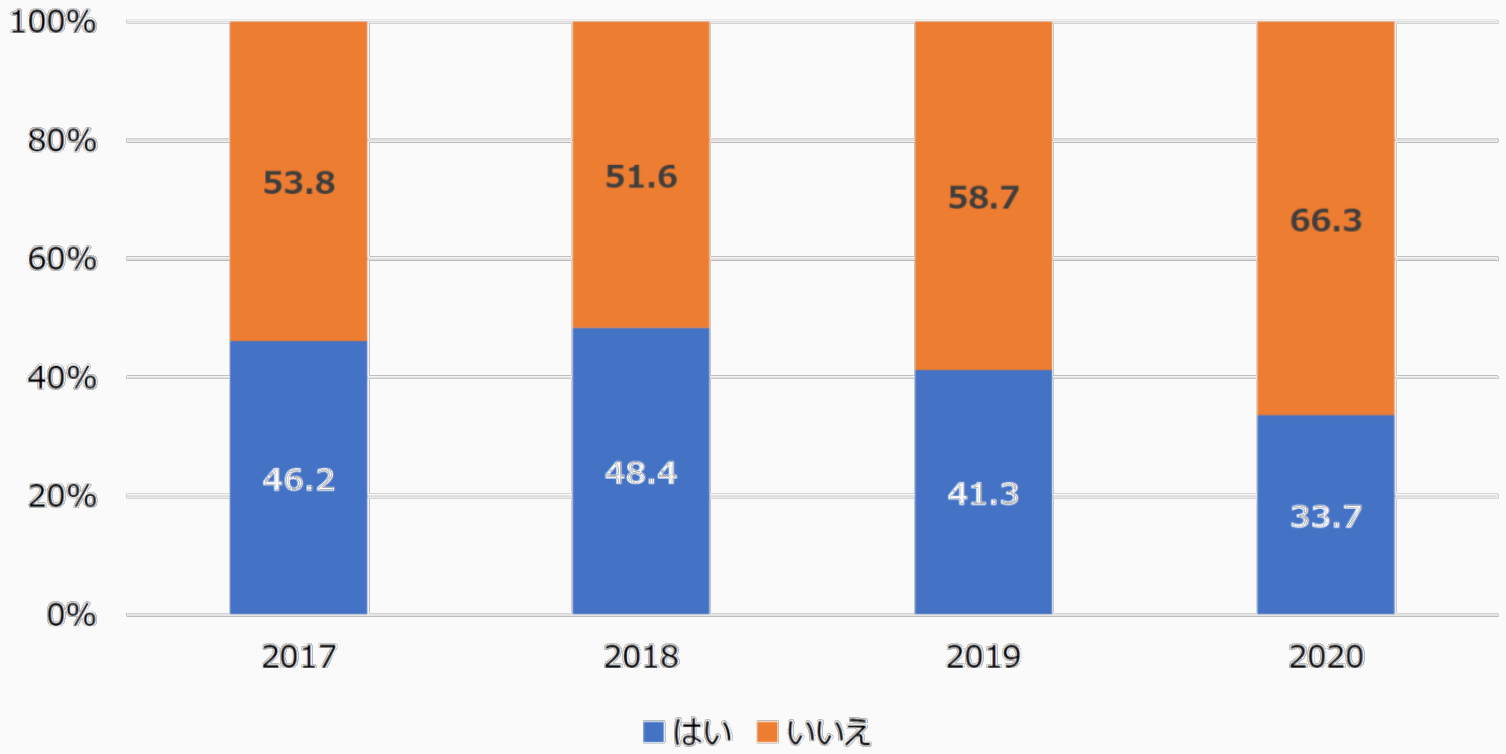
Have you taken any “antimicrobial” over the last year?



The percentage of people who had taken an antimicrobial is gradually decreasing

The frequency with which physicians are prescribing an antimicrobial for a cold is decreasing

