ANTIMICROBIAL RESISTANCE

Policy in Thailand

Background

AMR occurs when pathogens (bacteria, viruses, fungi and parasites) develop a resistance or tolerance to the medicines that are used to combat these microorganisms, such that these treatments are no longer effective.[1] AMR is a natural phenomenon, however the speed at which it occurs is impacted by how much exposure pathogens have to treatments. AMR has been increasing in low-, middle- and high-income countries around the world in recent years, and this trend is expected to continue.[2–4] This increase has been principally driven by the increase in global demand for antibiotics, which are overused and, in many cases, misused (e.g. the use of antibiotics for common viral infections, like the flu, in humans) and this has been compounded by falling investment in the development of new antimicrobial agents, which means that resistance to antimicrobials is growing at a quicker rate than new antimicrobial treatments are being developed. Eventually, this can lead to a situation where there are no viable treatments available for certain conditions.[5]

The indiscriminate use of antibiotics in the animal farming sector, where healthy animals are given antibiotics as a precaution, is just part of what makes the livestock industry responsible for an estimated 70-80% of the global total of antibiotic consumption.[6] However, antibiotics have undoubtedly been overused by humans and in agriculture practices (both livestock and crop farming).[7,8] Policy interventions need to consider the multisectoral nature of AMR if it is to be reduced as a public health threat, as resistant bacteria can reside in humans, animals and the environment – this is known as the One Health approach (Figure 1).[9] The United Nations also advocates the One Health approach to address AMR, and has formed a tripartite collaboration with The Food and Agriculture Organization of the United Nations (FAO), The World Organisation for Animal Health (OIE), and the World Health Organization (WHO).[10 *]

In 2019, the WHO listed AMR as one of the top ten threats to global health, due to the catastrophic impact it has the potential to cause.[7] The Review on Antimicrobial Resistance estimated that inaction in addressing AMR could result in an estimated 10 million deaths per year by 2050, and yield a much greater economic impact than that of the 2008-2009 financial crisis.[11] The WHO's 2015 Global Action Plan on AMR identified several key methods for reducing AMR as a threat, including through: 1) optimisation of the use of antimicrobials in both human and animal health; 2) reducing infections, through effective sanitation, hygiene and other infection prevention measures; 3) sustainable investment in the development of new antimicrobials, diagnostic tools and other interventions.[12]

