Course	Master of Science in Global Health and Medicine	Name	Thanawat KHONGYOT	
Thesis	Relationship between Fluoroquinolones Consumption and Levofloxacin resistance			
Title	Streptococcus pneumoniae in Japan: Ecological study.			

**Introduction:** Antimicrobial resistance (AMR) as a challenging problem in the world. Levofloxacin is a fluoroquinolone that uses for respiratory tract infections in both upper and lower parts. Levofloxacin is the top-consuming antibiotic among fluoroquinolones that might impact increasing AMR in Japan. Nowadays, we have limited data on the relationship between levofloxacin resistance *Streptococcus pneumoniae* (Levo-SP) and fluoroquinolone use in Japan.

**Objective:** This study will identify the geographic distribution of total fluoroquinolones consumption and levofloxacin resistance *Streptococcus pneumoniae* (Levo-SP) and elucidate the association among potential explanatory variables to Levo-SP.

Method: Ecological study is used for the analysis. The ecological variables were collected from three databases, including One health platform database Japan, e-stat, and the National Institute of infectious diseases (NIID). Levo-SP assigned as the dependent variable, fluoroquinolone consumption (DID, defined daily dose per 1,000 inhabitants) will be set as independent variables. The remaining variables will be the potential explanatory variables. All collected variables were described as prefectural level (47 prefectures, 141 observations) during 2014-2016. Regression diagnostic will use to control the quality of the variables by using multicollinearity, heteroscedasticity, linearity, normality, and interaction testing. The geographic distribution will use for univariate explanation. Scatter plot and Pearson's correlation explain as bivariate analysis. Multiple linear regression, stepwise (significant selection), stepwise (Bayesian information criterion (BIC) selection), best subset selection, and lasso "least absolute shrinkage and selection operator," are the tools to select the potential explanatory variables.

<sup>\*</sup> The abstract, containing the objective, method, result and conclusion should not exceed 300-500words and printed double sided on A4 paper)

## **Abstract of Master's Dissertation**

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Results: 30 ecological variables were included in this study. The geographic distribution of the mean Levo-SP (2014-2016) was the highest in Chugoku (6.61%), followed by Shikoku (5.47%) areas; meanwhile, the nationwide resistance was reported as 4.50%. Hiroshima (8.33%), Okayama (8.60%), and Saga (8.167%) were the highest resistance prefectures. Simultaneously, the total fluoroquinolone DID (A-DID) was highest in Shikoku (DID 3.594), follows by Kyushu (DID 3.316) and Chugoku (DID 3.188), respectively. Kagawa (DID 3.783), Ehime (DID 3.683), and Oita (DID 3.663) were showing the most intense fluoroquinolone consumption. Regression diagnostic was used to verify the variables before start regression analysis. Four variables (medical expense ratio) are excluded due to multicollinearity. 26 ecological variables are the final variables for analysis. Dependent variable (Levo-SP) used log transformation to improve homoscedasticity and linearity before starting variable selection. The analysis found the association between fluoroquinolone consumption and Levo-SP. Furthermore, the additional selected variables were the nurse assistants' number, levofloxacin resistance *Klebsiella pneumoniae* (Levo-KP), clinic bed number, and medical clinic number.

Conclusion: We confirmed the association between fluoroquinolone consumption and Levo-SP. Nurse assistants might be the possible explanatory factor of increasing AMR. Preventive measures should be a concern in health care professionals, along with the prescription of antimicrobial medication. Improve the primary care service is the potential strategy for reducing AMR. However, the ecological fallacy needs to consider; the individual analysis can help to verify the results.

## Word count: 463

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