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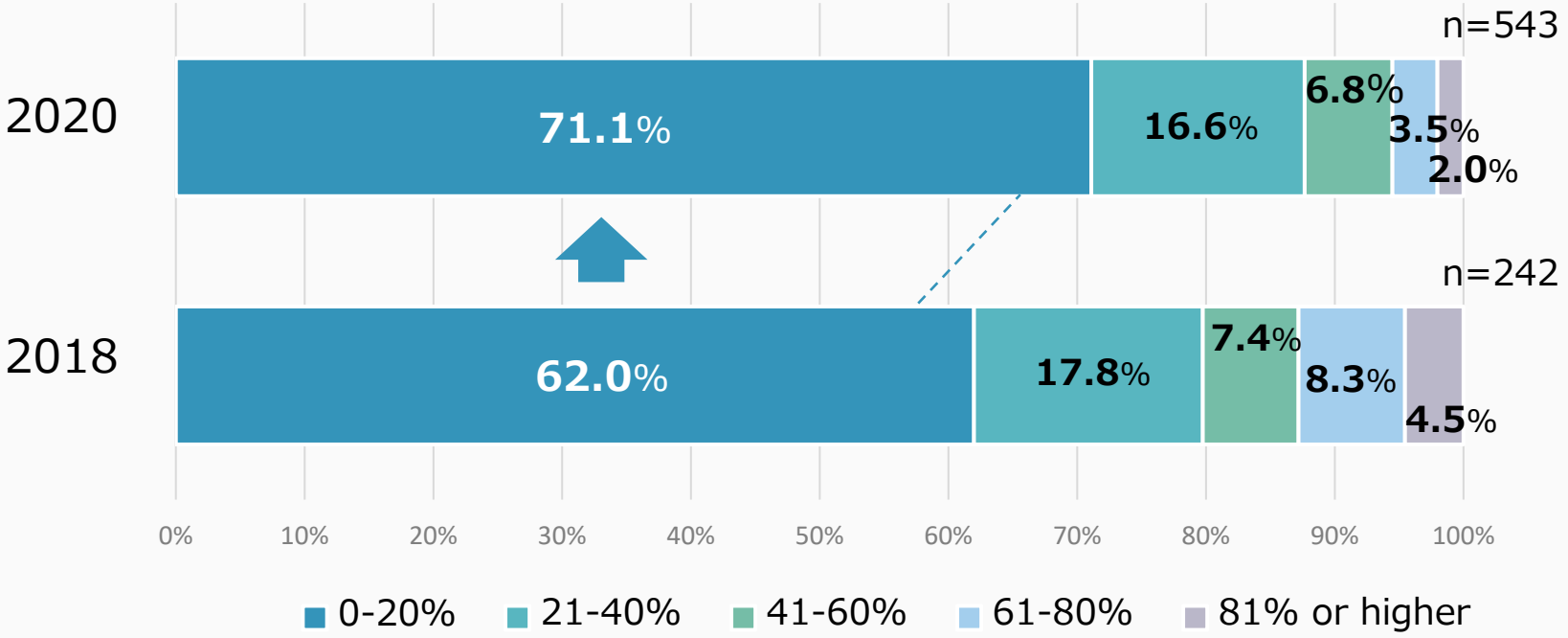
Percentage of physicians who prescribed an antimicrobial when they diagnosed a patient with a cold (over the past year)



Joint Committee to Study the Proper Outpatient Use of Antimicrobials of the Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases
(Second) Survey of physicians in clinics nationwide regarding the proper use of antimicrobials

The elderly are susceptible to infections

https://www.city.toshima.lg.jp/013/kuse/koho/hodo/r0304/2104301724.html

Issues with and the direction of education and educational campaigns

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1. Improvements in figures for public knowledge and awareness are not evident yet, but healthcare-seeking behavior has changed and instances where antimicrobials are prescribed are decreasing
2. Physician knowledge and awareness has improved according to figures, and prescribing has also improved

For the general public

1. More information is needed
2. Specific approaches in given areas
3. Increased health education (antimicrobials & vaccines) in schools

For medical personnel

1. Enhancing education provided in school
2. Infection control training (including COVID-19) in medical & care settings

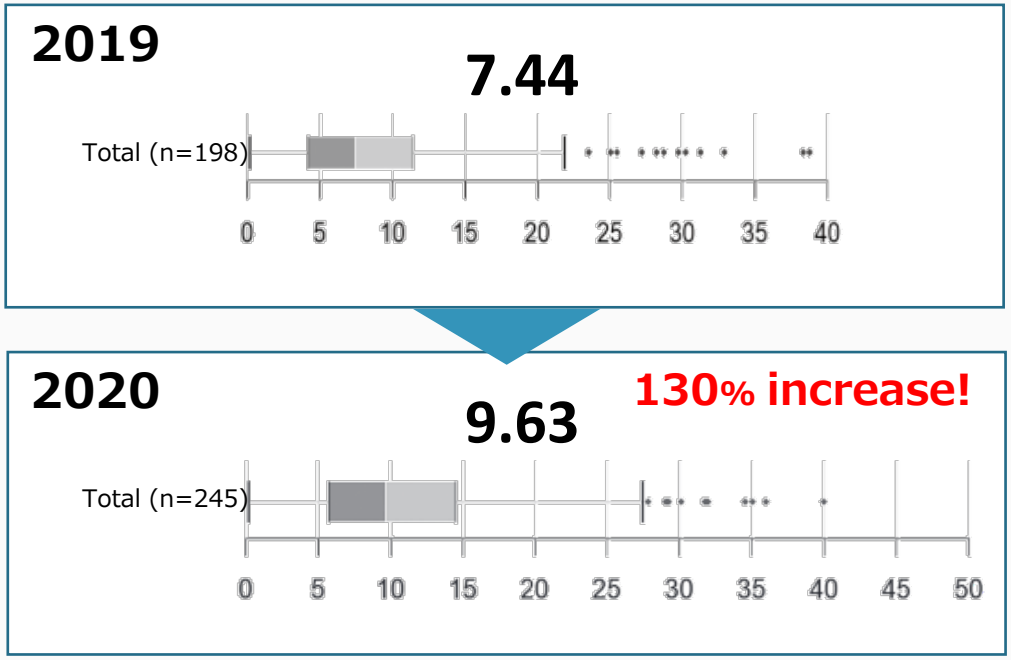
The current status of and issues with surveillance

