Brief Report

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Evaluation of the global action plan on antimicrobial resistance in Japan during its first eighteen months

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Summary **Antimicrobial resistance (AMR) has garnered the most attention among public health concerns worldwide. Japan formulated a national action plan for AMR in April 2016. The plan seeks to reduce the amount of antimicrobials used in 2020 to two-thirds of the use recorded in 2013. Prescription surveillance (PS) is being used to monitor trends in the amount of antimicrobials used. PS estimates the number of patients prescribed an antimicrobial each day. The number of patients who were prescribed an antimicrobial under the action plan was analyzed by including dummy variables with other control variables. Data from April 1, 2011 to 30 September 30, 2017 were analyzed. When the number of patients with an infectious disease (1 of 13 specified diseases) served as a dummy variable, estimates indicated that the coefficient of that dummy variable was not significant. If the number of patients with an infectious disease (1 of 13 specified diseases) was excluded as an explanatory variable, then the estimated coefficient was significant. The global action plan in Japan might not reduce the amount of antimicrobials used. The current results indicated that the number of patients who were prescribed an antimicrobial did not decrease significantly after initiation of the action plan. This finding does not exclude the possibility that the average amount of antimicrobials used per patient has decreased.**

Keywords: Action plan, antimicrobial resistance, evaluation, prescription surveillance, surveillance

1. Introduction

Antimicrobial resistance (AMR) has garnered the most attention among public health concerns since the World Health Organization (WHO) launched a global action plan in 2011 with the slogan "No action today, no cure tomorrow." According to the O'Neil Commission (*1*), 0.7 million persons were estimated to have died from AMR in 2013. The number of people dying due to AMR is estimated to increase to 10 million people if no countermeasures are taken. The rate of AMR will continue to increase by its current rate. Therefore, the nations of the world have started to take action. The WHO global action plan asks all member nations to formulate a national action plan. Following formulation of a national action plan in the UK and USA, Japan formulated such a plan in April 2016. The plan seeks to reduce the amount of used antimicrobials in 2020 to two-thirds of the use in 2013 and to reduce the rate of AMR.

A surveillance system, like the system started prior to 2013, is needed to monitor trends in the amount of antimicrobials used. Moreover, a timely and precise surveillance system is needed to evaluate measures intended to reduce antimicrobial use. If the surveillance system is not timely or precise, then measures cannot be modified to be maximally effective.

Fortunately, prescription surveillance (PS) is in operation in Japan. Since 2009, the PS system has been operated by the Japan Medical Association, the Japan Pharmaceutical Association, the School of Pharmacy of Nihon University, and EM Systems Co. Ltd. This nationwide syndromic surveillance system has reported the estimated number of patients with influenza and

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chicken pox and the number of patients prescribed certain types of drugs based on prescriptions filled at outside pharmacies (*2,3*). Under this system, the number of patients is estimated each day based on the number of prescriptions for neuraminidase inhibitors, anti-herpes virus drugs, antipyretic analgesics, and multi-ingredient cold medications as well as antimicrobials. The number of patients is estimated by prefecture and by age group. As of the end of April 2017, approximately 10,000 pharmacies were participating, accounting for about 20% of all pharmacies. The estimated number of patients is shown on a dedicated web page (*http://prescription.orca.med.or.jp/kanjyasuikei/*) the following morning.

2. Materials and Methods

2.1. *Data*

In fact, PS estimates the number of patients receiving a prescription each day. The number of prescriptions issued for certain medications by pharmacies participating in PS is tallied by prefecture. This number is multiplied by the reciprocal of the proportion of pharmacies participating in PS by prefecture and by the reciprocal of the percentage of off-site prescriptions by prefecture. Antimicrobials are classified into five types: penicillin, cephems, macrolides, new quinolones, and other antimicrobials (*2,3*). The current study focused on the total number of patients prescribed an antimicrobial while ignoring the specific type of antimicrobial.

2.2. *Analysis*

The number of patients who were prescribed an antimicrobial was included as a dummy variable with other control variables. An equation was calculated using the least-squares method

$$x_t = \alpha + \sum_{j=1}^{14} \beta_j d_{jt} + \sum_{k=2}^{52} \delta_k w_k + \sum_{l=2}^{7} \eta_l z_l + \zeta\ h_t + \psi\ n_t + \varepsilon_t \quad (1)$$

where x_t represents the number of patients prescribed an antimicrobial on day t, d_{jt} denotes the reported number of patients with an infectious disease j per sentinel site during a week with t days, and where w_k, z_l, h_t, and n_t are, respectively, dummy variables for the epidemiological week, day of the week, holidays, and the day after a holiday. In these variables, the subscripts k and l respectively indicate the number of the epidemiological week and days of the week in t days. Here, α_i is a constant term, and δ_{ik}, η_{il}, ζ_i, and ψ_i respectively represent coefficients for dependent variables. To assess the robustness of Eq. 1, the equation was also estimated while excluding the number of patients with an infectious disease (1 of 13 specified diseases).

