早稲田大学審査学位論文
博士（人間科学）

健康行動としての予防接種とそれに影響を与える因子の研究

－健康行動理論および公衆衛生学的見地から－

Vaccination as Health Behavior and Factors Influence on Vaccinations in Japan

－Behavior Theory and Public Health Perspectives－

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List of Abbreviations

Chapter I

WHO The World Health Organization

HBM Health Belief Model

SCT Social Cognitive Theory

TTM Transtheoretical Model

TRA Theory of Reasoned Action

TPB Theory of Planned Behavior

TMSC Transactional Model of Stress and Coping

FOBT Fecal Occult Blood Test

AFR African Region (WHO definition)

EUR European Region (WHO definition)

SEAR South East Asia Region (WHO definition)

GVAP Global Vaccine Action Plan

NIP National immunization program

DTaP Diphtheria, Tetanus, and acellular Pertussis (vaccination)

BCG Bacillus de Calmette-Guerin

Hib Haemophilus influenzae type B (vaccination)

HPV Human Papilloma Virus (vaccination)

MR Measles and Rubella (vaccination)

MMR Mumps, Measles, Rubella (vaccination)

RCV Rubella-containing Vaccines

CRS Congenital Rubella Syndrome

OPV Oral Polio Vaccine

VAPP Vaccine-associated Paralytic Polio

IPV Inactivated Poliovirus Vaccine

TB Tuberculosis

Flu Influenza

NIID National Institute of Infectious Disease (Japan)

VPD Vaccine Preventable Diseases

JRF WHO-UNICEF Joint Reporting Form on Immunization

OECD Organization for Economic Co-operation and Development

PRC People's Republic of China

SLV School-located Vaccination

Chapter II

OR Unadjusted Odds Ratio

aOR adjusted Odds Ratio

Chapter III

WTP Willing To Pay

Chapter IV

SRH Self Rated Health

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Introduction

Outline of the Studies

This dissertation examines immunization as a health behavior and investigates factors that influence vaccination acceptance. Chapter I describes the background and literature review, outlining a brief history of communicable diseases, public health and immunization development as well as the history and definitions of theories and models of health behavior and health promotion. The author explores the health belief model (HBM), the most popular health behavior model for vaccinations. Current and past vaccination systems in the world and Japan are also examined to find characteristics and issues that Japan currently must address. From the literature review, two current public health problems related to vaccinations were selected as research questions. They were the increase in complications from natural mumps because of the mumps vaccination rate drop and excess mortality during influenza seasons mainly in the elderly population due to the low vaccination rate of seasonal influenza vaccines.

Chapter II describes the common background and methodology in the studies in this dissertation for the two questionnaire surveys. Study I surveys the maternal population to investigate factors that influence not vaccinating their children against mumps; Study II surveys the elderly people in a community to investigate factors that affect seasonal flu vaccination uptakes. One of the major pillars in this dissertation is methodology research. This chapter presents the literature review and describes the mixed method research. Proper quantitative analysis is discussed and the reason for the method used in the studies in this paper.

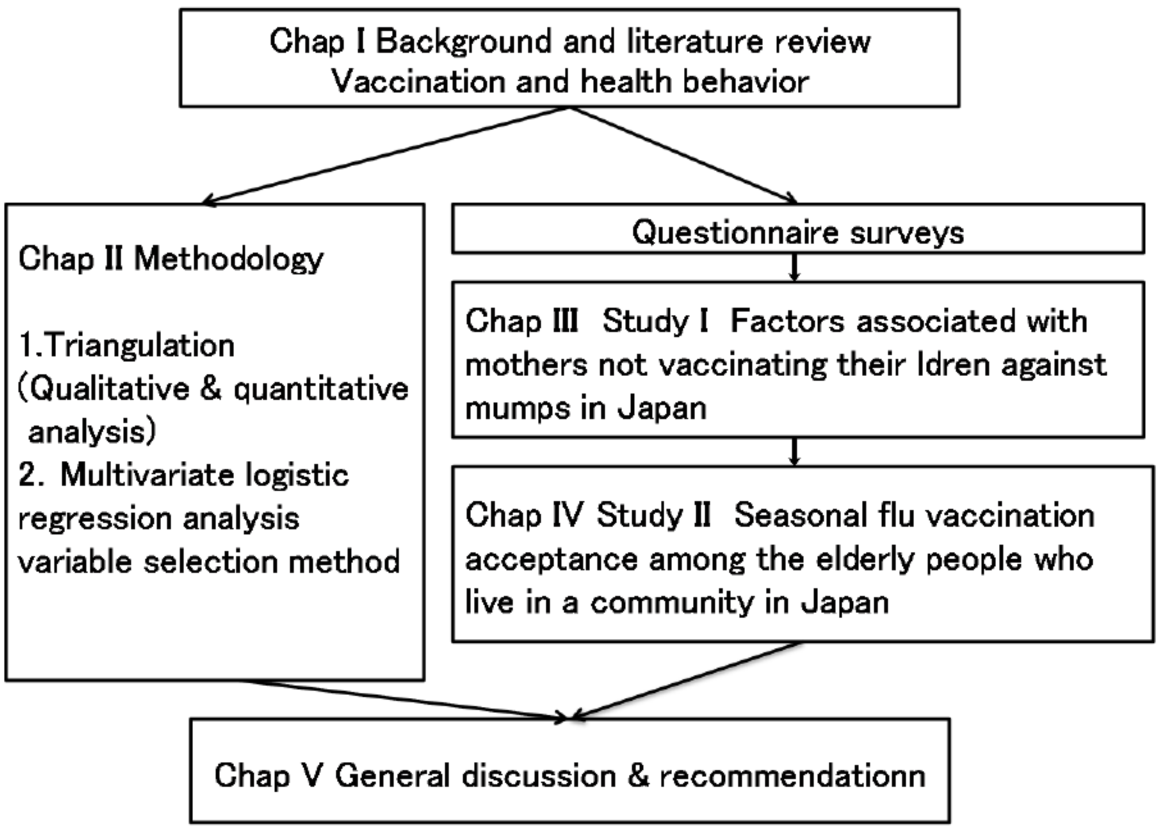
Chapter III describes Study I: Factors associated with mothers not vaccinating their children against mumps in Japan. In this chapter, the author targeted the maternal population to explore the factors influencing the low mumps vaccination rate of children. Another pillar of the studies in this paper was to investigate the HBM analysis of vaccination behavior. These factors were extremely helpful in the analysis. We found factors including HBM factors that affected maternal awareness for vaccine uptake of their children at the individual level and other factors that must be considered more broadly at ecological levels.

Chapter IV describes Study II: Seasonal flu vaccination acceptance among the elderly who live in a community in Japan. In Study II, we analyzed factors of characteristics, HBM factors and factors known to influence health for elderly populations such as Self-Rated Health and social activities and participation. We found factors affecting seasonal influenza vaccination uptakes among the population. HBM factors were proven to be useful predictors in the study. This chapter describes the results and findings of a quality analysis of an open-ended question to address the idea for influenza vaccinations.

Chapter V summarizes and presents the conclusions from Studies I and II. Chapter V especially focuses on the wrapping up methodology applied in the studies in this paper and the results of the HBM analysis focusing on common and different factors between Studies I and II, comparing them with previous studies. Chapter V includes implications obtained from the studies and proposes an ecological model for health promotion to address the public health issues as objectives presented in this paper.

The author shows the flow of studies in this thesis in Chart 1 below

Flow chart 1: Outline of the study



Chapter I

Background and literature review

1.1 Emergence of infectious diseases and establishing a vaccination system

In public health history, controlling infectious diseases and the invention of vaccinations are very important. The history of pneumonia started at least several thousand years ago. In the Middle Ages, infectious diseases cost many human lives; the spread of plague, smallpox and measles was severe in the 14th century; communicative disease fatalities were one-third of the total population (2). When 8 to 20 percent of the total death rate was due to smallpox in some European countries in the 18th century, E. Jenner (1749-1823) discovered people inoculated from cowpox residue did not develop smallpox later (1). L. Pasteur (1822-1895) further developed inoculation and established vaccination in the 19th century, focusing on immunology (2). K. Frankel (1861-1915), E. Behring (1854-1917) and S. Kitasato (1852-1931) developed serum therapy for tetanus that lead to immunization against other infectious diseases today (3). Along with this immunization development, the epidemiology development first established by J. Snow (1813-1858), who found the source of a cholera outbreak was a cholera germ named Vibrio Cholerae in London in 1854, contributed to modern public health history (1, 37).

1.2 Vaccinations as health behavior

1.2.1 Health behavior

Health behavior has many definitions. In the 1950s, the Medical Education Committee of the American Medical Association (AMA) recommended all medical education institutions incorporate human behavior as a basic academic discipline. Since then the role of human behavior in medical education and health promotion has attracted attention (28). Matarazzo defined *Behavioral health* as an interdisciplinary field dedicated to promoting a philosophy of health stressing *individual responsibility* in applying behavioral and biomedical science knowledge. He also established techniques for *maintaining* health and *preventing* illness and dysfunction through a variety of self-initiated individual and shared activities (29). Parsons analyzed that sickness goes beyond disease and defined that people who have fallen ill have rights and obligations within social norms: "1) The sick person is exempt from normal social roles, 2) the sick person is not responsible for their condition and obligations; 2) the sick person should try to get well, 3) the sick person should seek technically competent help and cooperate with the medical professional (16)." Kasl and Cobb (1966) define three categories of health behavior: 1) preventive health behavior, 2) illness behavior and 3) sick-role behavior(s) (19). Adhering to this definition, Gochman defines health behavior as an individual's beliefs, expectations, motivations, concepts and other such factors that include preventive and adaptive behavior relating to health maintenance, restoration and improvement (15, 20). According to this definition, health behavior includes utilizing health services such as physician visits, vaccinations and screenings, adhering to treatment and voluntary healthy behavior including a proper diet, sleeping, exercise and not smoking.

In this paper, the definition of health behavior follows Gochman's definition and considers the attitudes and actions concerning vaccination as a health behavior (21).

1.2.2 Health behavior and health promotion

Along with the development of health behavior study, epidemiological researchers focusing on health behavior and lifestyle factors including diet, smoking and exercise increased. The most well-known relevant research was the Framingham Heart Study, which started in the 1940s; clinical and physical factors as well as lifestyle factors were researched to study the risk factors for cardiovascular diseases of people in Framingham, Massachusetts, USA.

Health was defined as "… a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" in the Constitution of the World Health Organization in 1946.

After that the Declaration of Alma-Ata was adopted at the International Conference on Primary Health Care convened in Alma-Ata, Kazakhstan in September 1978, the member countries set "Health for All" as a goal and recognized the importance of primary health care and health promotion (163).

In the first International Conference on Health Promotion in Ottawa organized by The World Health Organization (WHO), health promotion was defined as "the process of enabling people to increase control over, and to improve, their health". The Ottawa Charter was established to achieve "Health for All by the year 2000 and beyond" (120). At this conference, the importance of supporting education and the social environment to facilitate healthy behaviors and lifestyles was proposed. To provide a framework for environment and public policies to urge healthy behaviors in the population, Healthy People 2000 in the United States and Healthy Japan 21 were established after (37).

1.2.3 Health behavior theories and models

1.2.3.1 Health Belief Model

Many health education intervention theories and models have been created to facilitate health education.

The oldest health behavior model that explains health behavior at the individual level is the Health Belief Model (HBM). Hochbaum (1958) first developed HBM in the 1950s to examine why people failed to undergo tuberculosis screening when they believed that they were susceptible to tuberculosis and recognized the benefits of the screening tests. HBM was later formulated by Becker *et al.* who defined key constructs such as perceived susceptibility to disease, perceived severity of disease, perceived benefits, perceived barriers, perceived self-efficacy and cues to action (17, 18). HBM has been and is still widely used to analyze individual preventive behaviors such as HIV/AIDS-related prevention behaviors (141, 147) and breast cancer screening behaviors (143, 144).

1.2.3.2 Another behavior models

Another significant development of health behavior and health education theory is Social Cognitive Theory as Social Learning, Miller et al. (1941) first established as Imitation Theory of behavioral change in the psychological field. Bandura conceptualized as Social Learning through Imitation (1962) where Rotter added concepts of expectancy to internal and external control for self-reinforcement in 1954 (165).

Bandura defined and named as Social Cognitive Theory (SCT) from Social Learning Theory in his 1986 paper (124). The current SCT components are the environment, situation, behavioral capability, expectations, self-control, observational learning, reinforcements, self-efficacy, emotional coping responses and reciprocal determinism (125, 126, 127). SCT has been applied to health education programs. One of the most popular health behavior intervention programs adopting SCT is the Gimme

5 "let's eat more fruits and vegetables" program to improve children's eating habits. This nutrition intervention program especially focuses on observational learning where children tend to imitate the behaviors of others and to improve their environments such as homes and schools. This program was established in 1993 (Domel and al.) and has repeatedly been used in schools and homes and become a national program in the US (146).

The next significant health education model is the Transtheoretical Model (TTM) that Prochaska first established from psychotherapy therapies in 1984 (123). The theory focuses on which stage individual behavior is on, using a continuum with contemplation, preparation, action, maintenance and termination. TTM looks for the leverage to intervene to change behaviors.

The Theory of Reasoned Action (TRA), which was first proposed by Fishbein in 1967 and formulated with Ajzen in 1975, is another health education theory. They insisted that the most important determinant factors for health behavior are subjective norms and the intention to perform a behavior (121). Later Ajzen and Driver added recognizable behavioral control as a new factor and established the Theory of Planned Behavior (TPB) in 1991 (122). Many programs for promoting participation in exercise and physical screening tests use TRA and TPB (128, 129).

The Transactional Model of Stress and Coping (TMSC) is another significant behavioral model. Lazarus and Cohen (1977) first formulated it in 1977 to address stressful events. They thought a stressful event was mediated by the first appraisal of the affected person, followed by the affected person's second appraisal of the psychological, social and cultural resources at his or her disposal (Lazarus & Cohen, 1977; Antonovsky & Kats, 1967; Cohen 1984) (140). TMSC has been used in stress coping programs for patients with HIV/AIDS and breast cancer or other stress coping programs (130, 131, 148).

1.2.3.3 Health Belief Model and vaccinations

As specifying each construct of HBM is comparatively easy, HBM has been used widely from the 1950s by health behavior researchers of preventive behaviors and to obtain insights and frameworks for health behavior interventions at the individual level.

HBM is the most popular health behavior model in vaccination behavior research covering influenza (134, 135), pertussis (136) and other uptake studies. Brewer *et al.* performed a meta-analysis of thirty-four HBM based vaccination behavior studies (N=15988) and analyzed each constituent of HBM such as perceived susceptibility, perceived severity and perceived likelihood. They found that all the constituents significantly associated with vaccination behaviors were effective determinant factors (137).

Some studies in health behavior such as nutrition uptake and smoking cessation have used HBM theory in Japan (158, 166). Recently we have observed vaccination studies based on HBM analysis in Japan, however, the number is still enough (57, 138).

1.3 Social factors and health

1.3.1 Social factors

Many studies investigate the influence of social factors such as income, living places, social activities, social connections or social networks and social support on health (151, 154, 155). Kondo *et al.* reported that not only life styles such as smoking, exercises, dietary habits, sleeping but also health outcomes such as oral health, anxieties, depression and others were influenced by social factors (31, 157).

Cohen defined social integration as including social roles, social participation, a sense of belonging to one's community, self-expectancy for one's status, social networks, contribution to the community and social networks of friends or families (1988). Cohen *et al.* indicated that as people are better socially integrated, they can more easily obtain beneficial information resources for their health (152). Social networks and social support have extended to social capital including social characteristics such as social norms, trust and social networks (Putnam 1993) (149). There are a various definitions about social capital from macro or micro perspectives and sociology or public health perspectives so that a definition is not made in this paper. Kawachi suggests in his book that people benefitting from better social capital have reported better health than those with lower social capital (176).

Social networks and social support are known to influence Health Behavior, including preventive behavior such as smoking secession and dietary habits. In immunization studies, cues to action factors of HBM such as friends' or relatives' recommendation, family doctor's advice and support relevant to social networks are shown to influence on immunization activities (135).

1.3.2 Social and cultural factors and health service usage

The Organization for Economic Co-operation and Development (OECD) utilizes preventive services such as the mammography, Pap smear screening test ratio and influenza acceptance ratio among the elderly 65 years and older as health care quality indicators. Many studies investigate social factor influences on these indicators; many of these studies suggest that these indicators decline in low socio-economic status and low hospital density locations such as rural places (53, 161, 54, 162). Casey *et al.* using a large scale database Behavioral Risk Factor Surveillance System (BRFSS) and Area Resource File in the Unites States, have shown that preventive service usage such as Fecal occult blood test (FOBT), proctosigmoidoscopy, mammogram, pap smear screening test and influenza vaccination significantly declined in the population living in rural places (53).

For immunization behaviors, Nagata (Jason) *et al.* suggested in their systematic review of 58 both qualitative and quantitative studies about seasonal influenza vaccine uptake in the elderly population and concluded that social determinants were the most important factors to influence seasonal vaccination uptakes (56).

Similarly, Cultural factors, genders, and ethnicity are known to influence on immunization acceptance (52). Ward *et al.* argued how culture determines cognition for immunization behavior of acceptance or rejection by adopting comprehensive sociocultural understandings (178). Pleis *et al.* reported a cultural and biological difference of gender (male and female) in seasonal influenza vaccination acceptance using a large scale data of the National Health Interview Survey (58).