J-SIPHE has collected data from hospitals

Hospital surveillance

(863 facilities participating, as of March 16, 2022)

1,000 patients, amount (L) of hand sanitizer used per day



Hand hygiene has tended to improve

Point prevalence surveys (PPSes) of facilities for the elderly are also being conducted

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Facilities [No. of facilities responding]	Antimicrobials Usage	Main infectious diseases treated with antimicrobials	Main types of antimicrobials
Convalescent beds (Medical facilities) [82]	9.4%	Pneumonia (39.5%) Urinary tract infections (26.8%) Bronchitis (3.8%)	Third-generation cephalosporin injections Oral quinolone-based antibacterials Carbapenems Penicillin-based antibiotics
Long-term care facilities for the elderly (LTC facilities) [126]	1.7%	Urinary tract infections (51.3%) Pneumonia (24.3%) Upper respiratory inflammation (9.9%)	Third-generation cephalosporins Quinolone-based antibacterials Penicillin-based antibiotics
Special nursing homes for the elderly (Special nursing homes) [137]	1.0%	Urinary tract infections (31.1%) Pneumonia (14.9%) Upper respiratory inflammation (12.2%)	Third-generation cephalosporin injections Oral quinolone-based antibacterials Oral penicillin-based antibiotics

As of February 2022, a second PPS of long-term care facilities for the elderly is in the planning stage

A system of medical records of institutional care of the elderly with certain conditions has been launched

Support for an additional fee to assess a facility's treatment and management of conditions such as pneumonia and a urinary tract infection in residents of long-term care facilities for the elderly

Clinical data and microorganism testing data need to be integrated

- JANIS data are data on drug-resistant microorganisms and provide no information on patients
- The administrative department of a medical facility handles the E & F files [indicating tests performed and care provided] and Form 1 [indicating patient information, the patient's illness, surgery, etc.]. Combined use of these documents will allow the duration of hospitalization, costs, outcomes, and other data to be tracked

Current state

In research using the E & F files and Form 1,
the duration of hospitalization for S. aureus and costs can be ascertained

S Tsuzuki et al. Public Health,198, 292-296,2021

Data from care facilities are used to control antimicrobial resistance

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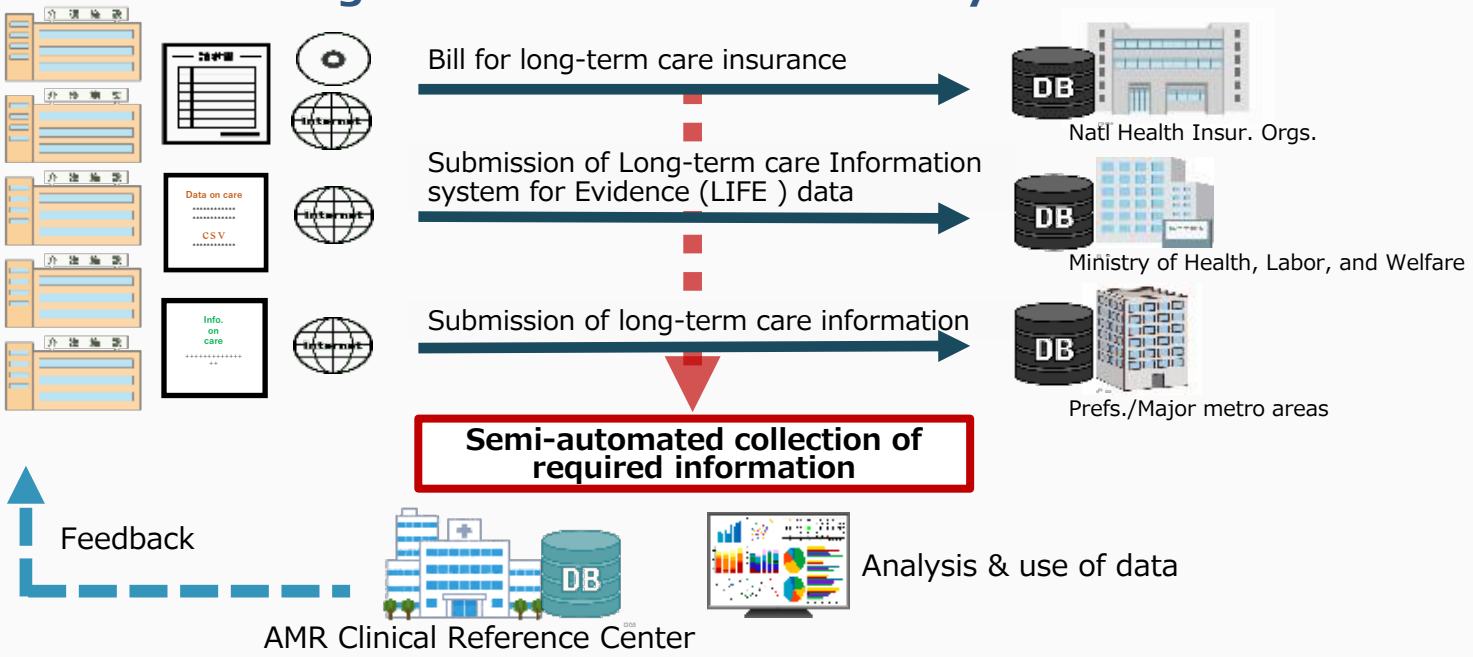
Establishing methods of studying trends in use of antimicrobials in long-term care facilities for the elderly