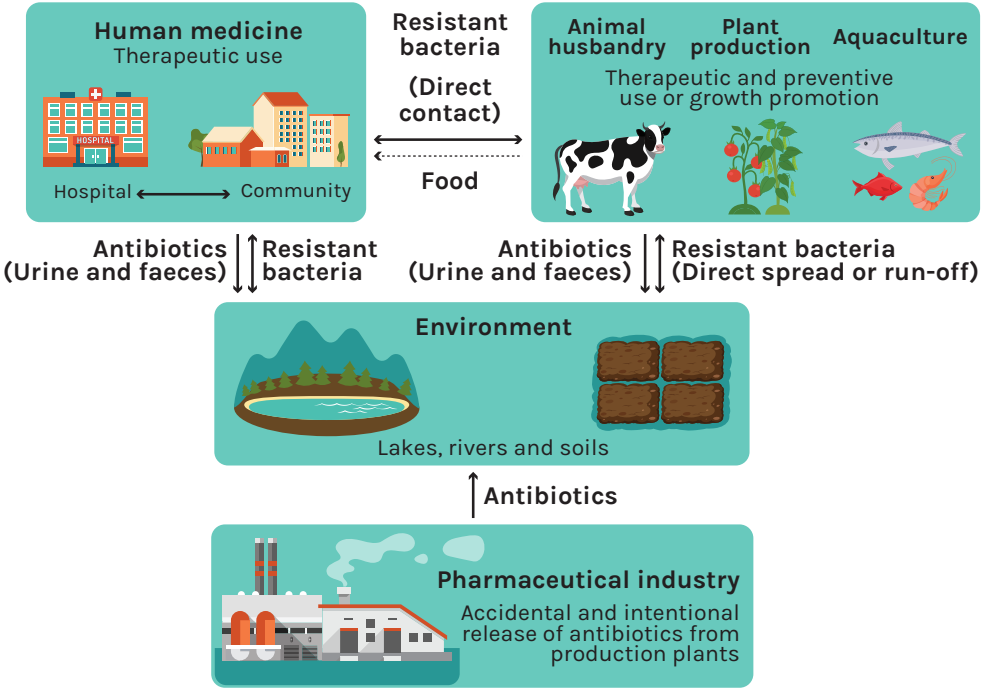

Figure 1. One Health depiction of antimicrobial resistance – adapted from White, A., Hughes, J.M. Critical Importance of a One Health Approach to Antimicrobial Resistance. EcoHealth.

Thailand and AMR

Antimicrobial drugs, including antibiotics, have been cheap and easily accessible for many years in south-east Asia; risk assessments conducted by the WHO have suggested that the region is at the highest risk for AMR in the world.[13] In 2010, it was estimated that 19,000 excess deaths were caused as a result of multidrugresistant bacterial infections.[14] Whilst in the USA and the European Union, it was estimated that between 23,000 and 25,000 excess deaths were caused by multidrug-resistant bacteria in these regions, respectively. Though the monitoring of pathogens and methods used varies between countries, making comparisons difficult, these statistics underscore the importance of addressing AMR in Thailand and the south-east Asia region.[14]

Thailand has been proactive in responding to the threat of AMR. In 2011, the independent, university-led Thailand Antimicrobial Resistance Containment and Prevention Program, or Thailand AMR Program, was founded; it estimated that there were 87,000 new AMR infections, an additional 3 million days of hospital stay, and 38,000 deaths of patients with AMR infections per year.[15, 16]

Separately in 2015, the Thai Ministry of Public Health (MOPH), sought to respond to the WHO's Global Action Plan on AMR which urged member states to develop national action plans within 2 years.[12] In 2017, Thailand then produced its first national strategic plan on AMR (NSP-AMR)[17] which was the product of The Coordination and Integration Committee on Antimicrobial Resistance, set-up in May 2015.[17] The goals of the 2017-2021 NSP-AMR to be achieved are:[18]

1. A 50% reduction in AMR morbidity
2. A 20% reduction in antimicrobial consumption in humans
3. A 30% reduction in antimicrobial consumption in animals
4. A 20% increase in public knowledge of AMR and awareness of appropriate use of antimicrobials
5. An increase in the capacity of the national AMR management system is increased to level 4 as measured by the WHO's Joint External Evaluation Tool (JEE) for International Health Regulations (2005)

To achieve these goals, a combination of six strategies to address key drivers of AMR (human, animal and environment) have been proposed a One Health approach with the outcome of stabilisation or decrease in AMR burdens across the country and minimisation of the socio-economic impacts from it (Figure 1).[10,19] Thailand's multi-stakeholder approach to AMR includes public, private and civil society groups, while also fostering global partnerships with the tripartite - WHO, OIE and the FAO – and through regional commitments (ASEAN).[10,20]