In Japan, there are studies about the effect of social factors on health care services. Endo *et al.* (2004) have shown unfair access for low-income people to health care services from 1984 due to the aging society (169). Some children's studies suggest that the parental income effect for their children's hospital or health service usage is limited (167, 168). In gerontology studies, Yamada suggested that elderly people with low income accessed home long-term care service below their needs, but this has been ameliorated since 1998 (170). However, the number of these studies especially about preventive service is still low in Japan, even if we include other preventive service studies such as cancer screening and mammographies (57, 157, 171).

1.4 Current vaccination systems

1.4.1 Vaccination in the world today

The WHO issues vaccine position papers for vaccine preventable diseases (VPD) to all member countries providing recommendations and strategic plans to achieve regional goals (39). The WHO also regularly disseminates information about infectious diseases, epidemiological reports and vaccine safety reports, using WER (Weekly Epidemiological Records) (40).

The Global Vaccine Action Plan (GVAP) adopted by the 194 Member States of the WHO in May 2012 provide clear five goals (118). They are 1) Achieve a world free of poliomyelitis, 2) Exceed the Millennium Development Goal 4 target for reducing child mortality, 3) Meet global and regional elimination targets, 4) Meet vaccination coverage targets in every region, country and community, 5) Develop and introduce new and improved vaccines and technologies in order to prevent millions of deaths by 2020 by expanding vaccination access for people in all communities.

GVAP strengthen routine immunization to meet vaccination coverage targets; accelerate control of vaccine-preventable diseases with polio eradication as the first milestone; introduce new and improved vaccines and spur research and development for the next generation of vaccines and technologies (41). Under this action plan, the WHO estimates that 24 - 26 million child deaths can be prevented if all countries use 10 vaccines (hepatitis B, Haemophilus influenza type b, human papillomavirus, Japanese encephalitis, measles, meningococcus A, pneumococcus, rotavirus, rubella and yellow fever) and targetted 94 countries to achieve the goal during this decade

(42).

1.4.2 Vaccination in Japan today

Modern infectious disease law in Japan started with the Communicable Diseases Prevention Law enacted in April 1897; only severe and fatal infectious diseases were stipulated such as cholera, dysentery, typhoid, variola, epidemic typhus, scarlet fever, diphtheria and plague. Due to the progress in sanitation, medicine and public health along with the vaccination system, we can now live free from problems concerning these communicable diseases. The modern Preventive Immunization Law was established in 1948 where smallpox, typhoid fever, diphtheria, tetanus, and acellular pertussis (DTP) was included as immunization program (2). The current infectious diseases and vaccination systems were established under the Infectious Diseases Control Law enacted in 1999 (2).

1.4.2.1 Routine immunization system

Under the current National Law amended in December 2013, Type I Disease care is defined as "implementing immunization to prevent outbreaks of infectious diseases or epidemics, contributing to the improvement and promotion of public health as well as providing swift relief for health damages resulting from vaccinations." The diseases include diphtheria, pertussis, polio, measles, rubella, Japanese encephalitis, tetanus, tuberculosis, Hib, HPV, pediatric streptococcus pneumonia and smallpox. Influenza vaccination was included in NIP as the classification of Type II Disease for those 65 years old and older and for those from 60 to 64 with chronic cardiac, respiratory and renal diseases. This was defined as "implementing immunization to prevent individuals from contracting a disease and, if they do contract the disease, to reduce the severity of the disease, thereby contributing to public health" in 2001.

Under the Preventive Vaccination Law, combined diphtheria, tetanus and acellular pertussis vaccination (DTaPI), combined diphtheria and tetanus II, combined measles and rubella (MR), Bacillus de Calmette-Guerin (BCG), polio and Japanese encephalitis are incorporated in the national immunization program and are recommended for mandatory vaccination (38).

With the recent amendment to the Preventive Vaccination Law in Japan, haemophilus influenza type b (Hib), human papillomavirus (HPV) and pediatric streptococcus pneumonia were added to the routine vaccination schedule in March 2013 by amending the Vaccination Law, Act No. 69 of 1976. However, the government had withdrawn a recommendation for HPV vaccine due to frequent reports of side effects.

Currently, the WHO recommends BCG, hepatitis B, polio, DTP, Hib, pneumococcal (conjugate), rotavirus, measles, rubella and HPV for all population and mumps, seasonal influenza and chicken-pox for certain populations (117). The Japanese vaccination system had a long delay compared to other developed nations (48). The term called 'vaccine gap' had been used for a long time to express the delay (82) up to amending the Preventive Vaccine Law to add the three vaccinations for Hib, HPV and streptococcus pneumonia in 2013. Following the amendment, chicken pox vaccination that was delayed significantly was included in 2014 (119). However, seasonal influenza, mumps, hepatitis A and B and rotavirus vaccinations are not mandatory yet.

1.4.2.2 Non-mandatory immunization system

Currently, seasonal influenza for those 64 years of age and below, mumps and hepatitis A and B vaccinations are not still mandatory. One hundred and seventy-seven WHO member countries have already included a hepatitis B vaccination program in NIP in 2008 and 118 have included mumps vaccination.

No national surveillance data exists for non-mandatory vaccinations so that the correct vaccination rates among eligible children are unknown, but it is estimated to be about 5 percent for Hib vaccination, 30 percent for mumps and 50 percent or below for seasonal influenza in children (1,2,3).

1.4.3 Immunization and related issues in Japan

1.4.3.1 MMR combination vaccine

The WHO recommends including the Mumps, Measles, Rubella (MMR) combination vaccine in mandatory vaccinations, but the MMR is not used in Japan. In 1989, the first MMR combination vaccine (Kitasato AIK-C measles, Biken's Urabe Am9 mumps and Takeda To336 rubella) was authorized and introduced as a mandatory vaccine in the national immunization program (NIP). Takeda MMR (Schwarz FF8 measles, Torii's mumps and To336 rubella), Kitasato MMR (Kitasato AIK-C measles, Hoshino mumps and Takahashi rubella) and Biken MMR (Tanabe measles, Urabe Am9 mumps and Matsuura rubella) followed this (67). During this period, many side effects, mainly aseptic meningitis, were reported, three children died, four were handicapped and 10,032 needed medical assistance (4). The incidence of aseptic meningitis was reported to be from 1 in 500 to 900 vaccines to 1 in 1200 (70, 71). There was concern that mumps vaccines contained in MMR vaccines caused these adverse events (67,83, 84, 85, 86, 87, 89); the Ministry of Health, Welfare and Labor conducted nationwide surveys and tested mumps viruses isolated from cerebrospinal fluid for their relation to the mumps vaccine, using nucleotide sequence analysis (67,68,88). As a result of these surveys and tests, the Urabe strain included in mumps vaccines was identified as the cause. In 1993, the MMR was subsequently withdrawn from NIP in Japan (4,70). Since then a measles and rubella (MR) combination vaccine has been given in NIP and a single dose mumps vaccine (Hoshino-L32 or Torii) has been used as a non-mandatory vaccine.

1.4.3.2 Measles outbreaks and measles immunization

Measles is a severe communicable disease; the fatality rate may reach 20 percent. In 2000, many lives were lost due to measles outbreaks and about 40 percent of a total of 1.4 million deaths from VPD worldwide was estimated to be from measles (118). The WHO established objectives to strengthen vaccine dissemination in the African Region (AFR) and the South-East Asia Region (SEAR) to decrease the number of measles deaths. The WHO verified measles elimination in the European (EUR) and the Eastern Mediterranean Regions (EMR) by 2010, and the Western Pacific Regions (WPR) including Japan by 2012. Under these goals, the annual estimated measles deaths declined by 72 percent in 2013 (118).

In Japan, a measles outbreak was observed mainly in a population of small babies in 2001 and 286,000 cases were reported. This outbreak was due to the measles vaccination rate decline caused by the MMR vaccination withdrawal from NIP in 1993 and the measles vaccination rate of the population was estimated to be about 50 to 60 percent (69, 104). Since then, the measles vaccination has been mandated to be taken twice and improving the national surveillance data system was set as a goal (103).

The Japanese Government partially amended the Preventive Vaccination Law on July 29, 2004; the first and the second doses of the MR combination vaccine were mandated to be taken 12 to 24 months and 5 to 7 years after birth. However, an outbreak was observed in 2007 and 2307 measles cases were reported mainly in the single dose vaccination population with a median age of 17 years old, of which 44 percent were ten years old and older and the highest age group was the 20 to 24 year old adult population with many severe cases (105). The United States had already declared measles eliminated in 2000 and Japan was regarded as a measles exporting country (106). For this reason, a temporary measure was taken for five years starting from 2008 and a third additional dose was given to first year junior high school students followed by a fourth dose for senior high school students. Due to this temporary measure, the measles vaccination rate increased to 95 to 98 percent; reported cases dropped as low as 232 in 2013.

1.4.3.3 Rubella outbreak and rubella-containing immunization

When children contract rubella, many cases are mild. However, when pregnant women contract rubella, 90 percent of fetuses contract the disease from vertical transmission from the mother. The transmission causes congenital rubella syndrome (CRS) including heart disease, hearing loss and eyesight and mental disorders in the fetuses. In 2000, WHO published its first position paper on rubella vaccine to guide the introduction of rubella-containing vaccines (RCVs) into national childhood immunization schedules (109). Under this recommendation, the Americas (WHO definition) achieved the goal of eliminating rubella and CRS by 2010, followed by

EUR in 2015. However, many countries in the WRPO, AFR and SEAR have lagged behind in introducing RCVs; many rubella and CRS cases were reported (109).

In Japan, vaccination with RCVs started in 1976 and they were incorporated in NIP for female junior high school students. As mentioned in the measles discussion above, MMR vaccinations started in 1976 in NIP and were withdrawn due to the aseptic meningitis in 1993. A single dose rubella vaccine has been used since then, but the rubella vaccination rate significantly declined. To resolve the low vaccination rate, additional rubella vaccinations were administered to students at junior high school in 2003. Reported vaccination rates of both males and females were as low as 20 to 30 percent. Under the Preventive Vaccination Law, two doses of MR were mandated from 2006 and two additional doses added for first year students at junior and senior high schools (103). However, from 2012 to 2013, rubella outbreaks were observed in Japan with approximately 15,000 cases including 32 CRS cases reported (107). The reported cases were mainly from the adult male population who did not have RCVs before 1979 when only girls had the RCVs. The majority of cases reported were from 20 to 45 year old males with the most frequent reported age of 35. Given these circumstances, RCVs were additionally administered to male adults; the number of reported cases dropped to 320 in Japan in 2014 (108).

1.4.3.4 Polio immunization

The WHO promotes the Polio Global Eradication Initiative; nearly one year has passed since the last wild polio case was reported on the African continent on August 11, 2014. In the entire world, only Afghanistan and Pakistan have not declared polio eradicated. The WHO set a new objective to eradicate polio by 2018 from the world

(110).

In Japan, the last polio outbreak was reported in 1960 when approximately 6500 cases were reported all over Japan. Live attenuated oral polio vaccine (OPV) made from monkey kidney cells was included in NIP from 1961. Due to this vaccine program, reported wild polio cases were eliminated by 1980 (103). However, due to the spread of OPV, 8 to 10 cases of vaccine-associated paralytic polio (VAPP) have been reported annually. In the US, OPV was changed to inactivated poliovirus vaccine (IPV), but OPV was continuously used in NIP until 2012 when OPV was changed to IPV and VAPP was been reported every year after wild polio was eradicated in 1980 (111).

1.4.3.5 Tuberculosis incidence and BCG immunization

Tuberculosis is still a life-threatening disease following HIV/AIDS and 9 million tuberculosis cases were reported in 2013 of which 1.5 million people, mainly in low socio-economic classes, died (112). The WHO set up an End Tuberculosis Strategy to 1) push down global tuberculosis (TB) incidence rates from an annual decline of 2 percent in 2015 to 10 percent by 2025 and to 2) Reduce the proportion of people with TB who die from the disease from 15 percent in 2015 to 5 percent by 2025 (113).

The most effective prevention for TB is BCG vaccination. However, infants with a depressed immunological state such as being HIV positive have revealed that they risk developing TB through BCG vaccines (116). Thus BCG vaccines have been withdrawn in some areas in the world, which has raised new concerns (114). In Japan, the Tuberculosis Prevention Act was enacted in 1951 when 500,000 cases were reported annually, of which 93,000 resulted in deaths (2). After BCG vaccines spread widely, a vaccination rate of more than 95 percent was achieved, especially for newborns. Reported TB cases have significantly declined, but 19,615 TB cases were reported in 2014 of which 58.2 percent of the cases consisted of the elderly who were 70 years old and older compared to 0.2 percent among those 0 to 14 years old. TB is still a major concern in Japan (115).

1.4.3.6 Seasonal influenza outbreak and immunization among elderly population

In 2009, the H1N1 influenza pandemic occurred in the world and Japan, people rushed to have swine flu vaccinations at hospitals and the H1N1 vaccine shortage became an issue. However, seasonal influenza outbreaks occurred cyclically before the swine flu panic and have become a significant public health issue, costing many lives in the world and Japan (91). Influenza specifically affects the elderly and people with fragile health, causing respiratory diseases such as pneumonia and bronchitis as well as aggravating cardiovascular and cerebral vascular diseases that cause many deaths every year (95). According to CDC, from 1990 to 1999 influenza seasons, more than 32,000 deaths in the US each year among the elderly population 65 years and older were caused by influenza complications (96). The WHO analyzes influenza virus surveillance data with an expert panel and issues recommendations for the world on the composition of the influenza vaccines for the following influenza season and on being vaccinated (92). The WHO recommends that high-risk populations such as pregnant women, the elderly, infants, the immune-compromised and people with chronic conditions have priority for immunization (93). In Japan, influenza vaccination for the elderly 65 years old and older, and 60 years and older in the high-risk group with chronic diseases such as diabetes and with cardiac, kidney, and respiratory diseases as well as compromised immune systems, was included in NIP in 2001.

Since 1970, the WHO has used the concept of excess mortality from respiratory diseases during influenza season, which estimates the total mortality caused by influenza (90). Excess mortality is the mortality estimate from influenza during an influenza outbreak from among the total death increase of the entire population. Under the WHO definition, Assad *et al.* adopted excess mortality from respiratory diseases (90). However, Takahashi *et al.* used Japanese data from 1987 to 2005 and noticed that respiratory diseases, cardiovascular and cerebral vascular diseases all increased during flu season; they established estimation including these diseases (94). They also suggested that 85 to 90 percent of the excess death occurred among people 65 years old and over. The most frequent cause of deaths are pneumonia and heart diseases followed by cerebral vascular diseases. The substantial excess mortality of the 2004 to 2005 influenza season was as many as 15,000 deaths with 80 percent of the mortality from the elderly who were 65 years and older (91). Following Takahashi's study, Tachibana *et al.* reported that acute respiratory diseases, ischemic heart diseases and cerebral vascular diseases all increased during the flu seasons from 1980 to 1994 in Japan (95). In Japan, the National Institute of Infectious Disease publishes the "National Institute of Infectious Diseases (NIID) Model" from the 1998-99 season based on stochastic frontier estimation, originally developed in economics by Aigner *et al.* (1977), Jondrow *et al.* (1982) and Shindo *et al.* NIID developed this model to estimate the excess mortality caused by influenza during influenza season (156). According to this model, several thousand excess deaths are reported during recent influenza seasons (Fig.1). However, this public health problem does not attract great attention from the public.

1.4.3.7 Mumps vaccination

The WHO recommends including mumps vaccinations in national immunization programs in their position papers, but as of 2015, Japan has not done so (5, 39). For currently mumps vaccinations, 2 MMR doses have been adopted worldwide and 120 of 194 WHO member countries provide more than 2 MMR doses while 11 countries provide only one MMR dose as of 2014 (21). According to the WHO-UNICEF Joint Reporting Form on Immunization (JRF) and WHO statistics reported from regional WHO offices, countries that mandate two doses of mumps vaccines reported almost zero cases (7).

Among 34 OECD member countries, only Japan does not include mumps vaccine or MMR in NIP. In nearby Asian countries, Hong Kong-China and the Republic of Korea adopt two MMR doses and the People's Republic of China (PRC) one dose (21). Due to the widespread of mumps vaccines in the world, reported cases of mumps in the world are mainly from the PRC and Japan.

China reported 479,518 cases; ranking at the top, followed by Japan's reported 71,549 cases in 2013, surpassing the number of cases reported by WHO countries in SEAR and AFR (42) (Fig.2).In Japan the estimated immunization rate of mumps among eligible children is only about 30 percent, raising public health concerns such as increased risk of meningitis, encephalitis and deafness caused by contracting natural mumps as many as more than one million reported cases (4).

1.4.3.8 Seasonal influenza vaccine among the child population

After the Asian flu (1957) and Hong Kong flu (1968) pandemics, seasonal influenza live attenuated vaccine became recommended and school-located vaccination

(SLV) became mandatory according to the Preventive Vaccination Law Amendment in 1976. Every child had the flu vaccine at school (103).

However, one report tracking the incidence of influenza for five years in Maebashi city was published in 1987, contesting the influenza vaccine efficacy. The report attracted great attention and the influenza vaccination was withdrawn from NIP in 1994. The influenza vaccination rate has continued to drop since then; the estimated seasonal influenza vaccination rate among children is around 30 percent (105).