- Information on antimicrobials (name of medication, dose, and duration of administration) cannot be obtained from long-term care insurance bills (integrated facilities for medical and long-term care and long-term care facilities for the elderly)
- Information on antimicrobials that can be obtained from medical bills is limited (For special nursing homes for the elderly, the only information available concerns antimicrobials prescribed in the facility)

Creating an effective surveillance system



Data on treatment of infections will be collected from clinics

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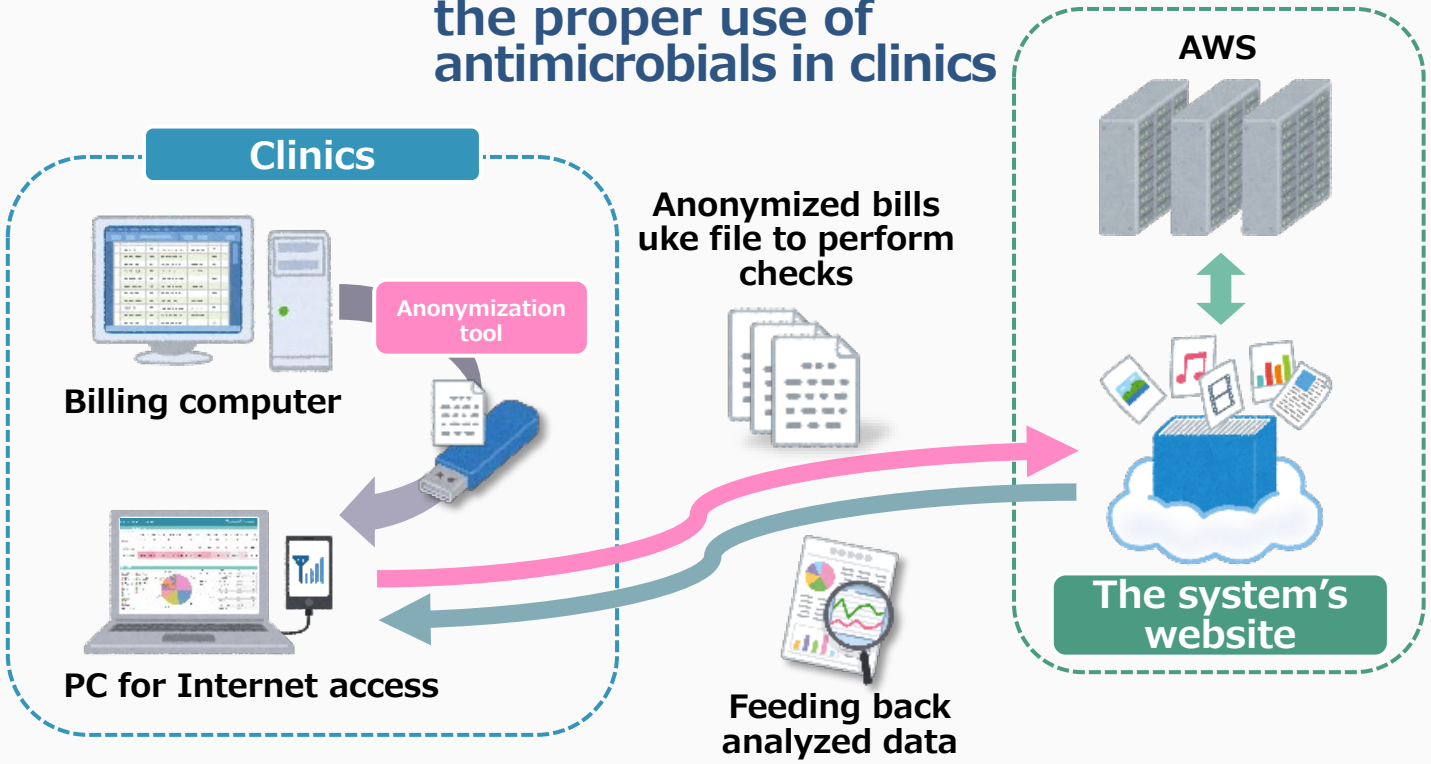
There is no way to collect information on trends in care at clinics