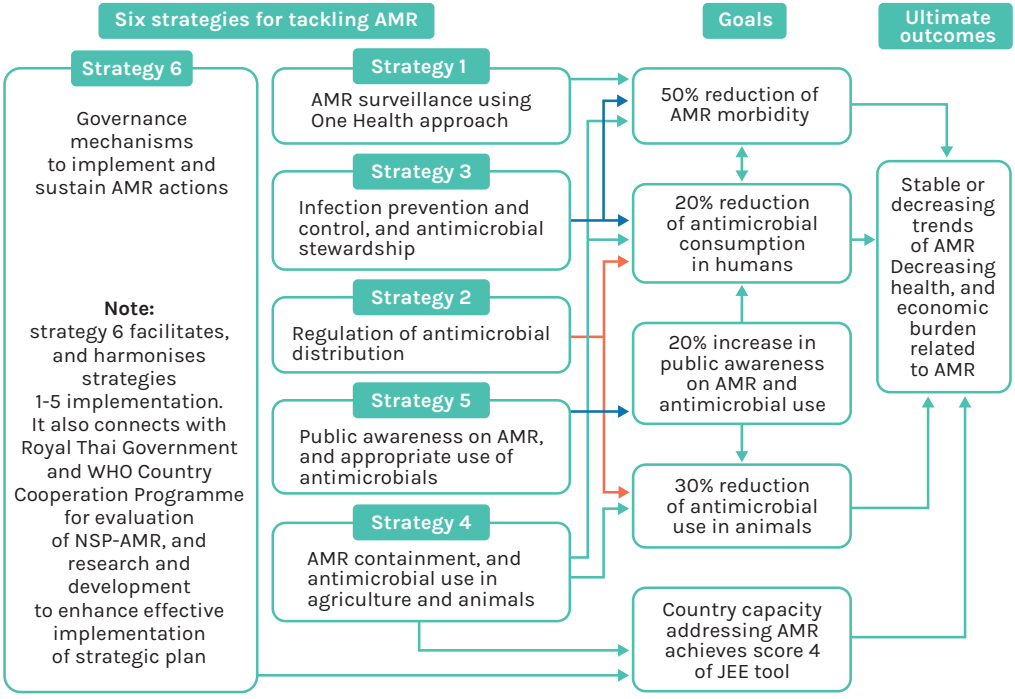

Figure 2. Six Strategies to Tackle AMR and achieve NSP goals – from Sumpradit N, Wongkongkathep S, Poonpolsup S, et al. New chapter in tackling antimicrobial resistance in Thailand. BMJ.

A national governance framework, referred to as the National Policy Committee on AMR, bringing together diverse stakeholders from across the country was set up to contribute towards the implementation of the NSP-AMR (implementation framework in Figure 2).[18] This Committee is further divided into 5 sub-committees to supervise and monitor progress towards each of these strategies. These sub-committees align with the One Health approach, each addressing important components such as antimicrobial drug management strategy (aligned with strategies 2 and 6), drug surveillance (strategy 1), addressing medicine use and medical belief systems in hospitals (strategy 3), antimicrobial management in agriculture and animals (strategy 4) and last, enhancing public trust in drugs and appropriate antimicrobial use (strategy 5). To ensure efficient engagement and benefit from pooled efforts of sub-committees, a working group has been instituted to coordinate activities and monitor progress.

As shown in Figure 2, progress towards Goals 1, 2 and 3 are keenly tied to the establishment of surveillance systems based on the One Health approach, as well as the regulatory mechanisms to supervise, manage and control the distribution and consumption of antimicrobials, both in hospitals and farming practices. Goal 4 and 5 focus on increased public knowledge and awareness on the risks and impacts of AMR through behaviour sensitisation as well as leadership and governance, acting as a foundation towards achieving the other objectives.

Steps taken so far

Goals 1, 2 and 3: 50% reduction in AMR morbidity, 20% reduction in antimicrobial consumption in humans and 30% reduction in antimicrobial use in animals [18-23]

Surveillance

Surveillance is vital for evidence-informed decision making and developing comprehensive awareness of AMR. In Thailand, the surveillance gap has been addressed through the National

Integrated AMR Surveillance System, also known as the Thai-SAC, which provides baseline antimicrobial consumption data from 2017 and outlines some processes for long-term AMR trend monitoring. Thailand's Food and Drug Administration (Thai-FDA) uses annual reports on the value and volume of all pharmaceutical products including antimicrobials, both human and animal, which pharmaceutical importers and manufacturers are mandatorily required to send, as per a 1987 Drug Act. This information forms the core of the national surveillance system and has been improved since the passing of the 2015 Animal Feed Quality Control Act, specifically for antimicrobial use in animals. Thailand has also set up a National Antimicrobial Surveillance Research Center (NARST) for monitoring AMR infections. NARST's enhanced surveillance capacity now makes it possible to differentiate between AMR rates and patterns across individual health districts, offering health professionals a better understanding of infection trends and prevalence in specific locations, targeting treatments accordingly. Recent implementation of the WHO Global AMR surveillance system (GLASS) in the country has also permitted identification of patients who have acquired AMR