School children of 5 - 18 years are a primary vector for influenza because they have a longer communicable period than adults (134, 177). Hull *et al.* reported that raising vaccination rate among school children could protect elderly population (159). In order to achieve herd immunity to protect vulnerable populations like the elderly people, it would be necessary to raise the low rate. But this issue has not attracted public attention enough.

Chapter I Chronology & Tables and Figures

Chronology 1

Events and issues related immunization in Chapter I

Tables and Figures

Figures

Chronology 1 Events and issues related immunization in Chapter I

Year	Events and issues related immunization
1897	Communicable Diseases Prevention Law
1948	Preventive Immunization Law Smallpox, typhoid fever, diphtheria, tetanus, and acellular pertussis (DPT) vaccination started.
1951	Tuberculosis Prevention Act 500000 tuberculosis (TB) cases were reported in Japan. Bacillus de Calmette-Guerin (BCG) vaccination started.
1957	Asian flu pandemic
1960	Last polio outbreak was reported in Japan. 6500 cases were reported.
1961	Oral Polio vaccination (OPV) started. Vaccine-associated paralytic polio (VAPP) have been reported annually.
1968	Hong Kong flu pandemic
1976	Rubella-Containing Vaccination (RCV) started only for girls. Seasonal influenza School-located vaccination (SLV) for children started.
1978	Measles vaccination started.
1989	Measles, mumps and rubella (MMR) combination vaccine was introduced in national immunization program (NIP). Many side effects of aseptic meningitis related MMR was reported.
1993	MMR was withdrawn from NIP.
1994	SLV terminated (Seasonal influenza for children became non-mandatory vaccination).
1999	Infectious Diseases Control Law
2000	Measles outbreak worldwide

Cont'd to next page

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2001	Measles outbreak in Japan 286000 cases were reported mainly in babies. Due to vaccination rate decline after MMR withdrawal. Two doses of measles vaccinations started. Seasonal influenza vaccine for 65 years older with high-risk population for 60-65 was included in NIP.
2004	Seasonal influenza excess death peak 15000 deaths due to total causes were estimated.
2005	Reported mumps case peak 1.35 million cases were estimated.
2006	Preventive Vaccination Law Amendment MR combination vaccine two dose started. 12-24 months and 5-7 years population
2007	Measles outbreak in Japan The adult population of two dose system (only one dose population).
2008	Third dose of measles vaccine was temporarily administered. (13 years old and 18 years old population).
2009	The 2009 H1N1 influenza (Swine flu) pandemic
2012	Rubella outbreak in Japan (adult male population) 15000 cases of rubella and 32 cases of Congenital Rubella Syndrome (CRS) were reported. Additional rubella vaccine was administered to the male population.
2013	Preventive Vaccine Law Amendment Haemophilus influenza type b (Hib), human papillomavirus (HPV) and pediatric streptococcus pneumonia were included in NIP. Reported measles cases were dropped. Side effects of HPV vaccine were reported.
2014	Preventive Vaccine Law Amendment Chicken pox vaccination was added in NIP Seasonal influenza under 65, mumps, rotavirus and hepatitis A and B are not included yet. Inactivated polio virus vaccine (IPV) was switched with OPV. Recommendation for HPV vaccine was withdrawn. 19615 TB cases were reported in Japan. Polio eradicated from African continent.

Note: Not all event and issues related immunization in history are included in this table.

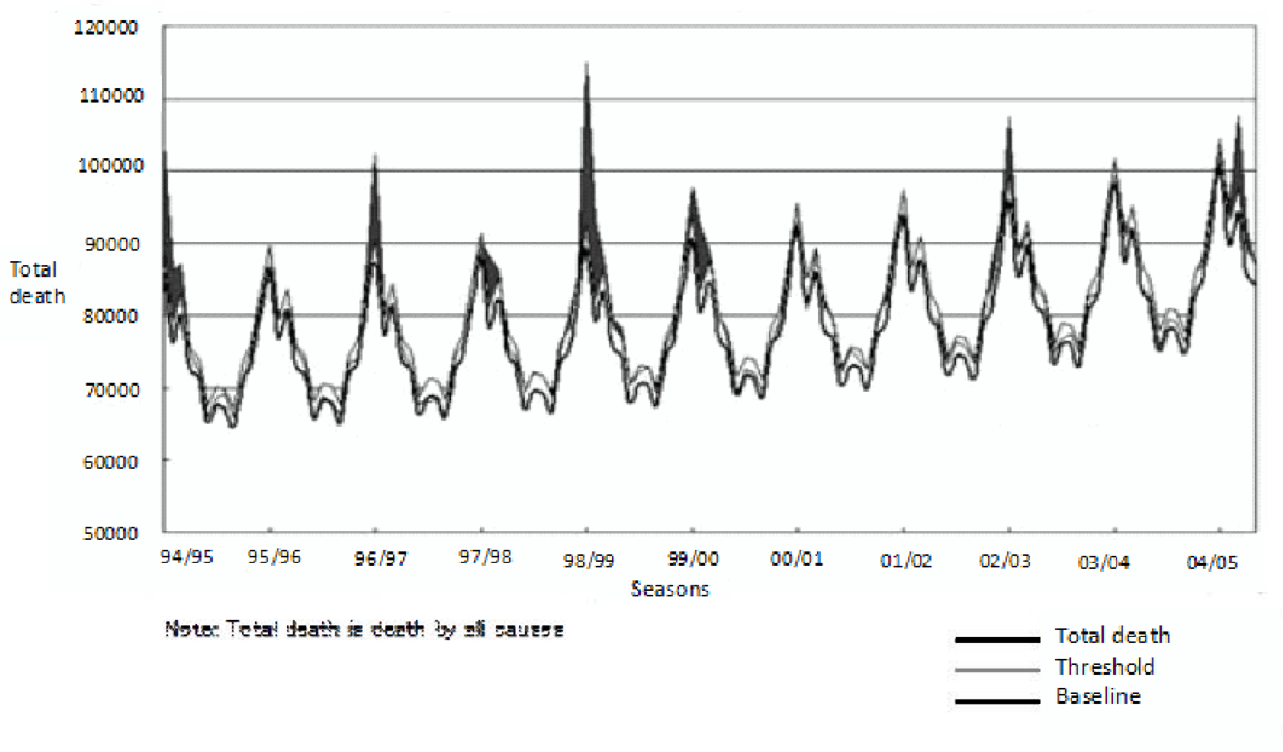

Figure 1 The excess mortality during the influenza epidemic periods (total mortality) Stochastic Frontier Estimation Model
Infectious Agents Surveillance Report (IASR); National Institute of Infectious Diseases (Accessed October 2015)

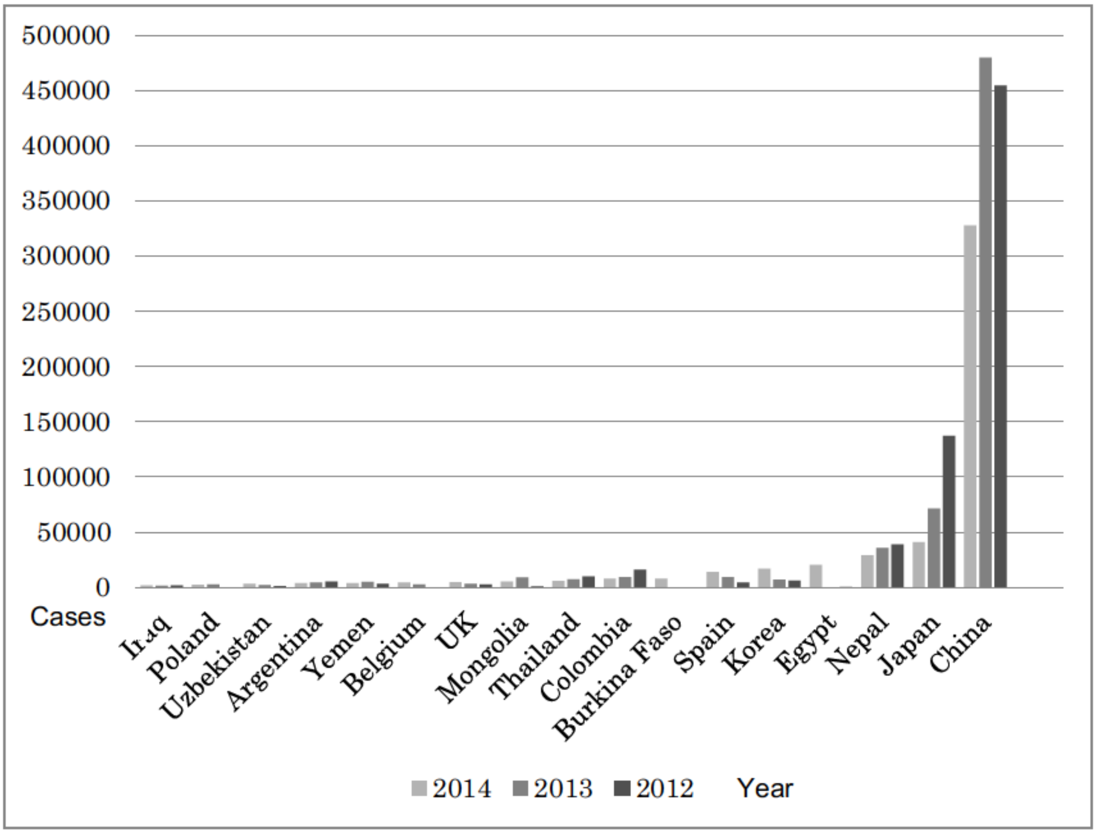

Figure 2 Mumps incidence reported cases；The WHO member countries
（Data are from World Health Organization. Immunization, WHO Data Statistics. Disease incidence. Mumps reported cases, accessed Oct.01, 2015）

Chapter II

About the studies in this paper

2. 1 Backgrounds and objectives

The above literature research demonstrates that Japanese immunization has many issues to address concerning public health. Mumps vaccination in the child population and seasonal influenza vaccination in the elderly population are two issues to be prioritized and addressed in Japan, but these issues have not been attracting great attention. We must focus on why the vaccination rates are low, considering vaccination as a preventive health behavior, and on factors that influence vaccination behavior.

As mentioned in the literature review, the Health Belief Model (HBM) has been proven very effective for exploring individual health behaviors such as being vaccinated or not in studies abroad. However, the number of vaccination behavior studies based on HBM constructs is still small and effective HBM utilization for health behavior and promotion studies in Japan is still little known and insufficient.

Under the circumstances, the author decided to choose the above discussed two issues of mumps vaccination among children and seasonal influenza vaccination among the elderly population 65 years and over. The backgrounds behind these issues were examined to investigate why the mumps vaccination rate among the child population and the seasonal influenza vaccination rate among the elderly population are low. The factors examined include HBM that influences vaccination, focusing on vaccination as the common objective in the studies in this dissertation.

2.2 Methodology

As no national database for non-mandatory immunization was available in Japan, two questionnaire surveys were organized, one targeting mothers with children for

Study I to investigate mumps vaccination in children and another targeting the elderly population for Study II. Study I "Factors Associated with Mothers not Vaccinating their Children against Mumps in Japan" was based on a maternal questionnaire survey undertaken from 2010 to 2011. Study II "Seasonal flu vaccination acceptance among the elderly people who live in a community in Japan" was undertaken in 2009 and in 2010.

For both questionnaire surveys, alumni lists obtained from offices officially agreed upon were used and a retrospective cross-sectional study was conducted. Along with each questionnaire, the author provided a cover letter explaining that study participation is completely voluntary and that responding to and returning the questionnaire would be regarded as informed consent to participate.

2.2.1 Mixed and triangulation methods

In the studies in this paper, even though many questionnaires were sent to potential participants randomly selected from alumni lists, the number of participants in the studies was smaller than expected and the collected data were limited. In order to increase the analytical quality of the studies, triangulation method of mixed method were adopted. A mixed method is a statistical analytical method where several analytical methods such as qualitative and quantitative methods are adopted in the same research and data are collected concurrently or sequentially. Research, especially in health and preventive care services, that uses mixed methods has been increasing over the past 10 years and will continue to increase in the future (181, 182). The mixed method is utilized in health care research such as examining primary and preventive care as well as in welfare, sociology and behavioral science research (180, 183). The triangulation method classified in the mixed method is to organize qualitative and quantitative methods together, collect data concurrently and integrate them into a study. In the studies in this paper, the two questionnaire surveys included open-ended questions where participants freely wrote their opinions to reply to designate questions.

2.2.2 Quantitative analysis

As quantitative analysis of the studies in this dissertation, first descriptive analysis was conducted. Then unadjusted univariate logistic regression analysis was performed for participant characteristics and HBM factors including social factors, using vaccination and non-vaccination statuses as dependent variables. Participant age was regarded as a continuing variable and immunization status was compared with Student's t-test. Other variables were entered into a univariate logistic regression analysis using the binary vaccination status of vaccination or non-vaccination as dependent variables to obtain unadjusted odds ratios (OR). As a dependent variable was not normally distributed and a binominal category variable was, discriminant function analysis was not considered. The author adopted univariate and multivariate logistic regression analysis. For variables that did not meet the assumption for the $\chi 2$ test, the p value was obtained by the Fisher Exact Test.

To improve analytical quality, HBM barrier factor variables of HBM constructs in Studies I and II were created by combining the questionnaire results of multiple selection responses of reasons for non vaccination and text responses of opinions about vaccinations in open-ended questions. A text analytical method was used to create new barrier factor variables.

2.2.3 Selection of variables for multivariate analysis

2.2.3.1 Rational for selection method

Harrell *et al.* suggested that uncritical application of modeling techniques can result in models that poorly fit the dataset at hand, or, even more likely, inaccurately predict outcomes on new subjects (22, 23). Previous studies suggested that automated subset algorithms, which are backward elimination, forward selection, and stepwise methods, are sometimes inaccurate, and noise variables are sometimes included in final models (160). Selections using these automated methods are affected by the correlation between variables and the number of candidate predictor variables, risking very important variables being eliminated from final models and noise variables entering (22, 27, 30). Considering these issues, the limited backward step-down method in multivariate analysis was adopted considering all interactions between the variables (22, 25).

In variable selection, all statistically significant variables (alpha<0.05) and noticeable variables, even if they were not significant for univariate analysis, and all interaction variables identified by Spearman's rank correlation tests (r>0.4) were candidates for multivariate logistic regression analysis, again using binary vaccination status such as vaccination or non-vaccination as the dependent variable. Variables for the adjusted analysis were selected with the step-down method by selecting a wide range of variables using a liberal p-value of 0.15 by backward elimination stepwise variable selection to build a final multivariate model (25).

As previous studies have suggested, over fitting variables in a multivariate method may lead to risking type I errors that may erroneously reject the null hypothesis, and a variable may incorrectly have no impact on the outcome. In analogy to type II errors, the analysis may lack the power to detect important variables and so type III errors may affect the outcome (26). Accordingly, the number of independent variables in the final multivariate model was determined and limited by the outcome number divided by 10 (23, 26).

Selected variables were included in a second multivariate analysis to evaluate the model's overall accuracy in predicting vaccination with the Hosmer-Lemeshow goodness-of-fit test and the C-statistic, which is the area under the receiver operating characteristics curve (23, 24). The results are reported as adjusted odds ratios (aOR) with 95 percent confidence intervals (CI). Alpha was set at 0.05, and all tests were two-tailed; data were analyzed with SPSS Statistics, version 21.

2.3 Ethical review

The Office of Human Research Ethics (Internal Review Board) at Waseda University established the Guidelines regarding Academic Research Ethics. In this study, the questionnaire was anonymous and data obtained from the questionnaire were completely de-identified so that this study did not need to be reviewed by the Internal Review Board (185). Papers consisting of parts of this dissertation were accepted by journals agreeing with the above mentioned conditions.

Chapter III

Study I: Factors associated with mothers not vaccinating their children against mumps in Japan

3.1 Background and objective

After MMR's withdrawal in 1993 from NIP due to a reported increase in aseptic meningitis, mumps vaccination became voluntary. Single dose vaccines have been consistently provided since then and the mumps vaccination coverage rate subsequently dropped from almost 90 percent to about 30-50 percent (4, 10, 67, 70). This low mumps vaccination rate among eligible children in Japan is a public health concern. In 2006, 1.18 million cases of mumps were reported in Japan (6). According to NIID, 1.35 million annual mumps cases were reported in 2005 and current annual estimates are 0.4 to 1 million cases, with about 60 percent being children between birth and six years old and the other 40 percent a large population including adults (6).

Increasing complications from mumps, including meningitis, encephalitis and deafness, are also a public health concern in Japan (8, 9). The correct numbers of these complications in Japan are unknown due to lacking a large national database for collecting and managing the data, but previous studies reported that 13 out of 1051 natural mumps cases resulted in meningitis (4) and approximately 1800-2000 natural mumps cases caused deafness annually in Japan (8, 9, 10). Given this low mumps coverage rate in Japan, understanding the barriers and factors influencing children’s mumps vaccination rates from a wide range of perspectives is necessary. Yet no published studies have been conducted to identify determinants for increasing mumps vaccinations in Japan. Studies suggest that maternal awareness including health belief model factors influences children’s vaccination uptakes (11, 12, 13, 14), but I believe other factors are specific to Japan. In Japan, mothers’ taking their children to be vaccinated is common. Accordingly, a group of mothers was surveyed to determine what factors influenced their decisions to have their children vaccinated, including the change in maternal consciousness from the 1990s when the mumps vaccination rate was 90 percent to today where the rate has dropped more than half.