A system to facilitate the proper use of antimicrobials in clinics



Issues with surveillance

1. Clinical data and microorganism testing data from medical facilities are separate
2. Obtaining data from facilities for the elderly is difficult
3. Data cannot be obtained from clinics

1. Improving methods of data collection in hospitals
   - Linking data on drug-resistant microorganisms to patient information
   - Genomic data will eventually be incorporated as well
2. Implementing clinic surveillance
3. Obtaining data from facilities for the elderly
   - Introduction of a semi-automated system to collect data rather than depending on human entry

Issues with and the direction of proper use of antimicrobials

Antimicrobial sales in 2021 decreased about 31.6% compared to 2013 (14.91 DID)

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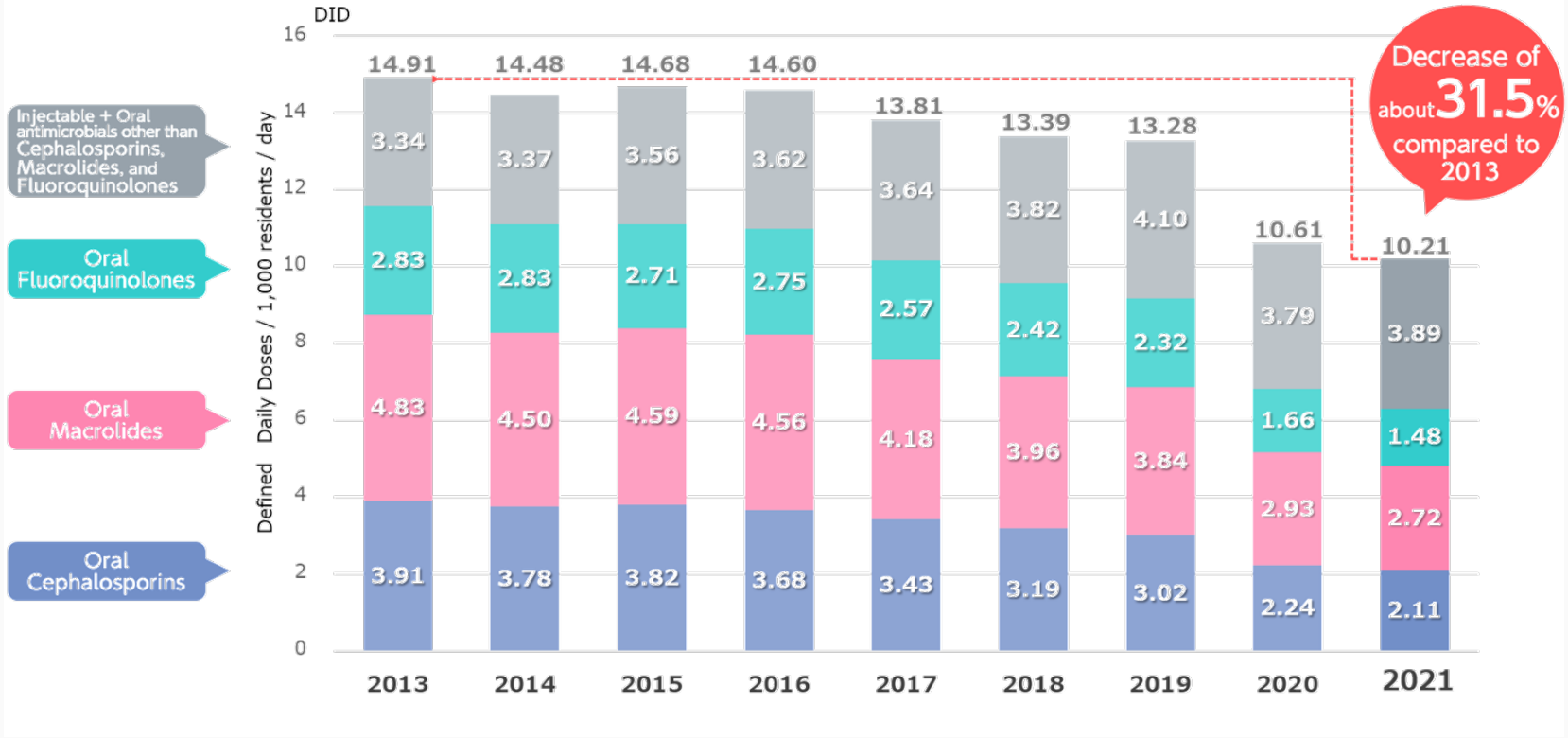
Changes in sales of antimicrobials nationwide 2013-2021 (Antimicrobials in the ATC3 class)