resistant infections, while alerting stakeholders to timely trends on AMR infections both in hospitals and communities. An exchange of AMR data and integrated reporting is now operational among human, animal, food and environment as per the One Health approach. The Ministry of Agriculture and Cooperatives (MOAC) which houses the Department of Livestock Development (DLD) and Department of Fisheries (DOF) are implementing agencies for the animal sector within this surveillance ecosystem.

Antimicrobial consumption and use

To minimise the spread of resistant bacteria, infection prevention and control (IPC) and antimicrobial stewardship programmes (ASP) have been in focus, each using separate protocols and guidelines.

With increasing attention on IPC as one of the strategies to combat AMR outlined in the NSP-AMR, it is important to recognise the strengths and gaps of these mechanisms by using the WHO IPC assessment tool. As per the WHO, IPCs are made up of 6 core components namely programmes, guidelines, education and training, surveillance, multimodal strategies and monitoring and feedback of IPC practices.

A report by the International Health Policy Program and Chiang Mai University identifies that despite Thailand's strengths in incorporating many of these components, its approach remains fragmented since it only involves successful local or sub-national and facility-level interventions; the inadequacy of a comprehensive national programme on hospital-acquired infections (HAIs) and AMR is crucial to address this. Currently much of the activity is conducted by the Bamrasnaradura Infectious Disease Institute (BIDI), where no legal mandate, budgets or dedicated staff time is available towards IPC.

Stewardship programmes are coordinated activities to improve and measure optimal antimicrobial use. One such initiative is the WHO funded Antibiotic Smart Use Program to encourage the rational use of medicines, particularly aimed at minimising their use for common, community-acquired infections. This programme began in 2007 as a community hospital -based intervention and has since expanded to the national level[23]. Thailand also piloted an initiative using an automated computer-based prescription system at a tertiary hospital, which required patients to renew their prescription on the completion of

one cycle and present the physical prescription to buy the medicines from the attached pharmacy. However, details of ASPs as part of the NSP-AMR are not widely available. Community pharmacists have been identified as the most important stakeholders as they dispense medication and are the first points of contact in the health system for most people seeking care. Therefore, ASPs must aim to train them and improve their competencies as outlined by the WHO Competency framework.

Stewardship for food producing and companion animals and for agriculture is implemented in conjunction with Strategy 1 on surveillance under the One Health approach and Strategy 2 on regulating antimicrobial distribution for animals and agricultural use. Outside the hospital setting, the MOAC along with the Veterinary Council is responsible for ASPs in the animal husbandry sector, implementing them in farms, animal clinics, hospitals and Thai FDA pharmacies. The Health Policy and Systems Research on Antimicrobial Resistance (HPSR-AMR) led by a Faculty from Veterinary Sciences at Mahidol University plans to study AMU trends in companion

animals in 2021,[22] which will be the first-step in launching a routine monitoring mechanism for these animals in 2022. The MOPH and MOAC surveillance of veterinary drug residue and AMR contaminants along the food chain is also being introduced. In addition, a public-private partnership to support farmers in reducing antimicrobial use is also operational. A recent initiative to provide a new choice of meat products called 'Raised without antimicrobials (RWA)' has been piloted in pig farms.

There has also been progress in controlling distribution of antimicrobials, with a drive for reclassification of drugs. For example, no antibiotics in any form are available over the counter unless dispensed by pharmacists, and important antibiotics need to first be prescribed by a physician before they can be purchased. Meanwhile, regulations to ban the use of antimicrobials as growth promoters in the animal husbandry sector have also been introduced.

The NSP-AMR also promotes advocacy efforts of the OIE to improve awareness, establish standards and provide recommendations to all '*agents of change*' (stakeholders) across the continuum of antimicrobial consumption in animals – manufacturers of animal feed, wholesale and retail distributors, farmers/animal owners and

veterinarians.[23] The OIE campaign notes the headlining influence of veterinarians as they work directly with animals and can regulate antimicrobial drug prescriptions as well as advise farmers on best practices, which may help achieve Goal 4 of improved AMR awareness.