Considering the low vaccination rate of mumps among children and an increase in natural mumps cases, the author determined to study maternal awareness in Study I to investigate factors including HBM that influence maternal decisions to have their children vaccinated.

3.2 Sample and method

In this study, a sample of women was selected from Waseda University between 1980 and 2003. We used alumna lists provided by the alumni office at Waseda University to conduct a retrospective cross-sectional study using a quantitative and qualitative mixed method. We set the target maternal age margin widely because the average age for the first birth of Japanese women was 27 years old in 1985 and 30 years old in 2011 (31); I wanted to research the change in their consciousness after MMR termination in 1993. We sent 1268 questionnaires with cover letters by postal mail including self-addressed, stamped return envelopes from 2010 to 2011. The cover letter explained that the questionnaire was completely anonymous, data obtained from the survey would be de-identified and only aggregated data would be used. The cover letter also added that participation was voluntary.

Only participants' first born children were subject to analysis in these studies.

3.2.1 Instruments

We developed a questionnaire consisting of 10 demographic questions on the respondent and her family and 18 questions regarding vaccinations and vaccination statuses for mumps and other vaccinations such as measles, rubella, poliovirus, DTP, Japanese encephalitis, influenza virus type B, pneumococcus, chicken pox and hepatitis A and B. We also asked for children's medical histories, subjective wealth and the maternal working status when the children were vaccinated. Other questions covered HBM factors such as the perceived efficacy of mumps vaccination for their children, perceived severity of mumps on their children, cues to the action that encouraged them to take their children to be vaccinated, perceived barriers influencing non-vaccination for each illness and who takes their children to be vaccinated. Willing to pay (WTP) was a 5-point scale of less than 1000 yen, 2000 yen, 3000 yen, 4000 yen and over 4000 yen. We asked concerning the maternal commitment to vaccination in the questionnaire as to how mothers think of vaccinations in Japan. They were asked to choose one of the following responses: a) vaccinations have side effects so they should all be voluntary, b) current Japanese vaccinations mainly based on single doses are okay and more vaccinations are unnecessary, c) an improved vaccination system is necessary with informed consent from parents, d) Japan should adopt a stricter vaccination system such as that in the USA. The responses resulted in a maternal commitment to vaccination that was divided into a 4-point scale of weak, moderate, strong and very strong. We also asked for maternal preferences concerning combination vaccines from among a) single doses, b) combination double vaccinations, c) combination triple vaccinations and d) quadruple combination vaccinations. In an open-ended question, I asked the mothers to write down their opinions of vaccination.

3.2.2 Statistical methods

According to the statistical analysis described in the methodology in this section, first descriptive statistics analyze participant characteristics, immunization statuses, reasons for non-vaccination, HBM constructs, maternal commitment to vaccination and maternal preference for combination vaccinations. The age variables of mothers who had and had not immunized their children against mumps and of the children were compared with Student's t-test. For the HBM barrier variable, barrier factors were extracted by text analysis of responses from open-ended questions. These barrier factors were combined with reasons for non-vaccination, creating new HBM barrier variables. After descriptive analysis, univariate analysis was performed for each variable being an independent variable for non-vaccination of mumps and calculated non-adjusted ORs were obtained. For variables that did not meet the assumption for the $\chi 2$ test, the p value was obtained by the Fisher Exact Test. Univariate analysis was not performed for maternal preference constructs because of the similarity of questions concerning maternal obligation constructs.

We also used Spearman's rank correlation tests to analyze all interaction variables. Univariate analysis as described in the methodology section used selected variables from all candidate variables A final multivariate logistic regression analysis model of non-vaccination of mumps as a dependent variable was established by selected variables from all candidates variables from univariate analysis using the method described in methodology section.

3.3 Results

In 2010, the author mailed 1268 questionnaires. Of these, 628 (49.5%) were returned as undeliverable; of the remaining 640 that were delivered, 226 (35.3%) returned the questionnaires. Among 226 respondents, two questionnaires were incomplete, leaving a sample of 224 women (35.0%). This recovery rate (35%) may be inevitable because of the low birth rate (TFR: total fertility rate) of 1.39 for Japanese women as shown by national demographic data in 2011 of the Ministry of Health, Welfare and Labor (31).

3.3.1 Descriptive analysis results

3.3.1.1 Vaccination status of the participants

Table 1 shows a descriptive analysis of all vaccination statuses including NIP and non mandatory vaccinations in this population with the national average published by NIID. The NIP vaccination rates in this population such as polio (96.9%), BCG (95.1%), measles (94.2%), DTP1(92.4%) and rubella (88.8%) were as high as expected except for DT2 (DTP3[62.9%]), but non-mandatory vaccination rates at the time of the survey such as Mumps (61.6%), Varicella (37.5%) and seasonal influenza (41.7%) were low compared with NIP rates. Vaccination rates of influenza type b (9.8%), hepatitis B (9.8%), pneumococcus (2.2%) and hepatitis A (1.3%) were especially low and many participants responded that they did not know about the vaccines.

3.3.1.2 Characteristics of participants and mumps vaccination status

Characteristics of participants

Table 2 shows the descriptive analysis results including mothers' and children's characteristics; a total of 224 mothers with children participated. The mean (SD) age of the 224 mothers responding at the time of this survey was 44.7 (SD=5.02; 30-55 years) and the mean age of mothers during the recommended vaccination period was 30.52 (SD=3.94; 20-43 years). The number of children the participants had was two children

(48.7%), one child (31.7%) and three children (17.9%). In responses to who took the children to be vaccinated, 204 (90.7%) responded mothers (myself) regardless of their age and only 17 (7.6%) responded others. For child characteristics, the mean (SD) age of the 224 children was 14.16 (SD=6.71; 0-22>years) and the average age was higher than expected. The ratios of males to females were 50.0: 46.5. Those who lived with children during the children's vaccination period were mothers and fathers (79.2%), others such as grandparents, aunts and uncles (9.7%) and mothers alone (7.1%). In this population, 92.4 percent of mothers responded that they took their children by themselves to be vaccinated.

Mumps vaccination status

Of the 138 (61.1% of 224) children vaccinated for mumps, 47 (34.1%) had the MMR vaccination. Among them, 20 had MMR abroad, 14 had MMR from unknown sources and 13 appeared to have had MMR before 1993 when it was withdrawn from NIP. The remainder had the vaccination as a single dose. The reasons for non-vaccination of mumps, if any, are shown in Table 3.

3.3.1.3 Maternal commitment and vaccination preferences

Maternal commitment to vaccinations and maternal preferences for combination vaccinations analyzed by descriptive statistics are shown in Table 4. For maternal commitment to vaccinations, nearly 63 percent of mothers responded that more progressed vaccination system was necessary; however, mothers who thought a strict vaccination system like in the US necessary were only 14.2 percent. For responses about maternal preferences for combination vaccines, mothers who preferred the double combination vaccination were 32.2 percent, followed by the triple combination vaccination at 28.6 percent, the quadruple combination vaccination at 18.5 percent and the single dose at 11.9 percent (Table 5).

3.3.1.4 HBM factors

According to the method described in the statistical method section, HBM barrier variables created by combining reasons for non-vaccination (Table 3) and key words extracted from text responses in open-ended questions by text analysis (Table 6) are included in Table 7. A number of responders to reasons for non-vaccination question and open-ended question was 55 and 139 respectively.

Table 7 shows the descriptive statistics of HBM constructs. About 9 percent of mothers thought the mumps vaccine ineffective for their children and about 5 percent of mothers did not understand the severity of mumps contracted after maturity. The most frequent information source about vaccines (cues to action) was communication from local government (61.6%), learning from booklets or brochures obtained (58.5%) and checking the maternity handbook (54.9%). The most frequent perceived barriers were offered at inconvenient geographic locations (29.9%), fear of harmful side effects (19.9%) and vaccination being expensive (17.4%). About 33 percent of mothers responded that they were willing to pay more than 4000 yen, but 22 percent of mothers responded 1000 yen followed by 2000 yen (21.7%).

3.3.1.5 Social factors

Table 2 also includes social factors such as areas where the mothers lived during the vaccination period for their children. The participants' residential areas when vaccinated were urban (35.7%), rural-adjacent (51.8%) and rural (12.5%); nearly half lived in the Kanto Area. The participants who lived abroad when the children were vaccinated were 8.98 percent, which was probably a higher rate than the average population. Subjective life standards when vaccinated were very good (12.0%), good (40.6%) and average (39.7%); poor was only 5.8%.

Focusing on cue to action factors, mothers who received information only through non human relationships of non social such as learning from communication from local government, booklets or brochures obtained in public places, checking maternal handbooks and media were 59 (26.3%) (Table 7).

3.3.2 Univariate analysis results

3.3.2.1 Characteristics of participants

Table 1 also contains the results of Student's t-test for the age characteristics of mothers and children, and unadjusted logistic regression analysis for other demographic characteristics. From the results of Student's t-test and univariate analysis, children were more likely to be vaccinated for mumps during the vaccination period if their mothers were older ($p<0.01$) or living abroad (OR=0.16; $p=0.015$) (Fig. 3), and less likely if their mothers had three children (OR=2.25; $p=0.045$) (Fig.4) or were living in rural regions (OR=2.86; $p=0.049$) (Fig.5). Boys were more likely than girls to be vaccinated (OR=0.82; $p=0.48$), although not significantly. For family types, neither type affected children's vaccination status nor with or without support for their children for vaccination did not affect children's vaccination status in this study either.

3.3.2.2 Maternal commitment

The unadjusted analysis results of maternal commitment to vaccination for predicting non-immunization of mumps are shown in Table 4. From this analysis, mothers who think 'stricter vaccination systems are necessary' were significantly more likely to have their children vaccinated (OR=0.23; p=0.02) (Fig.6).

3.3.2.3 HBM factors

Table 3 shows Health Belief Model Constructs such as the perceived efficacy of mumps vaccination, perceived severity of mumps on their children, cues to action, perceived barriers, willingness to pay (WTP) and results of univariate analysis on non-vaccination as the dependent variable. From the univariate analysis, children were more likely to be vaccinated when mothers had recommendations from doctors (OR=0.53; p=0.023) (Fig.7). Moreover, they were less likely to be vaccinated when their mothers thought the vaccinations ineffective (OR=5.62; p=0.002) (Fig.8), the disease not severe (OR=5.08; p=0.018) (Fig.9), the vaccinations not mandatory (OR=2.99; p=0.03) (Fig.10), the side effects scary (OR=2.42; p=0.01) (Fig.11) and they were busy (OR=2.84; p=0.02) (Fig.12).

3.3.2.4 Social factors

In this study, children who lived in rural areas were significantly less likely to be vaccinated for mumps by the unadjusted model (OR=2.86; p=0.049), but not significantly by the adjusted model (aOR=1.55; p=0.09).

Subjective life standards did not influence vaccination status in this population according to univariate analysis (p=0.28-0.72).

In this study, univariate analysis showed that nonsocial network factors such as 'learning from booklets or brochures obtained at hospitals or public places' (OR=1.16;

p=0.59), ‘learning from the media’ (OR=1.44; p=0.27) and ‘communication from municipal governments (municipal governments usually communicate with mothers only by postal mail)’ (OR=1.64; p=0.08) raised the odds ratio of non-vaccination, but not significantly. If the population was divided into two groups, however, mothers who rely on social networks through relationships with others to obtain vaccination information and mothers who do not rely on social networks through relationships with others to obtain information, the mumps vaccination rate decreased significantly in the non social network group (OR=2.21; p=0.01) (Fig. 13).

3.3.3 Multivariate analysis results

Following the methodology described in the methodology section, variables for multivariate analysis were selected. As interaction variables (above r=0.4) were also candidates for an adjusted logistic regression model, the author tested interactions for all variables.

The candidate variables were maternal age, the residence area being urban, rural-adjacent or rural, fearing harmful side effects or not, believing the vaccine effective or not, the vaccination being mandatory or not, living abroad when vaccination usually occurs or not, the number of children mothers had, perceived severity of mumps on their children, recommendation from the family doctor to vaccinate or not, being too busy to vaccinate their children and maternal commitment to vaccination (4 point scale). The ‘only through non social network factor’ variable was significant after univariate analysis, but excluded from the candidate variables because this variable was not independent of other social network factors. From similar reason maternal age and children’s age were highly dependent each other and according to the method in the methodology section, the estimated number of variables in a final multivariate analysis was mothers reported having non-vaccinated children (n=86) divided by ten equaling around 8.6. To avoid over-fitting the model, only maternal age was included in the candidate variables. The process and result of step-down variable selection method are shown in Table 8. 'The number of children mothers had' variable that was not significant in the multivariate model was also excluded for the same reason to avoid over fitting. Among all interaction variable, child age and maternal age was interacted, but only maternal age was selected a candidate so that this interaction variable was excluded for candidates.

As a result, the variables selected for the final adjusted multivariate analysis were maternal age, recommendation from the family doctor to vaccinate or not, living abroad when vaccination usually occurs or not, maternal commitment to vaccination (4 point scale), being too busy to vaccinate their children or not, the vaccination being mandatory or not, fearing harmful side effects or not, believing the vaccine effective or not and the area of residence being urban, rural-adjacent or rural. The multivariate analysis result was shown in Table 9.

This result has shown that mothers who thought the vaccine was ineffective (aOR=6.21; $p<0.01$), who knew that the vaccination was not mandatory (aOR=3.30; $p<0.01$), who feared harmful side effects (aOR=2.55; $p=0.03$) and who reported being too busy to vaccinate their children (aOR=3.30; $p=0.02$) were significantly less likely to have their children vaccinated. Moreover, mothers who were older (aOR=0.91; $p<0.01$), living abroad when vaccination occurred or not (aOR=0.10; $p=0.02$) and cue to action factors of the recommendation from the family doctor (aOR=0.35; $p<0.01$) became significant. Mothers who had more commitment to vaccination were more likely to have their children vaccinated and those who lived in more rural areas were less likely to have their children vaccinated, but both were not significant (Table 5).

3.4. Discussion

3.4.1 Maternal and child characteristics

In this study, maternal age became significant after adjusted analysis and older mothers were more likely to have their children vaccinated against mumps. This is partially because the average age of this population was high and older mothers (n=13) who appeared to have had their children vaccinated against mumps before the MMR was withdrawn from NIP were included in this population. Children who lived abroad were more likely to be vaccinated, presumably because many countries have stricter vaccination requirements before children go to kindergarten or school than Japan (35) and parents living abroad might have been more likely to be aware of the need for vaccinations. One mother wrote as follows:

"We were thoroughly informed that we should have our children vaccinated when we lived overseas. The knowledge is not well communicated in Japan and the intake has not been enough."

Previous studies have shown that maternal employment can be associated with lower childhood vaccination rates (46, 172, 173). In this study, 61.6 percent of mothers were not working during their children's vaccination period, and maternal employment did not significantly affect vaccination in the unadjusted analysis. This is because there were two groups. One found working and taking their children to be vaccinated difficult; the other thought vaccination was effective for them to avoid taking sick-leave to care for their children. One of the former wrote: "Vaccinations were not available on holidays so that I had to take a day off to have my children vaccinated, which was very annoying." One of the latter wrote: "I worked and it was difficult to take off days when children got sick so that my children got vaccinations for VPDs as much as possible."

For the number of children factor, some Japanese studies suggest that the number of children in one family affects the vaccination rates for their children (13) or that when mothers have many children, vaccination incompletion risk increases (173). In our study, mothers with three children became significant by unadjusted analysis. Mothers with more than one child commented on the difficulty, writing as follows:

"It was hard to wait for a long time with two children at the hospital."

"It was hard to travel some distance with the children to get their shots."

Mothers still usually take their children to be vaccinated by themselves in Japan, which may be a strong barrier against small children being vaccinated and raises another concern.

3.4.2 Maternal awareness and HBM factors

Parental health beliefs, especially maternal vaccination awareness, influence the decision to vaccinate children (44, 45, 46). HBM constructs are a very effective tool to analyze or predict vaccination behaviors abroad, including maternal awareness. Brewer *et al.* reported in their meta-analysis (N=15, 988) that risk perception, severity and susceptibility were an effective tools to predict vaccination behavior (137). HBM vaccination studies in Japan are still few in number, but some studies show HBM constructs to influence vaccination rates (138). In addition, the perceived cost barrier reduced maternal awareness for Hib vaccine uptake (13). Supporting this conclusion, mothers who did not perceive the efficacy of mumps vaccination in adjusted models and who did not perceive the severity of mumps for their children in an unadjusted model were shown to be significant in this study. Some mothers thought mumps vaccine was ineffective and that natural immunity was better to acquire immunity. They wrote:

"Contracting mumps for acquiring immunity was more effective."

"I do not trust vaccinations at all. Natural immunity or hygiene is more important to prevent communicable diseases."

Orchitis among boys is a better-known risk among the complications caused by natural mumps; correct knowledge of complications such as increasing risks of meningitis or deafness will have to be disseminated.