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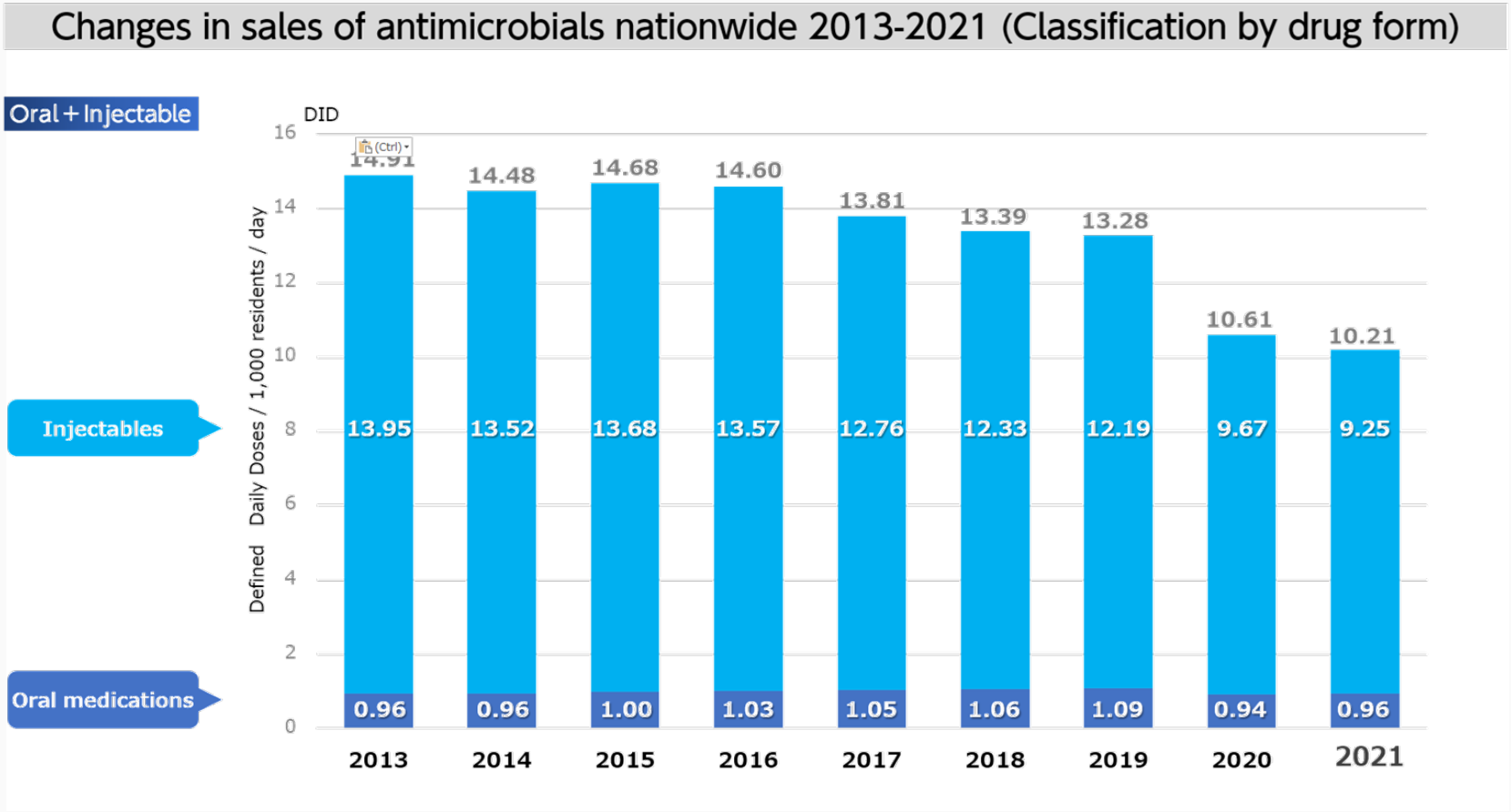
https://amrcrc.ncgm.go.jp/surveillance/020/20190902163931.html