Goal 4: 20% increase in public knowledge of AMR and awareness of appropriate use of antimicrobials[24]

The NSP-AMR mandated the Ministry of Public Health (MOPH) to promote the appropriate use of antibiotics.[25] Similarly, Thai Health was mandated to partner with civil society organisations and the media to create public awareness campaigns on the same topic.[25] Furthermore, Thailand has encouraged researchers to generate and disseminate evidence on AMR through academic channels, to improve the public's understanding. The National Statistical Office and International Health Policy Program of the MOPH jointly developed an AMR module, which was added to the Health and Welfare Survey (HWS), a survey carried out in Thailand every 2 years.[26] The AMR module has four sections in total, assessing:

- Public recall of receiving information on the appropriate use of antibiotics and AMR
- Knowledge underlying appropriate antibiotic use and AMR
- Awareness of appropriate antibiotic use and AMR
- One-month point prevalence of antibiotic use among the public, including the source of acquisition and reason for taking antibiotics

The results of the 2017 HWS AMR module were used as the baseline for monitoring progress of Goal 4, with the second AMR module score assessed in 2019. The AMR module score will next be assessed in 2021. Three sub-indicators were developed to assess the knowledge and awareness of appropriate antibiotic use and AMR:

1. The percentage of Thai adults who provided correct answers to more than 60.0% of the true/false statements and one question on knowledge about appropriate antibiotic use and AMR
2. The mean score of the adult population on awareness of the importance of appropriate antibiotic use and awareness of AMR (maximum score of 5)
3. The percentage of adult population who have received information about AMR and appropriate antibiotic use

The 2017 and 2019 results of sub-indicators 1-3 are reported in Table 1 below.

Sub-indicator	2017	2019	Percentage change from baseline
1	23.7%	24.3%	2.5%
2	Not recorded in 2017	3.3	N/A
3	17.8%	21.5%	20.8%

Table 1. Objective 4 sub-indicator results for the Thailand National Strategic Plan on Antimicrobial Resistance 2017-2021

Table 1 shows that whilst sufficient progress has been made in sub-indicator 3, significant progress is still required on sub-indicator 1 to achieve Goal 4. Sub-indicator 2 was not recorded in 2017. 82.7% of survey respondents noted that health professionals were one of their information sources on antibiotic use and AMR, highlighting the key role these workers play in educating the public. Improving the effectiveness of messaging provided by health professionals may prove key to meeting Goal 4.

Goal 5: An increase in the capacity of the national AMR management system to level 4, as measured by the WHO's Joint External Evaluation Tool (JEE) for International Health Regulations (2005)[27–29]

The JEE Tool for the International Health Regulations serves as an implementation guide to address AMR in both humans and animals, including in the agricultural sector. The tool employs four indicators (each indicator has five scores or levels):

1. Detection of antimicrobial resistant bacteria by designated laboratories
2. Surveillance of infections caused by AMR pathogens at designated sentinel sites
3. Healthcare associated infection prevention and control programmes at designated facilities
4. Antimicrobial stewardship activities at designated centers

The criterion for achieving level 4 is the continued implementation of all aspects of the national plans for the four dimensions of AMR, listed above, achieving demonstrated capacity in designated laboratories, facilities, centers or sentinel sites for at least one year.

Thailand first used the JEE to assess the AMR management system in 2017, which indicated scores of 4, 3, 2 and 2 for each of the indicators described above, respectively. The next JEE assessment will take place in 2022. By implementing the NSP-AMR, existing sub-committees and working groups that were previously unconnected began working together with more oversight, coordination and alignment. In recognition of Thailand's progress, in the 2019 Global Health Security Index Report Thailand was ranked 22nd out of 195 countries in the world for prevention of AMR, which explicitly considered the capacity of countries to conduct effective AMR surveillance, detection, reporting and control.