One cue to action factor, recommendations from family doctors, is known to be a significant predictor for vaccination uptake elsewhere (35, 44, 49, 59, 133,135). Brown *et al.* reported that the maternal relationship with their health professionals differentiated between MMR acceptors and rejecters in many cases (49). In our study, recommendations from family doctors significantly predicted positive vaccination uptakes by both unadjusted and adjusted analysis. One mother commented as follows:

"It was difficult to obtain information about non-mandatory vaccination and the family doctor's advice was very helpful."Another mother, however, was unhappy with the information from her doctor and commented: "I do not believe in vaccinations. Doctors do not provide enough information." This suggests that if doctors do not provide information, mothers may avoid vaccinations. Bonanni *et al.* suggested that that family doctor advice significantly influenced maternal vaccination uptakes and that the GP's knowledge level influences the recommendation levels (44).

Another cue to action factor, knowing of government vaccine subsidies, decreased non-vaccination significantly by unadjusted analysis. One mother commented: "Non-mandatory vaccinations are about 10,000 yen and very expensive. Why don't governments provide more subsidies?"

Currently, parents have to pay between ¥5,000 to 8,000 (US$50-80) for mumps vaccination. Only 61 of 1,727 municipalities subsidized mumps immunization in 2010, and at most, only 15 provide a subsidy large enough to cover the cost of the vaccination (60, 61). This low subsidy rate by local governments may explain the low mumps vaccination rate in Japan. Endo *et al*. researched a municipality that provided a subsidy for mumps vaccination with a high acceptance ratio and suggested that the subsidy was effective for raising the vaccination rate (169).

For barrier factors, mothers who chose being busy in this study as a perceived barrier were less likely to have had their children vaccinated.

In our study, maternal working status did not affect mumps vaccine uptakes, but the barrier factor of maternal busyness was significant after adjusted analysis irrespective of maternal working status. One mother wrote: "I have to wait in long lines in hospitals with children to have them vaccinated, which is always annoying."

Japan has universal insurance that enables Japanese to access medical care, but hospitals are commonly crowded and patients wait for a long time to see doctors. Also, only physicians are allowed to provide vaccinations under Japanese law, which may cause mothers to wait for a long time. To raise the vaccination rates, ameliorating the environment for busy mothers such as introducing combination vaccines to have their children vaccinated is necessary.

Among other barrier factors, 'the shot is not mandatory' was a significant barrier to children's vaccination. Some mothers decided not to have mandatory vaccinations for their children and one mother commented: "I did not get mandatory immunizations for my children because I am busy and they were expensive." Bonanni *et al*. reported in their study in Italy that non-mandatory vaccination rates are dramatically lower than mandatory ones and maternal awareness especially affects non-mandatory vaccinations uptakes (44), which is concordant with this study as shown in Table 1.

Another barrier factor, fear of harmful side effects, was a significant predictor of non-vaccination in the adjusted model in our study. One mother commented: "Doctors did not explain about vaccination side effects because doctors are always busy." This lack of knowledge may have led to maternal fear of side effects as a barrier for children to be vaccinated: "When I asked doctors about the side effects, they said that mothers had to decide for children to have the shot or not. I do not have enough knowledge so that I did not have my children vaccinated." Cheung *et al.* suggested in their influenza vaccination study of parental population that mothers with higher education were more prone to worry about side effects of vaccine than mothers who were lower education (134). The participants of study I in this paper were all with higher education of university graduates so that it is suggested that fear of side effects may not be associated with education levels of parents, but this needs to be studied further.

Endo *et al*. suggested that there was no influence of fear concerning side effects for the mumps vaccination uptake in their study and concluded that the MMR withdrawal issue in 1993 described in Chapter I had no effect on maternal awareness (172). However, their subject maternal age was young and their study was a non-adjusted study with potential confounding factors so that it may be early to conclude that. Brown *et al*. reported in their study in UK that one paper reported that MMR vaccine caused autism increased rejection of MMR which had affected more than 10 years (49).

In our study, some mothers commented as follows: “I remember the withdrawal of MMR due to side effects. I need more information” or “MMR was withdrawn during my first child’s vaccination period. The side effects are scary, but I let our children be immunized due to a sense of obligation.” In our study it was shown that this predictor, the post-vaccination aseptic meningitis and withdrawal of MMR in 1993 discussed above, may have influenced the maternal awareness that led to the current low vaccination rate.

3.4.3 Social factors

Many studies have reported that residential areas and socioeconomic factors affect health care utilization, including vaccination rates (51-54). In this study, children who lived in rural areas were significantly less likely to be vaccinated by the unadjusted model, which supported the previous study.

One Japanese study reported that household income affected Hib vaccination uptake (13); vaccination was non-mandatory at the time of survey. However, subjective life standards were not significant predictors in our study, which may have been due to population bias because respondents who had children who ‘lived in rural areas when vaccinated’ and who identified as poor were only 12.4 percent and 6.2 percent. However, considering some mothers commented that non-mandatory vaccines were expensive, the cost issue is relevant.

Social network factors also influence vaccination rates as one of healthcare utilization. These previous findings reported that social networks better predict parental especially mothers choice of vaccination choices and messages transmitted by interpersonal networks strongly influence motivation to obtain vaccinations (62, 63, 64,132). Marsh *et al*. reported that message framing strategy by interpersonal relationship was effective to raise maternal awareness (63).

In this study, children of mothers who did not rely on relationships with others to obtain information about vaccinations were significantly less vaccinated by univariate analysis. The raised odds ratio may suggest that children of mothers with less-extensive social networks and poorer communication skills will be less likely to have their children vaccinated. This supports the findings of previous studies and the theory of Cohen *et al*. and Putnam described in the introduction. A further study concentrating on social networks including social capital will be necessary.

3.4.4 Safety of vaccines

Currently MMRII, containing the Jeryl Lynn strain is widely used worldwide and more than 400 million doses of MMRII have been used in 72 countries as combination vaccines (73). The incidence of aseptic meningitis from the MMRII is very low (74, 75, 76, 77, 78, 79).

In Japan, the MMRII vaccine is not officially authorized yet. The incidence of aseptic meningitis of the single dose mumps vaccines currently used in Japan are estimated to be 400 in 1 million doses that are not as low as expected (80, 81). To improve the mumps vaccination rate, a national government subsidy and correct vaccine policies are necessary. Also mumps vaccine must be included in NIP. It will be necessary to review the safety of the current mumps vaccinations available in Japan and to introduce new and safer vaccines if possible.

It may be more attributable to the lack of a national government subsidy and policies that are unaware of the importance of mumps vaccination (43).

3.5. Conclusion

My paper support several conclusions. First the potential HBM on vaccination behavior was determined. In this study, factors associated with mothers not vaccinating their children against mumps were the fear of harmful side effects, the vaccination not being mandatory, the belief that the vaccine was not effective and being too busy to have their children vaccinated. Still, recommendations from family physicians to have children vaccinated could have been associated with reduced non-vaccination risk in this study. Given these conclusions and the absence of mandatory vaccinations, the author can provide a conclusion to raise the vaccination rate at the individual level. In addition, going beyond individual education for health behavior change and a public education campaign about mumps to also address social and political change such as institutional and policy change from ecological model perspectives could help review the current mumps vaccinations available in Japan. Introducing new and safe vaccines would be necessary.

3.6. Study limitations

The study was a cross-sectional study with a population of 224 mothers who were university graduates. According to published data from Ministry of Education, Cultural, Sports, Science and Technology Japan, the recent ratio of women who graduated from universities including colleges and graduate schools is 56 percent. However this excludes women who go to universities in their later life. That means that this research population cover majority of education levels in Japan but it may be necessary to conduct an additional longitudinal study targeting a wide range of the population of mothers with differing education levels to generalize the results obtained here.

Chapter III Tables and Figures

Tables

Figures

Table 1 Vaccination rate in this population (N=224)

Vaccine		n	%	National average as of 2011	
Measles	Yes	211	94.2	94	
	No	13	5.8		
Rubella	Yes	199	88.8	94	
	No	25	11.2		
BCG	Yes	213	95.1	94	
	No	8	3.6		
Polio	Yes	217	96.9	96	
	No	6	2.7		
DTP1	Yes	207	92.4	99	a
	No	9	4.0		
DT2 (DTP3)	Yes	141	62.9	102	a
	No	77	34.4		
Mumps	Yes	138	61.6	30–50	b
	No	86	38.4		
Chicken Pox	Yes	84	37.5	30	b
	No	130	58.0		
Seasonal influenza	Yes	91	41.7	30	b
(Routine vaccination)	No	117	52.2		
Hib	Yes	22	9.8	–	
	No	191	85.3		
Pneumococcus	Yes	5	2.2	–	
	No	202	90.2		
Hepatitis	Yes	22	9.8	–	
	No	190	84.8		
Hepatitis A	Yes	3	1.3	–	
	No	209	93.3		

DPT (diphtheria, and tetanus toxoids and, acellular pertussis)

DPT1 denotes percentage of population who completed 1st dose of DPT.

DT2 (diphtheria, acellular pertussis)

Total % is not necessarily 100% due to missing values.

National average for NIP vaccines were published data from the National Institute of Infectious Diseases as of 2011.

a Data are overestimated due to duplicating reporting.

b The rate is an estimate from literatures due to a lack of national database.

Pneumococcus, Influenza type b, Hepatitis B were excluded due to low number of children who took these vaccinations.

Table 2 Demographic characteristics of mother and child and mumps vaccination status (N=224)

	n (%)	Mumps Vaccination Yes	No	Unadjusted OR (95%CI)	p value	
Mother characteristic						
Age (Ave.±SD)	44.67±5.02	45.45±4.96	43.60±4.95	(0.49 – 3.20)	<0.01 **	a
30-40	42 (18.6)	23 (54.8)	19 (45.2)	1		
41-50	158 (70.5)	99 (62.7)	59 (37.3)	0.70 (0.35-1.40)	0.31	†
51-60	21 (9.4)	14 (66.7)	7 (33.3)	0.58 (0.20-1.73)	0.33	†
Maternal age during recommended vaccination period						
Age (Ave.±SD)	30.52±3.94			(-0.43-1.73)	<0.01 **	a
20-28	75 (33.5)	44 (58.7)	31 (41.3)	1		
29-35	116 (51.8)	69 (59.5)	47 (40.5)	0.97 (0.54-1.75)	0.91	†
36-42	26 (11.6)	19 (73.0)	7 (27.0)	0.42 (0.15-1.18)	0.1	†
Maternal working status when vaccinated						
Yes	79 (35.3)	43 (54.4)	36 (45.6)	1.69 (0.96-2.97)	0.07	†
No	138 (61.6)	90 (65.7)	47 (34.3)	1		
Residential area when vaccinated						
Urban	80 (35.7)	57 (71.3)	23 (28.7)	1		
Rural-adjacent	116 (51.8)	68 (58.6)	48 (41.4)	1.75 (0.95-3.22)	0.07	†
Rural	28 (12.5)	13 (50)	13 (50)	2.86 (1.12-6.94)	0.049 *	†
Prefecture: Tokyo (59, 26.3%), Kanagawa (27, 11.4%), Saitama (7, 3.1%), Chiba (7, 3.1%), Others (104, 46.4%)						
Subjective life standards when vaccinated						
Very good	27 (12.1)	15 (55.6)	12 (44.4)	1		
Good	91 (40.6)	61 (67.0)	30 (33.0)	0.62 (0.26-1.48)	0.28	†
Average	89 (39.7)	53 (59.6)	36 (40.4)	0.85 (0.36-2.03)	0.71	†
Poor	13 (5.8)	8 (66.7)	5 (33.3)	0.63 (0.15-2.59)	0.52	†
Living abroad when vaccinated						
Yes	20 (8.9)	18 (90)	2 (10)	0.16 (0.04-0.70)	0.015 *	†
No	204 (91.1)	120 (58.8)	84 (41.2)	1		
Number of children						
One child	71 (31.7)	46 (64.8)	25 (35.2)	1		
Two children	109 (48.7)	71 (65.1)	38 (34.9)	0.99 (0.53-1.84)	0.96	†
Three children	40 (17.9)	18 (45)	22 (55)	2.25 (1.02-4.96)	0.045 *	†
Four children	3 (1.3)	2 (66.7)	1 (33.3)		0.56	b
Child characteristics						
Age (Ave.±SD)	14.16 ±6.71	14.65±6.80	13.36±6.54	(-0.53 – 3.12)	0.16	a
0-1yrs	10 (4.4)	5 (50)	5 (50)	1		
2-5 yrs	15 (6.6)	9 (60)	6 (40)	0.67 (0.13-3.35)	0.62	†
6-10 yrs	39 (17.3)	26 (66.7)	13 (33.3)	0.50 (0.12-2.04)	0.33	†
11-20 yrs	115 (50.9)	65 (56.5)	50 (43.5)	0.77 (0.21-2.80)	0.69	†
>20 yrs	42 (18.6)	31 (73.8)	11 (26.2)	0.36 (0.09-1.47)	0.15	†
Sex						
Male	113 (50.0)	73 (52.9)	40 (35.4)	0.82 (0.48-1.41)	0.48	†
Female	105 (46.5)	62 (44.9)	43 (41.0)	1		
Unknown	6 (3.5)	3 (2.2)	3 (3.5)			

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	n (%)	Mumps Vaccination Yes	No	Unadjusted OR (95%CI)	p value	
Mumps vaccine status						
Yes	138 (61.6)					
MMR	47 (34.1)					
Single	91 (65.9)					
No	86 (38.4)					
Those who lived with children during children's vaccination period						
Mothers and fathe	179(79.2)	112 (62.6)	67 (37.4)	1		
Mothers only	16 (7.1)	11 (68.8)	5 (31.3)	1.37 (0.46-4.08)	0.58	†
Others	22 (9.7)	12 (54.5)	10 (45.5)	1.42 (0.59-3.46)	0.44	†
Those who took children to vaccinations						
Mother	204 (90.7)	78 (38.2)	126 (61.8)	0.82 (0.33-2.02)	0.66	†
Others	17 (7.6)	6 (35.3)	11 (64.7)	1		
Father (2), Mother or father (6), Grand parents (3), Mother or grand parents (6)						

** denote significance of p value is less than 0.01.

* denote significance of p value is less than 0.05.

a. p value and 95%CI were obtained by student t test for mother's age and children's age.

b. p value was obtained by Fisher Exact Test due to assumption for χ 2 test was unmet.

†. Unadjusted ORs were obtained from univariate logistic regression analysis of dependent variable as non vaccination of mumps.

Total % is not necessarily 100% due to missing values.

Table 3 Reasons for non-vaccination of mumps (Multiple choice) (N=224, n=86 Res=55)

Reasons	n	%
Offered at inconvenience in geographic location	27	12.1
Fear of harmful side effects	25	11.2
The vaccination is non-mandatory	23	10.3
The shot is expensive	16	7.1
The system is complicated	15	6.7
The vaccine is not effective	15	6.7
Being busy	14	6.3
I don't know mumps vaccine	8	3.6
Total	143	

Table 4 Maternal commitment to vaccination (N=224)

Mother's commitment		unadjusted OR(95%CI)	p
Vaccination should be all voluntary	17 (7.5)	1	
Prefer current vaccination system	28 (12.5)	0.70 (0.21-2.37)	p=0.57
Prefer more progressed vaccination system	141 (62.9)	0.40 (0.14-1.10)	p=0.07
Prefer most strict vaccination system such that in the USA is necessary	32 (14.2)	0.23 (0.07-0.82)	p=0.02 *

** denote significance of p value is less than 0.01.

* denote significance of p value is less than 0.05.

unadjusted ORs were obtained from univariate logistic regression analysis of dependent variable as non vaccination of mumps.

Total % is not necessarily 100% due to missing values.

Table 5 Maternal preference to vaccination system (N=224)

Preference	n (%)
Prefer single injection system	27 (11.9)
Prefer double combination vaccination system	73 (32.2)
Prefer triple combination vaccination system	65 (28.6)
Prefer quaduple combination vaccination system	42 (18.5)

n is a number of mothers

** denote significance of p value is less than 0.01.

* denote significance of p value is less than 0.05.

Total % is not necessarily 100% due to missing values.