Use of injectables has generally leveled off



https://amrcrc.ncgm.go.jp/surveillance/020/20190902163931.html

Honing in and addressing areas where antimicrobials are used inappropriately

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To members of the media

News Release

AMR Clinical Reference Center

Center Hospital of the National Center for Global Health and Medicine

AMR Clinical Reference Center

Commissioned by the Ministry of Health, Labor, and Welfare, Japan

January 27, 2022

Acne treatment for the 2020s and beyond:

The condition can now be treated at its source, but drug-resistant bacteria are a problem

In order to consider the problem of antimicrobial resistance (AMR) in acne treatment, the AMR Clinical Reference Center spoke with Dr. Ichiro Kurokawa, Head of Dermatology and Head of the Acne Center at Meiwa Hospital Acne is a familiar problem that most people suffer from at one time or another. How is AMR related to acne? And how have the circumstances of acne treatment changed over the past few years?

Acne is a full-fledged skin disease known by the scientific name “acne vulgaris.” It often develops during adolescence and is exacerbated by ”excessive sebum,” ”clogged pores (comedones),” and inflammation caused by the proliferation of Propionibacterium acnes. In the past, treatment primarily involved antibacterial to suppress inflammation, but now there are several topical agents that alleviate comedones, allowing prompt treatment of the condition at its source. However, the rate of Dermatology consults is low (about 16%*1), and many people exacerbate their condition with care of their own devising. Over the past few years, P. acnes has increasingly become drug-resistant. This may be due to acne treatment as well as antimicrobial treatments in other departments. This press release describes the relationship between acne treatment and drug-resistant bacteria.

*1 Tanizaki H et al. Jpns J Dermatol. 2000:130,1811.

Dr. Ichiro Kurokawa,
Head of Dermatology and Head of the Acne Center at Meiwa Hospital

Dr. Kurokawa graduated from Kansai Medical University in 1983. He worked at facilities such as Nakatsu Hospital and Mie University, and he has been in his current position since 2011. He is a member of the Japanese Dermatological Association’s committee to draft “Acne Vulgaris Treatment Guidelines.” He has been continued to research and treat acne since his residency. The Acne Center at the Hospital is visited by various patients from those with minor to severe acne to those with refractory acne-related conditions.

Summary

1. Acne originates as clogged pores (comedones); treatment should be started as soon as possible before inflammation develops
2. The appearance of topical agents that effectively treat comedones has allowed definitive treatment starting in the early stages
3. Topical and oral antibacterials are also used to treat acne with severe inflammation
4. P. acnes is increasingly resistant to macrolide antibacterials
5. Antibacterial treatment is, in principle, ”only for acute inflammation,” ”moderate or more severe acne,” and ”provided for up to 3 months.”

1. Improving use by identifying areas where antimicrobials are used inappropriately
2. Incorporation of forms of disease management other than antimicrobials

Improving patient prognosis by improving the quality of care for major infectious diseases

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<S. aureus>

- High fatality rate (20-50%)
- Deaths 28 days after onset have decreased 56% due to the involvement of infectious disease experts, but they are only involved in 32.6% of cases (111/341)

  Honda H, et al. Am J Med 2010

<Candidemia>

- High fatality rate (25-60%)
- Deaths 30 days after onset have decreased 46% due to the involvement of infectious disease experts, but they are only involved in 44.5% of cases (126/283)

  Ishikane M, et al. PLoS ONE 2019
- According to a 2018 Japanese study, only 25.6% of facilities (10/39) used antifungals properly

  Moriyama Y, et al. BMC Infect Dis 2021

An antibacterial or antifungal targeting *S. aureus* bacteremia or candidemia must be used properly (an evidence-based approach, e.g., selection of the appropriate medication and duration of administration)