Conclusion

Thailand's commitment to the issue of AMR as evidenced by the NSP-AMR goals and strategies offers promise as a good blueprint for other low- and middle-income countries navigating the challenges of AMR. However, like many others, this plan too will need to ensure that the most significant challenges of implementation and multi-stakeholder collaboration is addressed. As has been documented, the One Health approach will require that technical capacities be strengthened across these sectors and their efforts united, towards combating the burdens of AMR in Thailand.

Lessons Learned

- Develop a comprehensive National Action Plan for AMR: WHO recommends the establishment of a national action plan for AMR offers support on how to build out its components including implementation and monitoring and evaluation
- Follow a One Health approach: Recognise the interdisciplinary, multi-sectoral nature of AMR and ensure that the animal, environmental and human sectors work together. Also bring together a multitude of stakeholders from different government, non-government and civil society sectors form finance, governance, and infectious disease to work together
- Human resources for AMR: Provide additional routine training for healthcare professionals, pharmacists and community health workers on antimicrobial resistance to increase awareness, improve prescribing practices, and optimise antimicrobial use. Intro duce measures to improve hygiene and sanitation procedures within healthcare to reduce avoidable infections
- Implement or adjust regulations to restrict the availability of antimicrobials without a prescription, particularly antibiotics of strategic importance
- Conduct public information campaigns to improve the understanding of AMR in the general population

Bibliography

1. World Health Organization. What is Antimicrobial Resistance? Published 2017. https://www.who.int/features/qa/75/en/

2. Organisation for Economic Co-operation and Development. Antimicrobial Resistance: Policy Insights.; 2016. https://www.oecd.org/health/health-systems/AMR-Policy-Insights-November2016. pdf

3. Van Boeckel TP, Laxminarayan R. Global Trends in Antimicrobial Resistance in Animals in Low- and Middle-Income Countries. The Center for Disease Dynamics, Economics & Policy. Published 2019. Accessed May 12, 2020. https://cddep.org/publications/global-trends-in-antimicrobial-resistance-in-animals-in-low-and-middle-income-countries/

4. Sharma A, Hill A, Kurbatova E, et al. Estimating the future burden of multidrug-resistant and extensively drug-resistant tuberculosis in India, the Philippines, Russia, and South Africa: a mathematical modelling study. Lancet Infect Dis. 2017;17(7):707-715. doi:10.1016/S1473-3099(17)30247-5

5. Shallcross LJ, Davies DSC. Antibiotic overuse: a key driver of antimicrobial resistance. Br J Gen Pract. 2014;64(629):604-605. doi:10.3399/bjgp14X682561

6. Ritchie H. How Do We Reduce Antibiotic Resistance from Livestock? Our World in Data. Published 2017. Accessed May 14, 2020. https://ourworldindata.org/antibiotic-resistance-from-livestock

7. World Health Organization. Ten threats to global health in 2019. Published online 2019. https://www.who.int/news-room/feature-stories/ten-threats-to-global-health-in-2019

8. Review on Antimicrobial Resistance. Antimicrobials in Agriculture and the Environment: Reducing Use and Unnecessary Waste.; 2015. https://ec.europa.eu/health/amr/sites/amr/files/amr_studies_2015_am-in-agri-and-env.pdf

9. White A, Hughes JM. Critical Importance of a One Health Approach to Antimicrobial Resistance. Ecohealth. 2019;16(3):404-409. doi:10.1007/s10393-019-01415-5

10. World Health Organisation. FAO/OIE/WHO Tripartite Collaboration on AMR. Accessed May 14, 2020. https://www.who.int/foodsafety/areas_work /antimicrobial-resistance/tripartite/en/

11. Jonas O, Team W. Drug-Resistant Infections: A Threat to Our Economic Future.; 2017.

12. World Health Organization. Global Action Plan on Antimicrobial Resistance .; 2015. https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf? sequence=1

13. World Health Organization. Antimicrobial Resistance in the South East Asia. Accessed May 14, 2020. https://www.who.int/thailand/healthtopics/ antimicrobial-resistance