Table 6 Barrier keywords extracted from open-ended question about vaccination by text analysis (N=224, n=139)

Keywords	n	%
Busy (no time etc.)	28	12.3
Expensive (Subsidy need etc.)	24	10.6
Side effect, Safety (worry, scary etc.)	24	10.6
Information (scarce, scarcity etc.)	20	8.9
System, Schedule (complicated etc.)	16	7.0
Natural immunity (contract mumps, etc.)	12	8.6
Inconvenient, access (long distance, bad, etc.)	10	4.4
Waiting time (long, etc.)	10	7.2
Knowledge (need, more, etc.)	8	3.5
Efficacy (not effective, doubtful, etc.)	7	3.1
Total	159	

Table 7 Health Belief Model factors and mumps vaccination status (N=224)

		n (%)	Mumps Vaccination Yes	No	Unadjusted OR (95%CI)	p value	
Perceived efficacy of mumps vaccine to their children							
Do you think the vaccine is effective to your children?							
	Yes	204 (90.3)	133 (65.2)	71 (34.8)	1		
	No	20 (8.8)	5 (25.0)	15 (75.0)	5.62 (1.96-16.10)	0.002 **	†
Perceived severity of mumps to their children							
Do you think the disease is severe to your children when they are contracted?							
	Yes	212 (93.8)	130 (62.5)	78 (37.5)	1		
	No	12 (5.4)	7 (58.3)	5 (42.6)	5.03 (1.4-19.07)	0.018 *	†
Cue to the action							
Recommendation from family doctor							
	Yes	99 (44.2)	72 (72.7)	27 (27.3)	0.53 (0.30-0.91)	0.023 *	†
	No	125 (55.8)	66 (52.8)	59 (47.2)	1		
Knowing subsidy to the vaccine							
	Yes	10 (4.5)	9 (90)	1 (10.0)		0.093	a
	No	214 (95.5)	129 (60.3)	85 (39.7)			
Learning from experienced mother's recommendation							
	Yes	37 (16.5)	23 (62.2)	14 (37.8)	0.91 (0.44-1.88)	0.8	†
	No	187 (83.5)	115 (61.5)	72 (38.5)	1		
Learning from friends							
	Yes	60 (26.8)	40 (66.7)	20 (33.3)	0.62 (0.33-1.16)	0.14	†
	No	164 (73.2)	98 (59.8)	66 (40.2)	1		
Communication from local government							
	Yes	138 (61.1)	79 (57.2)	59 (42.8)	1.64 (0.94-2.88)	0.084	†
	No	86 (38.4)	59 (68.6)	27 (31.4)	1		
Baby's physical examination							
	Yes	68 (30.4)	41 (60.3)	27 (39.7)	0.998 (0.56-1.79)	0.996	†
	No	156 (69.6)	97 (62.2)	59 (37.8)	1		
Leaning from kindergarten or daycare							
	Yes	31 (13.8)	20 (64.5)	11 (35.5)	0.66 (0.31-1.42)	0.29	†
	No	193 (86.2)	118 (61.1)	75 (38.9)	1		
Leaning from booklets or brochures obtained at hospitals or public places							
	Yes	131 (58.5)	77 (58.8)	54 (41.2)	1.16 (0.67-2.00)	0.59	†
	No	93 (41.5)	61 (65.6)	32 (34.4)	1		
Learning from media (Magazine, TV)							
	Yes	47 (21.8)	26 (55.3)	21 (44.7)	1.44 (0.76-2.76)	0.27	†
	No	177 (79.0)	112 (63.3)	65 (36.7)	1		
Checking maternity handbook							
	Yes	123 (54.4)	76 (61.8)	47 (38.3)	0.99 (0.58-1.71)	0.97	†
	No	101 (44.7)	62 (61.4)	39 (38.6)	1		
Only through non social network information source b							
	Yes	59 (26.3)	28 (47.5)	31 (52.5)	2.21 (1.21-4.05)	0.01 *	†
	No	165 (73.7)	110 (66.7)	55 (33.3)	1		

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		n (%)		Mumps Vaccination Yes	No	Unadjusted OR (95%CI)	p value	
Perceived barriers								
The vaccination is not mandatory								
	Yes	38 (16.8)		15 (39.5)	23 (38)	2.99 (1.46-6.14)	0.03 *	†
	No	186 (82.3)		123 (66.1)	63 (33.9)	1		
Fear of harmful side effects								
	Yes	45 (19.9)		19 (43.2)	25 (56.8)	2.42 (1.24-4.70)	0.01 *	†
	No	179 (79.2)		119 (66.5)	60 (33.5)	1		
Being busy								
	Yes	24 (10.6)		10 (41.7)	14 (58.3)	2.84 (1.18-6.81)	0.02 *	†
	No	200 (88.5)		128 (64)	72 (36)	1		
Offered at inconvenience in geographic location								
	Yes	67 (29.9)		40 (59.7)	27 (40.3)	1.12 (0.62-2.01)	0.07	†
	No	157 (70.1)		98 (62.4)	59 (37.6)	1		
The system is complicated								
	Yes	35 (15.5)		20 (57.1)	15 (42.86)	1.26 (0.61-2.63)	0.53	†
	No	189 (84.4)		118 (63.30)	70 (37.7)	1		
The vaccination is expensive								
	Yes	39 (17.3)		23 (59.0)	16 (41.0)	1.14 (0.57-2.31)	0.71	†
	No	185 (81.9)		115 (62.2)	70 (37.8)	1		
Long waiting time at hospital								
	Yes	10 (4.5)		5 (50.0)	5 (50.0)		0.51	a
	No	213 (95.5)		133 (62.4)	80 (37.6)			
Information is scarce								
	Yes	20 (9.0)		13 (65.0)	7 (35.0)	0.86 (0.33-2.26)	0.76	†
	No	203 (91.0)		125 (61.6)	78 (38.4)	1		
Willing to pay								
1000 yen		50 (22.1)	‡	28 (56.0)	22 (44.0)	1		
2000 yen		49 (21.7)	‡	32 (65.3)	17 (34.7)	0.65 (0.31-1.35)	0.25	†
3000 yen		44 (19.5)	‡	31 (70.5)	13 (29.5)	0.88 (0.41-1.85)	0.73	†
4000 yen		3 (1.3)	‡	1 (33.3)	2 (66.7)	1.01 (0.46-2.18)	0.99	†
>4000 yen		74 (32.7)	‡	45 (61.1)	28 (37.83)	1.15 (0.99-13.27)	0.91	†

** denote p value is less than 0.01.

* denote p value is less than 0.05.

† Unadjusted ORs were obtained from univariate logistic regression analysis of dependent variable as non vaccination of mumps.

a. p value was obtained by Fisher Exact Test due to assumption for χ 2 test was unmet.

‡ Total % is not necessarily 100% due to missing values.

b Non social = Number of mothers who do not rely on relationships with others to obtain information only through; checking maternity handbook, learning from media, leaning from booklets or brochures obtained at hospitals or public places and communication from local government.

Table 8 Multivariate analysis variable selection by step-down method

Variables in Equations

		B	SD	Wald	df	p value	Exp (B)	EXP (B) 95% Lower	Upper
Step 1a	Mother's age	-0.11	0.07	2.36	1	0.12	0.89	0.77	1.03
	Residential area	0.33	0.28	1.38	1	0.24	1.39	0.80	2.40
	Fear of side effects	1.18	0.46	6.65	1	0.01	3.26	1.33	8.01
	Not effective	1.75	0.64	7.38	1	0.01	5.75	1.63	20.31
	Not mandatory	1.25	0.45	7.65	1	0.01	3.48	1.44	8.42
	Living abroad	-2.46	0.98	6.33	1	0.01	0.09	0.01	0.58
	Number of children	0.24	0.27	0.83	1	0.36	1.28	0.76	2.16
	Perceived severity	0.21	0.72	0.09	1	0.77	1.24	0.30	5.10
	Recommendation from family doctor	-0.97	0.37	6.95	1	0.01	0.38	0.18	0.78
	Being busy	1.50	0.58	6.77	1	0.01	4.48	1.45	13.88
	Maternal obligation	-0.27	0.25	1.20	1	0.27	0.76	0.47	1.24
	Child's age by Mother's age	0.00	0.00	0.06	1	0.80	1.00	1.00	1.00
	Constant	3.69	3.02	1.49	1	0.22	40.14		
Step 2a	Mother's age	-0.10	0.04	6.62	1	0.01	0.91	0.84	0.98
	Residential area	0.33	0.28	1.42	1	0.23	1.39	0.81	2.41
	Fear of side effects	1.20	0.46	6.88	1	0.01	3.31	1.35	8.07
	Not effective	1.74	0.64	7.33	1	0.01	5.70	1.62	20.12
	Not mandatory	1.26	0.45	7.90	1	0.00	3.52	1.46	8.48
	Living abroad	-2.45	0.98	6.26	1	0.01	0.09	0.01	0.59
	Number of children	0.27	0.25	1.20	1	0.27	1.31	0.81	2.13
	Perceived severity	0.23	0.72	0.10	1	0.76	1.25	0.30	5.17
	Recommendation from family doctor	-0.98	0.37	7.07	1	0.01	0.38	0.18	0.77
	Being busy	1.48	0.57	6.74	1	0.01	4.40	1.44	13.47
	Maternal obligation	-0.27	0.25	1.18	1	0.28	0.76	0.47	1.24
	Constant	3.10	1.89	2.68	1	0.10	22.11		
Step 3a	Mother's age	-0.10	0.04	6.61	1	0.01	0.91	0.85	0.98
	Residential area	0.32	0.28	1.34	1	0.25	1.37	0.80	2.36
	Fear of side effects	1.21	0.45	7.04	1	0.01	3.34	1.37	8.13
	Not effective	1.72	0.64	7.30	1	0.01	5.59	1.60	19.47
	Not mandatory	1.26	0.45	7.92	1	0.00	3.53	1.47	8.48
	Living abroad	-2.44	0.98	6.26	1	0.01	0.09	0.01	0.59
	Number of children	0.26	0.24	1.12	1	0.29	1.29	0.80	2.08
	Recommendation from family doctor	-0.97	0.37	7.02	1	0.01	0.38	0.18	0.78
	Being busy	1.47	0.57	6.70	1	0.01	4.36	1.43	13.30
	Maternal obligation	-0.28	0.25	1.23	1	0.27	0.76	0.47	1.24
	Constant	3.25	1.82	3.18	1	0.07	25.90		

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		B	SD	Wald	df	p value	Exp(B)	EXP(B) 95% Lower	Upper
Step 4a	Mother's age	-0.09	0.04	5.94	1	0.01	0.92	0.85	0.98
	Residential area	0.37	0.27	1.85	1	0.17	1.44	0.85	2.45
	Fear of side effects	1.19	0.46	6.85	1	0.01	3.30	1.35	8.06
	Not effective	1.70	0.63	7.28	1	0.01	5.47	1.59	18.79
	Not mandatory	1.26	0.45	7.91	1	0.00	3.51	1.46	8.44
	Living abroad	-2.43	0.97	6.24	1	0.01	0.09	0.01	0.59
	Recommendation from family doctor	-1.00	0.37	7.43	1	0.01	0.37	0.18	0.76
	Being busy	1.50	0.57	6.87	1	0.01	4.50	1.46	13.88
	Maternal obligation	-0.28	0.25	1.27	1	0.26	0.76	0.47	1.23
	Constant	3.38	1.81	3.47	1	0.06	29.29		
Step 5a	Mother's age	-0.09	0.04	6.31	1	0.01	0.91	0.85	0.98
	Residential area	0.41	0.27	2.40	1	0.12	1.51	0.90	2.55
	Fear of side effects	1.28	0.45	8.07	1	0.00	3.58	1.49	8.63
	Not effective	1.74	0.64	7.49	1	0.01	5.71	1.64	19.90
	Not mandatory	1.30	0.44	8.54	1	0.00	3.66	1.53	8.72
	Living abroad	-2.26	0.93	5.94	1	0.01	0.10	0.02	0.64
	Recommendation from family doctor	-1.06	0.36	8.51	1	0.00	0.35	0.17	0.71
	Being busy	1.46	0.57	6.56	1	0.01	4.29	1.41	13.05
	Constant	2.58	1.64	2.46	1	0.12	13.19		

a. Step 1: Variables in equations; Mother's age, Residential area, Fear of side Number of children, Perceived severity, Recommendation from family doctor, Recommendation from family doctor, Maternal obligation, Child's age * Mother's age
Backward elimination stepwise variable selctions was done by setting probability for stepwise entry 0.15 and removal 0.15 (SPSS Statistics 23)

Table 9 Multivariate analysis findings for predicting non immunization of mumps vaccine (N=224)

	Adjusted OR (95%CI)	p value
Mother's age	0.91 (0.85–0.96)	<0.01 **
Residential area	1.55 (0.93– 2.61)	0.09
Living abroad when vaccination	0.10 (0.02–0.68)	0.02 *
Maternal commitment	0.72 (0.46–1.15)	0.18
Perceived efficacy of mumps vaccine		
The vaccine is not effective	6.21 (1.85–20.91)	<0.01 **
Cue to the action		
Recommendations from family doctors	0.35 (0.17–0.71)	<0.01 **
Perceived barriers		
Being busy	3.30 (1.21–9.01)	0.02 *
The shot is not mandatory	3.30 (1.41–7.72)	<0.01 **
Fear of harmful side effects	2.55 (1.10–5.89)	0.03 *

** denote p value is less than 0.01

* denote p value is less than 0.05

Adjusted ORs were obtained from multivariate analysis of dependent variable as non vaccination of mumps

Hosmer Lemshaw test, ROC analysis, R2=0.32

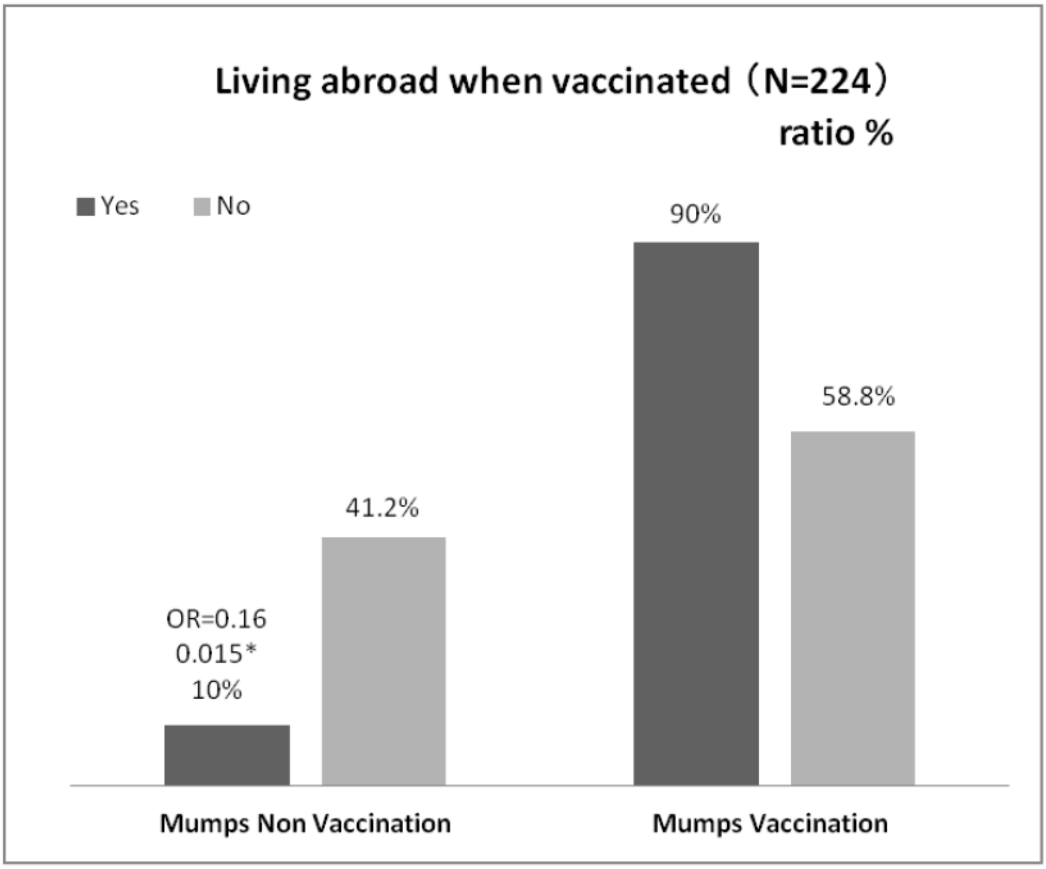

Figure 3 Univariate analysis result of mumps vaccine study: Living abroad when vaccinated (N=224)

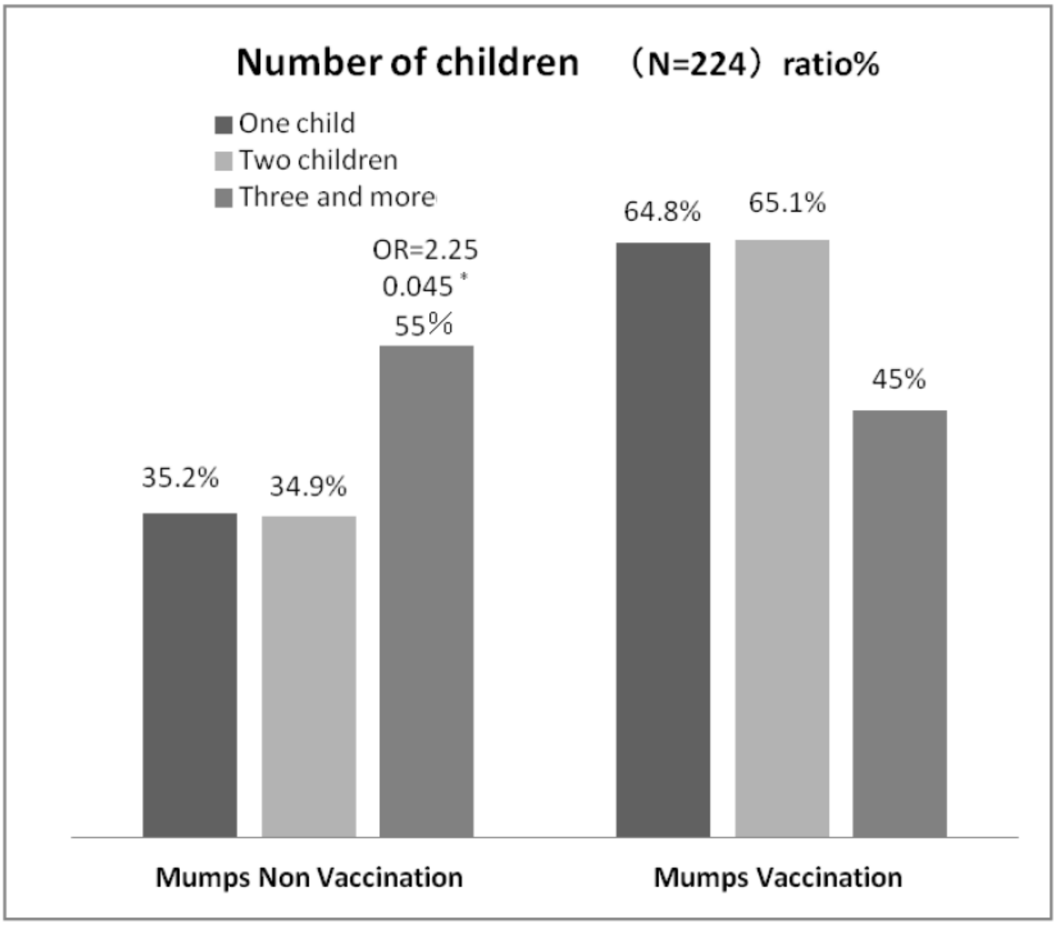

Figure 4 Univariate analysis result of mumps study: Number of children (N=224)