Improving the quality of care through sufficient use of testing

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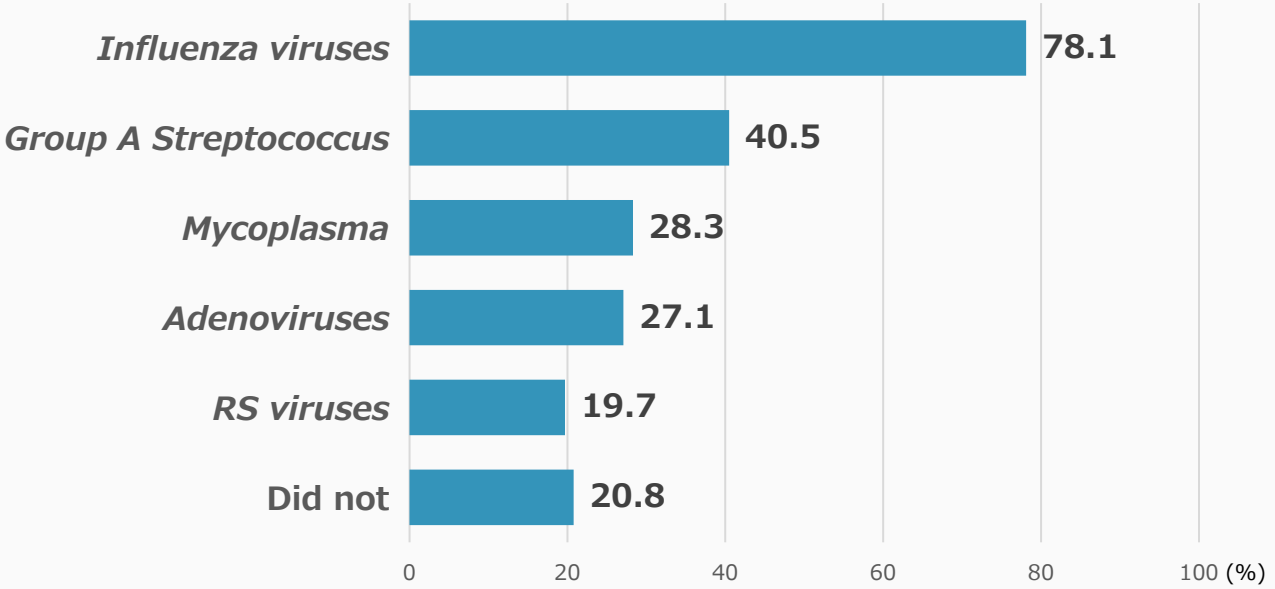
Is rapid testing not widespread enough to facilitate appropriate treatment?

Rapid diagnostic tests that can be performed in the hospital

(n=269, multiple answers allowed)



February 2018 survey

Joint Committee to Study the Proper Outpatient Use of Antimicrobials of the Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases
(First) Survey of physicians in clinics nationwide regarding the proper use of antimicrobials

Issues with and the direction of proper use of antimicrobials

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1. Use of oral antimicrobials is decreasing but use of injectable antimicrobials has not changed
2. Use of antimicrobials is increasing due to an increase in the elderly population
3. Colds are being treated more appropriately, but what about other conditions?
4. Can sometimes not lead to an improved prognosis
5. There may be other inappropriate treatments as well, but the overall picture is unclear
6. The criticism that “Isn’t the goal to reduce use?”

1. Seeking to reduce the disease burden due to drug-resistant microorganisms and to improve patient prognosis by improving the quality of care
2. Examining measures to deal with an increase in the elderly population
3. Identifying areas where antimicrobials are used improperly and measures focusing on those areas
4. Examining approaches (including education and educational campaigns) for each patient demographic, such as age
5. Improving care to directly improve patient prognosis

Measures for specific microorganisms that are hard to control

The fluoroquinolone resistance of *E. coli* and the methicillin resistance of *S. aureus* are persistent problems

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Drug resistance of index microorganisms

	Index	2013	2016	2019	2020	2020 (target)
Medicine	Penicillin insensitivity of *Pneumococci*	47.4	36.4	32.0	**33.3**	15% or lower
	Fluoroquinolone resistance of *E. coli*	35.5	39.3	41.4	**41.5**	25% or lower
	Methicillin resistance of *S. aureus*	51.1	47.7	47.7	**47.5**	20% or lower
	Carbapenem (IPM) resistance of *Pseudomonas aeruginosa*	17.1	17.9	16.2	**15.9**	10% or lower
	Carbapenem resistance of *E. coli* and *Klebsiella pneumoniae*	0.1- 0.3	0.1- 0.2	0.1- 0.2	**0.1-** **0.2**	0.2% or lower (same rates for both)

https://janis.mhlw.go.jp/report/open_report/2020/3/1/ken_Open_Report_202000.pdf

Responses to the fluoroquinolone resistance of *E. coli* and the methicillin resistance of *S. aureus*

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Will the situation be improved by just a decrease in unnecessary use of antimicrobials and a decrease in the use of broad-spectrum antimicrobials?

Measures to prevent infections

- Reducing infections themselves
  → Decreased viral infections with the aid of measures against COVID-19
- Measures to improve the ADL of the elderly
- Measures to prevent urinary tract infections in the elderly

Use of new approaches such as vaccines

- Ex.: *E. coli* lineages that colonize humans, such as ST131, are increasing, and the disease burden of fluoroquinolone-resistant *E. coli* infections is increasing (as mentioned earlier)

There is ample opportunity to research and develop new interventions