14. Lim C, Takahashi E, Hongsuwan M, et al. Epidemiology and burden of multidrugresistant bacterial infection in a developing country. Elife. 2016;5. doi:10.7554/eLife.18082

15. Thamlikitkul V, Rattanaumpawan P, Boonyasiri A, Sirijatuphat R, Jaroenpoj S. Operational Actions of the Thailand Antimicrobial Resistance (AMR) Containment and Prevention Program in Response to the World Health Organization (WHO) Global Action Plan on AMR. J Heal Syst Res. 2017;11(4).

16. Pumart P, Phodha T, Thamlikitkul V, Riewpaiboon A, Prakongsai P, Limwattananon S. Health and economic impacts of antimicrobial resistance in Thailand. J Heal Syst Res. 2012;6:352-360.

17. Health Systems Research Institute. Thailand National Strategic Plan on Antimicrobial Resistance 2017-2021.; 2017. http://www.fda.moph.go.th/sites/drug/Shared Documents/AMR/04.pdf

18. Ministry of Public Health. National Strategic Plan on Antimicrobial Resistance 2017-2021 Thailand: At a Glance.; 2017. http://www.fda.moph.go.th/sites/drug/Shared Documents/AMR/05.pdf

19. Sumpradit N, Wongkongkathep S, Poonpolsup S, et al. New chapter in tackling antimicrobial resistance in Thailand. BMJ. 2017;358:j3415. doi:10.1136/bmj.j2423

20. ASEAN. ASEAN Leaders' Declaration on Antimicrobial Resistance (AMR): Combating AMR through One Health Approach. Published 2017. https://asean.org/asean-leaders-declaration-on-antimicro bial-resistance-amr-combating-amr-through-one-health-approach/

21. Thai FDA. Antimicrobial resistance. Accessed June 25, 2020. https://amrthailand.net/

22. Thamlikitku V, Rattanaumpawan P, Boonyasiri A, et al. Operational Actions of the Thailand Antimicrobial Resistance (AMR) Containment and Prevention Program in Response to the World Health Organization (WHO) Global Action Plan on AMR. Journal of Public Health Research. 2017; 453-470

23. Malathum K. Antimicrobial Stewardship in Thailand. Accessed Jul 20, 2020. https://www.hsri.or.th/sites/default/files/attachment/4.1_KM_Antimicrobial_Stew.pdf

24. Thai Working Group on Health Policy and Systems Research on Antimicrobial Resistance. Thailand Surveillance of Antimicrobial Consumption in 2018 (Thailand SAC).; 2018.

25. World Organization for Animal Health (OIE). We Need You!

26. National Statistical Office, International Health Policy Program. Knowledge and Awareness of Antibiotic Use and Antimicrobial Resistance: The 2019 National Health and Welfare Survey in Thailand.; 2020.

27. Sommanustweechai A, Tangcharoensathien V, Malathum K, et al. Implementing national strategies on antimicrobial resistance in Thailand: potential challenges and solutions. Public Health. 2018;157:142-146. doi:https://doi.org/10.1016/j.puhe.2018.01.005

28. Chanvatik S, Kosiyaporn H, Lekagul A, et al. Knowledge and use of antibiotics in Thailand: A 2017 national household survey. PLoS One. 2019;14(8):e0220990. doi:10.1371/journal.pone.0220990

29. World Health Organization. Joint External Evaluation Tool: International Health Regulations (2005).; 2016. https://apps.who.int/iris/handle/10665/204368

30. Thai Working Group on Health Policy and Systems Research on Antimicrobial Resistance. 2019 Midterm Progress Report for Thailand's National Strategic Plan on AMR.; 2020.

31. Nuclear Threat Initative, John Hopkins Center for Health Security, The Economist Intelligence Unit. Global Health Security Index 2019: Building Collective Action and Accountability.; 2019. https://www.ghsindex.org/wp-content/up ads/2020/04/2019-Global-Health-Security-Index.pdf

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