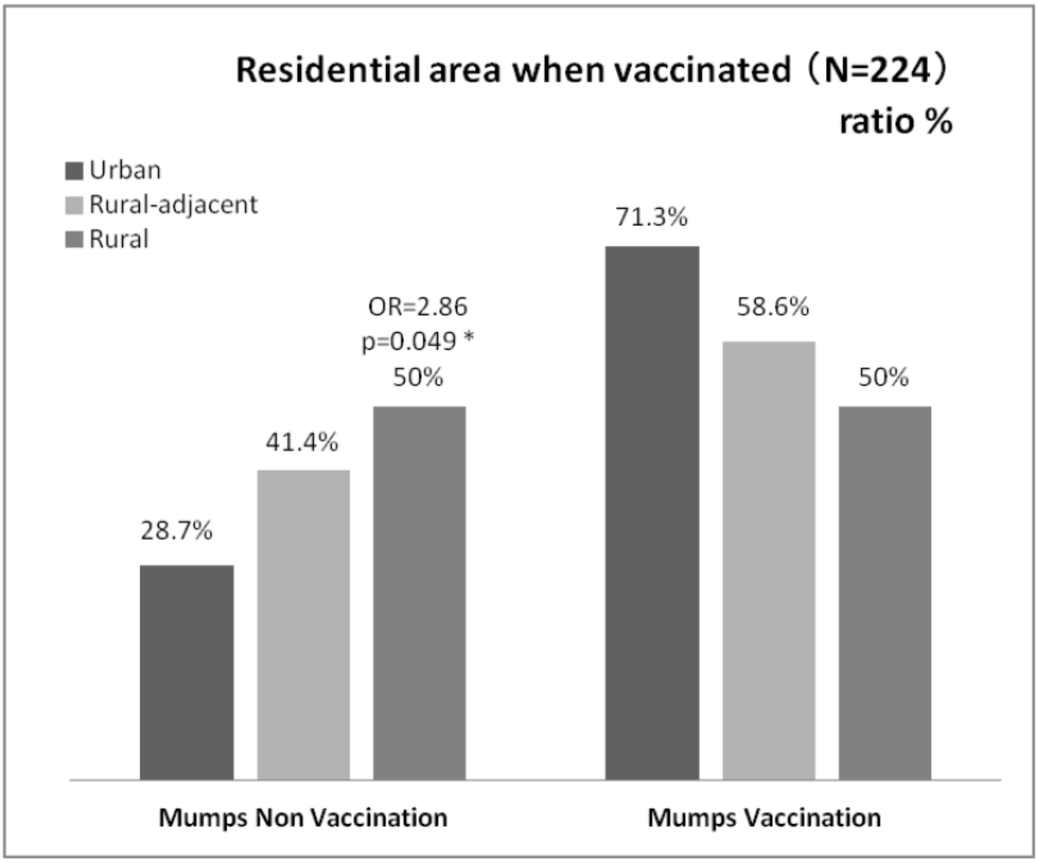

Figure 5 Univariate analysis result of mumps study: Residential area when vaccinated (N=224)

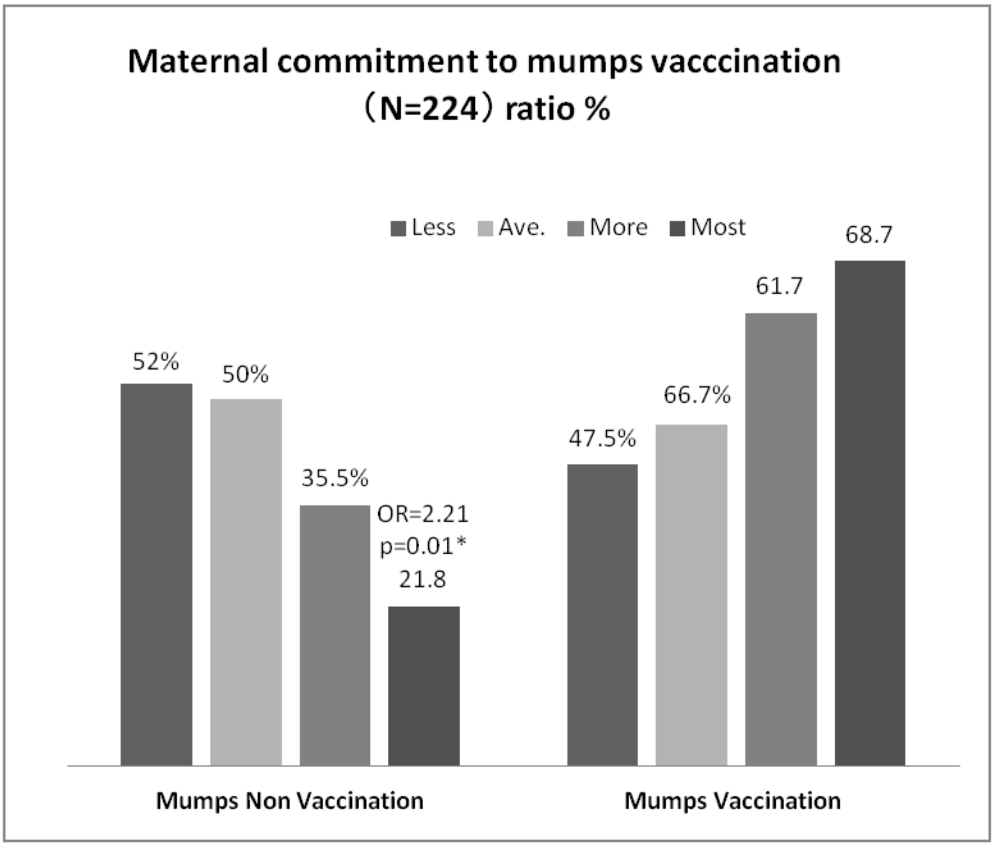

Figure 6 Univariate analysis result of mumps study: Maternal commitment to mumps vaccination (N=224)

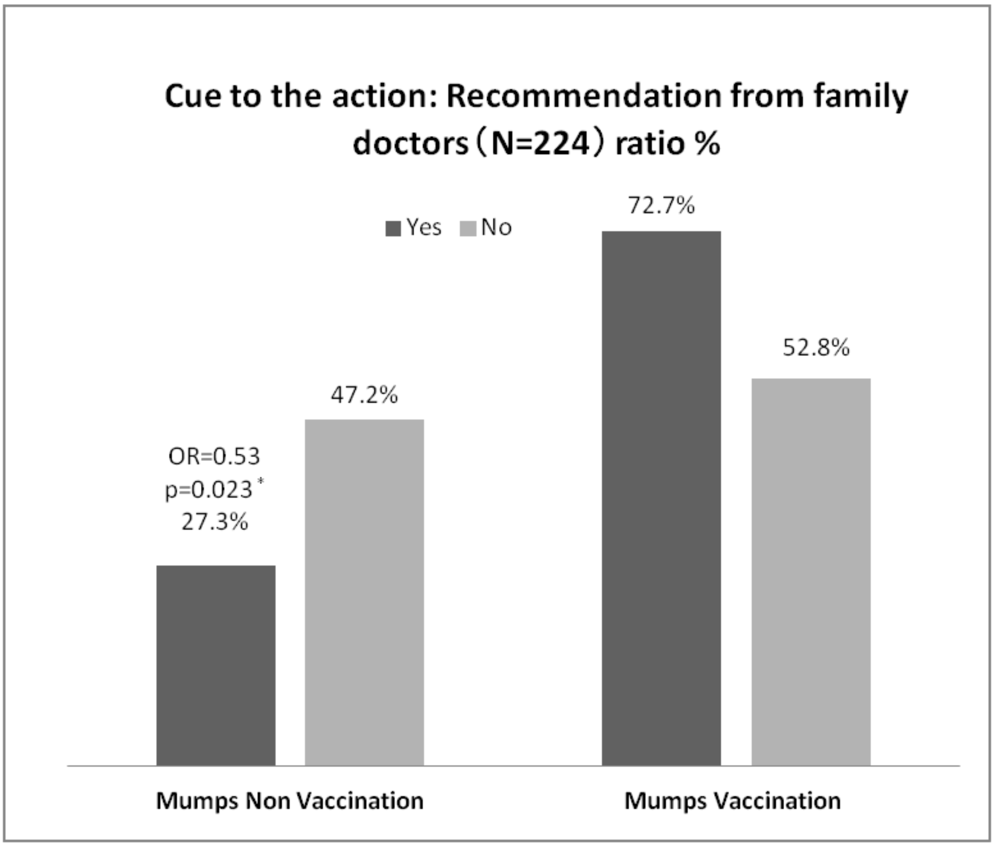

Figure 7 Univariate analysis result of mumps study: Cue to the action; Recommendation from family doctors (N=224)

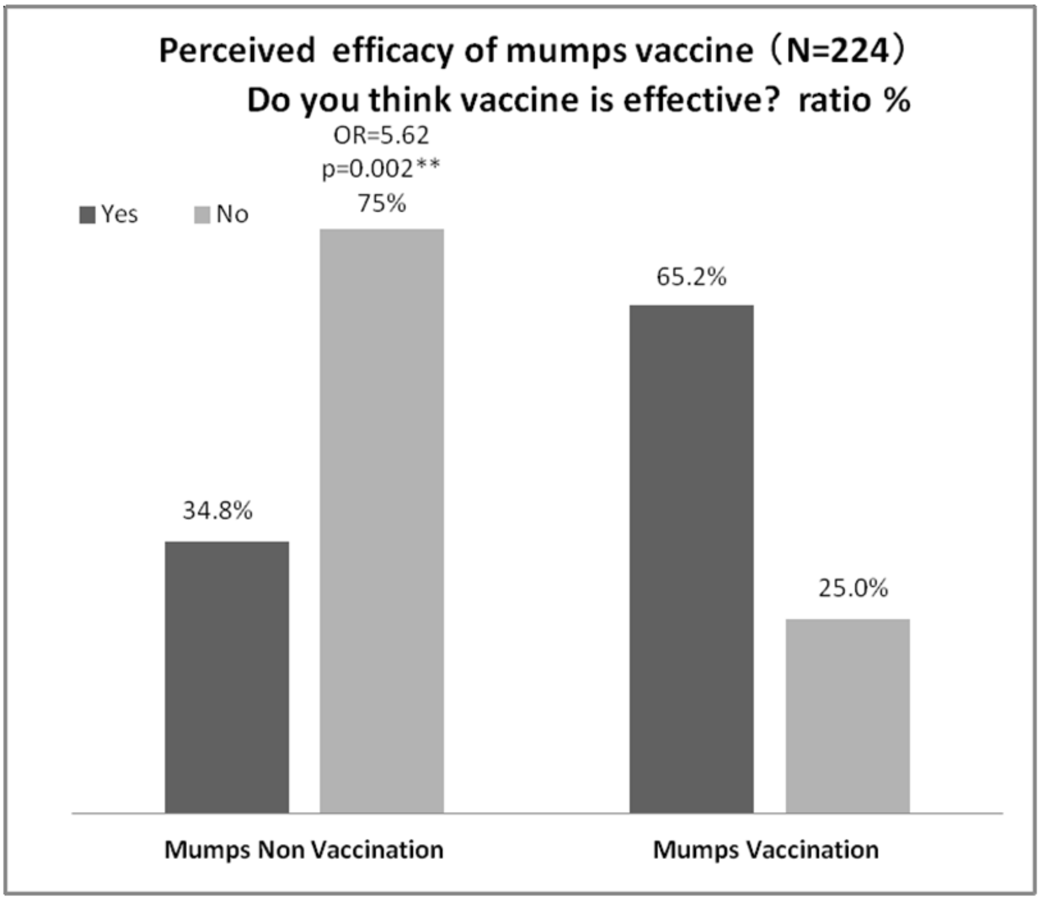

Figure 8 Univariate analysis result of mumps study: Perceived efficacy of mumps vaccine (N=224)

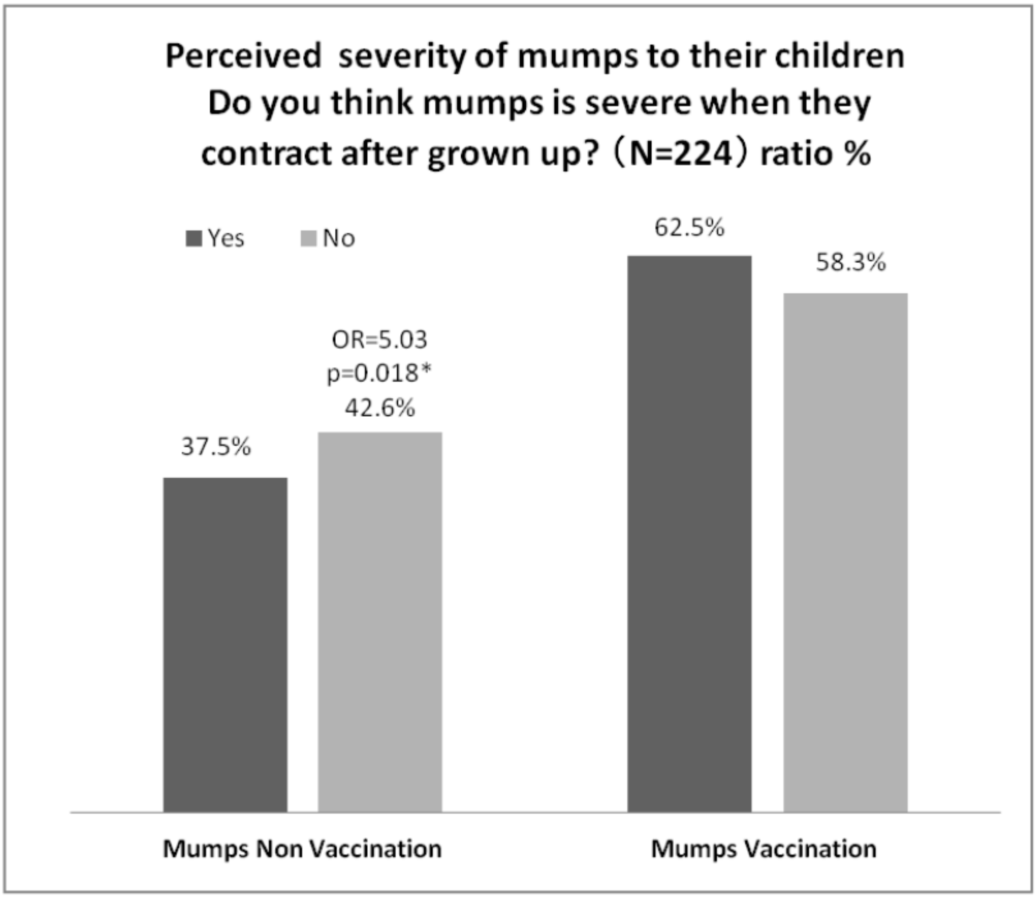

Figure 9 Univariate analysis result of mumps study: Perceived severity of mumps (N=224)