The number of patients with certain specified infectious diseases at a sentinel site is reported officially each week. These infectious diseases are influenza, RS virus infection, pharyngoconjunctival fever, group A streptococcal pharyngitis, gastrointestinal infections, varicella, hand, foot and mouth disease, erythema infectiosum, exanthem subitum, pertussis, herpangina, mumps, and mycoplasma pneumonia. For RS, official surveillance figures only indicate the total number of patients per week. This information has been published officially and continually by the Ministry of Health, Labor, and Welfare.

Data from April 1, 2011 to September 30, 2017 were examined.

2.3. *Ethical considerations*

Data from PS were aggregated and not linked to personal information related to patients, medical institutions, and pharmacies, thereby yielding anonymous data. Therefore, there are no ethical concerns raised by the use of these data in this study.

3. Results and Discussion

Figure 1 shows variations in the number of antimicrobial prescriptions. The average number of antimicrobial prescriptions was 480,280 overall, 491,065 before initiation of the action plan, and 441,635 afterwards.

According to Eq. 1 where the number of patients with an infectious disease (1 of 13 specified diseases) served as a dummy variable, the coefficient of that dummy variable was –9876.085, and its p was 0.581. The adjusted R^2, which represents the overall goodness of fit, was 0.6607. Therefore, approximately 70% of the variation in the number of patients prescribed an antimicrobial was explained by Eq. 1. Moreover, if the number of patients with an infectious disease (1 of 13 specified diseases) is excluded as an explanatory

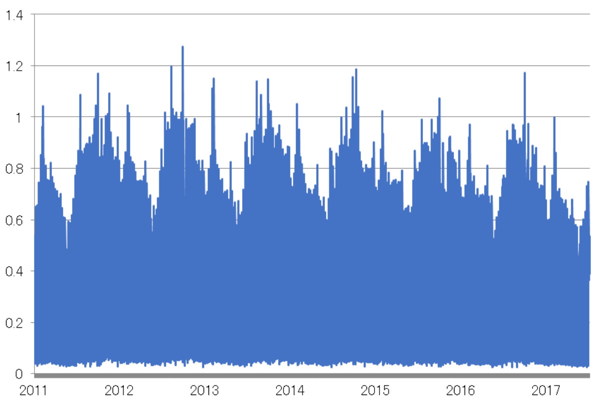

Figure 1. Variations in the number of patients prescribed an antimicrobial according to prescription surveillance (million patients). *Note*: Represents the daily estimate of the number of patients prescribed an antimicrobial according to prescription surveillance.

variable, then the estimated coefficient is –34109.6, and its p is less than 0.001. The adjusted R^2 was 0.6486.

Results indicated that the global action plan in Japan will significantly reduce the amount of antimicrobial use when the number of patients with an infectious disease (1 of 13 specified diseases) is excluded as an explanatory variable. However, including that number resulted in an insignificant reduction. The significant reduction in antimicrobials appears to reflect a lower incidence of the 13 specified infectious diseases after the plan was initiated than before it was initiated. Moreover, the estimated coefficient –34109.6 was only 7.1% of the average of the amount of antimicrobials used in all periods. Therefore, the global action plan in Japan might not reduce the amount of antimicrobials used.

However, the current finding does not necessarily mean that the global action plan in Japan has failed to reduce antimicrobial usage. Here, the amount of antimicrobials used was defined as the number of patients who were prescribed an antimicrobial each day. The amount of the antimicrobial is not specified. To be more accurate, the current results suggest that the number of patients prescribed an antimicrobial has not decreased markedly since initiation of the action plan. This finding does not exclude the possibility that the average amount of antimicrobials used per patient has decreased

4. Conclusion

This study examined the amount of all antimicrobials used without considering the type of antimicrobial. The action plan in Japan seeks to decrease all antimicrobials as well as certain type of antimicrobials. Therefore, the effects of the action plan must be assessed in terms of the type of antimicrobial. This is a topic for future study.

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