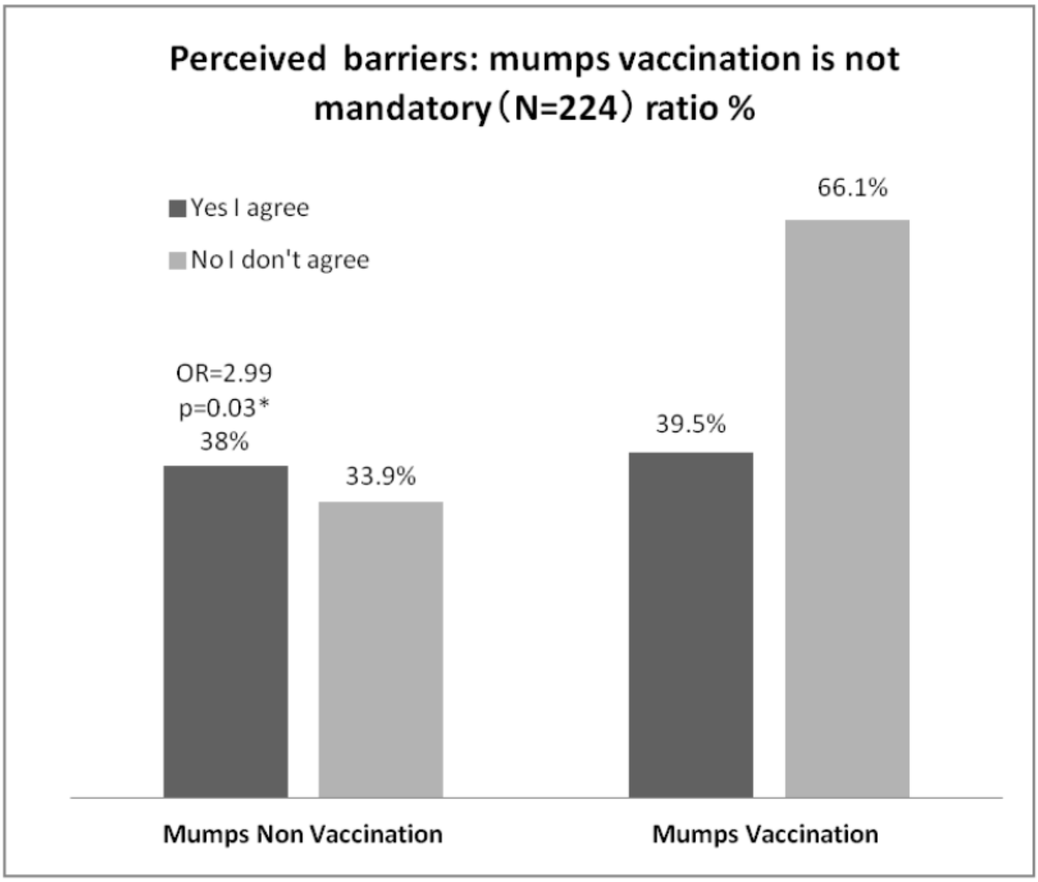

Figure 10 Univariate analysis result of mumps study: Perceived barriers: mumps vaccination is not mandatory (N=224)

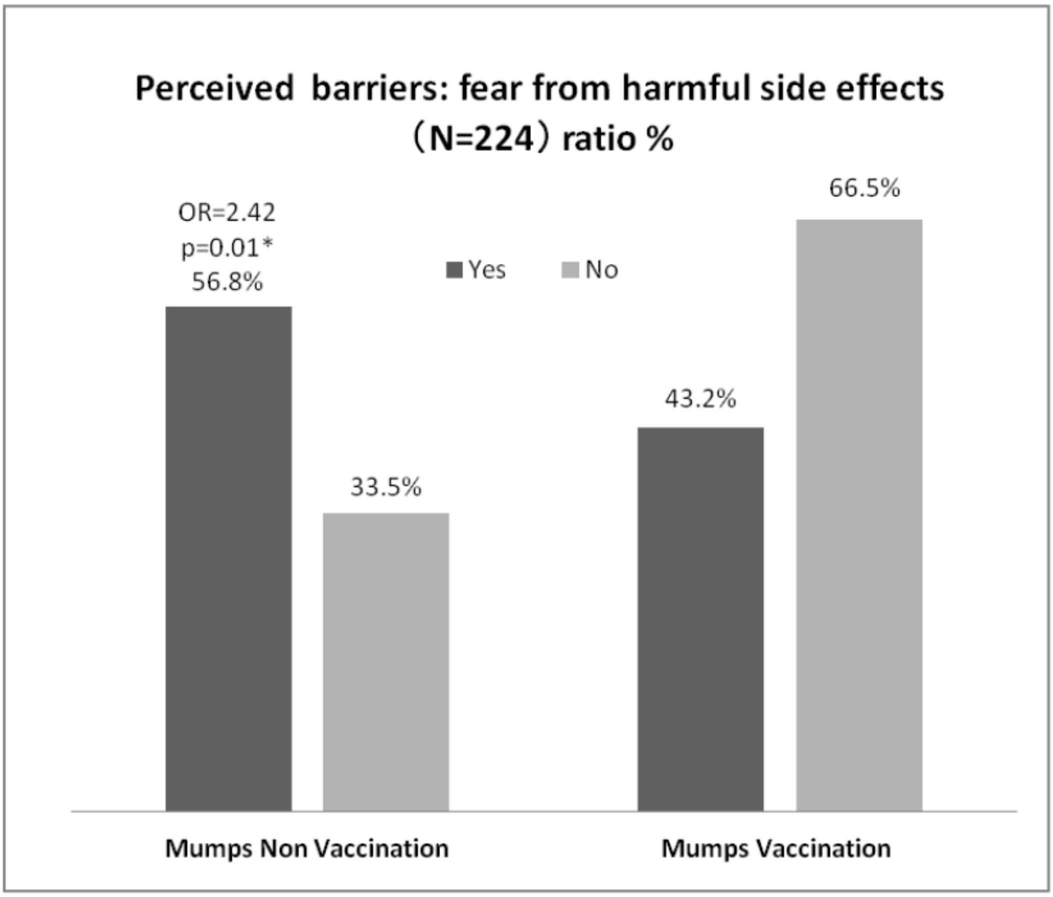

Figure 11 Univariate analysis result of mumps study: Perceived barriers: fear from harmful side effects (N=224)

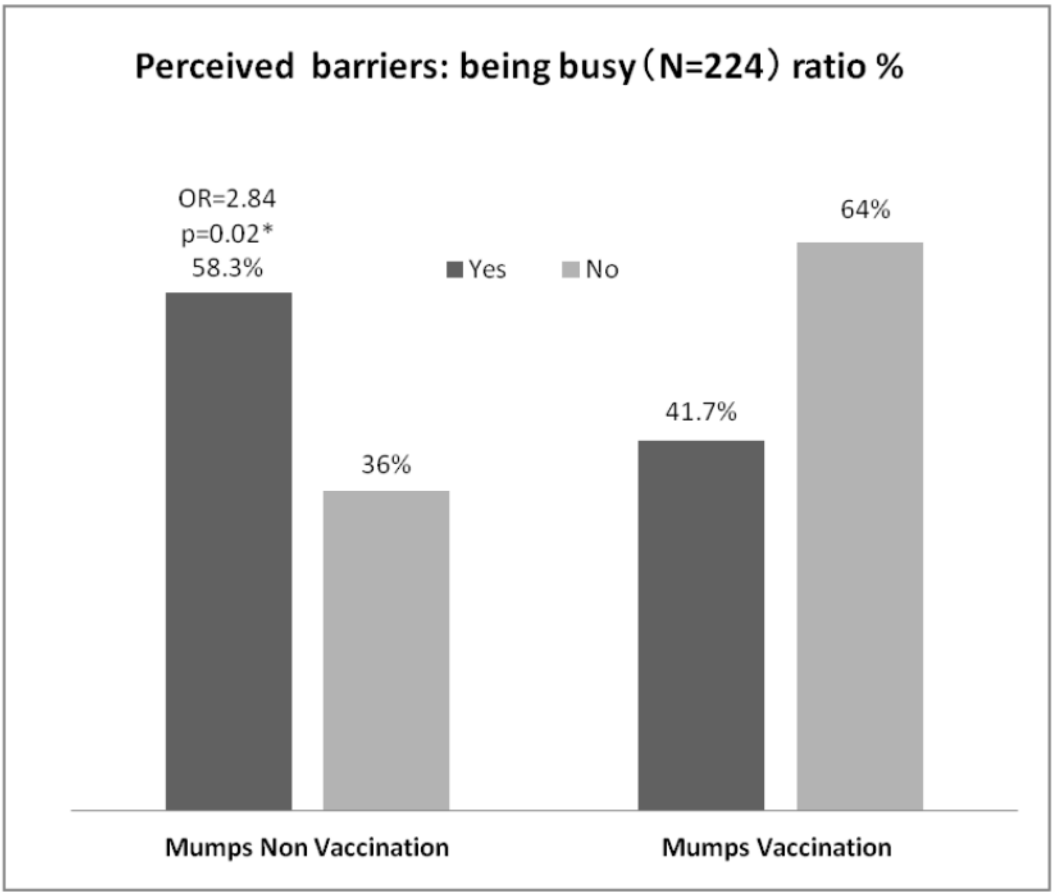

Figure 12 Univariate analysis result of mumps study: Perceived barriers: being busy (N=224)

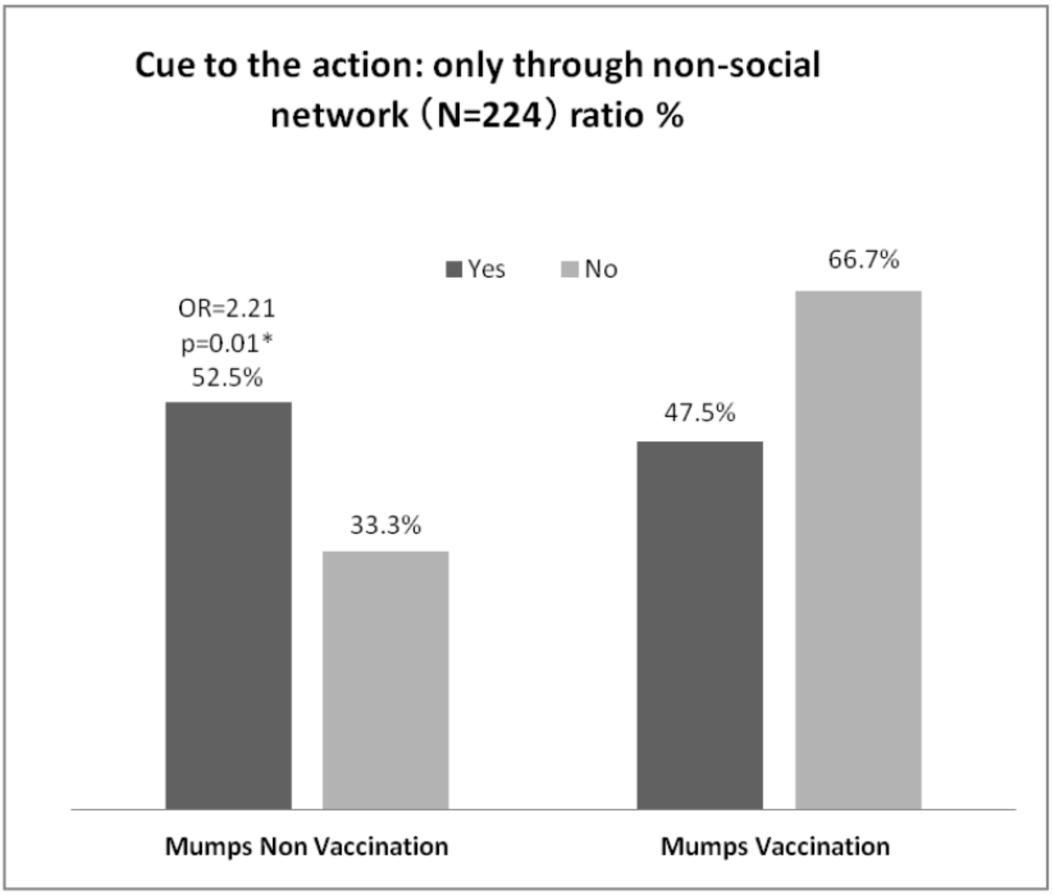

Figure 13 Univariate analysis result of mumps study: Cue to the action: information obtained only through non social network (N=224)

Chapter IV

Study II: Seasonal flu vaccination acceptance

among

the elderly people who live in a community in Japan

4.1 Background and objective

In Japan, the number of people dying from influenza is still increasing; influenza causes pneumonia, bronchitis and influenza-related respiratory illnesses that raise excess mortality. The majority of the deceased are the elderly and vulnerable populations such as those with chronic diseases.

Given these circumstances, the Japanese government amended the Preventive Vaccination Law in 2001 to include flu vaccinations as routine immunizations for this age group. People 65 years old and over can now receive flu vaccinations subsidized by their local governments. This caused the government to reconsider influenza vaccination among the elderly who were 65 years old and older, and 60 years and older in a high-risk group of those who have chronic diseases such as diabetes, cardiac, renal and respiratory diseases. They were included in NIP in 2001 by amending the Preventive Vaccination Law. Although people 65 years old and over now can receive subsidies for flu vaccinations from local governments where they live, the decreased vaccination rate did not recover sufficiently. The estimated vaccination rate among the elderly and vulnerable populations is below 50 percent while that among children is approximately 30 percent (195), ranking in the lower range of OECD member countries (Fig. 14). For example in the US, the coverage of total population with six months and older are reported to be nearly 50 percent (97). Additional concern exists that the elderly Japanese who belong to high-risk groups may not receive sufficient seasonal flu vaccinations.

Under the circumstances, we must consider the low vaccination rate of seasonal influenza vaccination among the elderly population, even though the Japanese government included the vaccination in NIP in 2001. Addressing the issue of increasing excess death cases during the flu season, the author determined to study the awareness of elderly people 65 years and older to investigate factors including HBM with the objective of influencing their decisions to be vaccinated. Another goal in this study is to examine the vaccination situation of high-risk groups with chronic diseases. The author set two objectives in Study II.

4.2 Sample and method

The author sent questionnaires in 2009 and 2010 to university graduates 65 years old and over who were not institutionalized. The candidates were randomly selected from lists obtained from university alumni books separately in 2009 and 2010 from alumni offices that were authorized to provide information on those 65 years and older. Unfortunately, less than 10 percent of the alumni were female so female graduates were excluded to avoid bias due to gender difference. A total of 1457 questionnaires were sent in 2009 and 2010 with cover letters by postal mail including self-addressed and stamped return envelopes. The cover letter noted that the questionnaire was completely anonymous, data obtained from the survey will be de-identified and only aggregated data will be used. Also, the letter noted that participation was completely voluntary.

4.2.1 Instruments

The author developed a questionnaire with 30 questions such as demographic questions on the respondents and their families and questions regarding seasonal influenza vaccinations and vaccination status. It asked their ages, working statuses, subjective life standards (very good, good, average, poor), self-rated health (SRH; very good, good, average, poor), regions where they live (urban, rural-adjacent, rural) and prefectures, living with family or not (not, with spouse, with spouse and children, with spouse, children and grandchildren, other). It also asked their influenza immunization status (annual, sometimes, never), a multiple choice question about their reasons, if any, for non-vaccination (unnecessary, ineffective, expensive, bothersome, fear of side effects, being busy, other) and history of flu-like symptoms within the past two years (yes, no). In addition, prevention measures against the flu if any such as gargling, wearing masks in public, having sufficient sleep and good nutrition were included. Furthermore, respondent knowledge about flu and cold symptoms (high fever, low-grade fever, joint or muscle pain, exhaustion, sore throat, sneezing) were asked. The questionnaire also asked for current and past medical histories, including strokes, hypertension, cardiovascular, liver, gallbladder, gastroduodenal diseases, diabetes, tuberculosis, asthma and chronic bronchitis, anemia, rheumatism and arthritis, cancer, bone fractures, pneumonia, allergies and more. Lifestyle questions of healthy habits such as exercise, sports hours per week, measuring weight regularly, measuring blood pressure regularly, resting regularly, quitting smoking, quitting drinking and relieving stress were included. For social participation and activity questions, groups and organizations they are participating in such as elderly clubs, neighborhood associations, hobby clubs, fitness and sports related clubs, study and culture clubs, civic activity clubs, religious organizations, volunteer organizations and NPOs, commerce and industry associations, retiree organizations, alumni clubs and employment center services for the elderly were asked about. Questions about activities they participate in such as sports, hobbies, community involvement, environmental activities, education and culture, work productivity, support activities for the elderly, neighbor security, support activities for children and home care were also asked. The same as in the mumps vaccine study, HBM constructs such as perceived flu severity, knowing the difference between flu and ordinary colds (yes, no), perceived vulnerability to flu and colds, perceived efficacy of influenza vaccine, cue to action factors of the information sources (open-ended) asking how participants obtain information about flu vaccinations and knowing about flu vaccine subsidies, and WTP (willingness to pay) were asked about. Two open-ended questions where participants could write freely were included; one was on their opinions about influenza vaccines and the other was about their concerns on health care, policy and the health care system.

4.2.2 Statistical method

As separate data from independent lists in 2009 and 2010 was collected, the goodness of fit test was undertaken to test if differences existed in participant characteristics between the two groups. Then, according to the statistical analysis described in the methodology in this section, participant characteristics, seasonal influenza immunization statuses, medical histories, health habits and HBM constructs were analyzed by descriptive statistics. For analysis, the 'have never had seasonal flu vaccines' group was defined as a non-vaccination group. Age was considered as a continuous variable and the difference between who had and had not been immunized with flu vaccines were compared with student's t-test. SRH was skewed, dividing into the 'bad' or 'good' categorical variable. Other categorical and ordinal variables were entered into a univariate logistic regression analysis using non-vaccination as a dependent variable to obtain unadjusted odds ratios (OR). The total hours spent on sports per week, a total number of medical issues and WTP variables did not fall within normal distribution assumptions so that the p values were obtained by the Mann-Whitney U test comparing vaccinated and non-vaccinated groups. HBM barrier factors were created from one open-ended question on opinions about flu vaccinations by text analysis extractions and combined with reasons for non-vaccinations (IBM SPSS Text Analytics for Surveys 4.0). The questionnaire had a question about groups and organizations being participated in and a question about social activities being participated in, but the variables included in the questionnaire were twenty-one and ten respectively. Some of them overlapped so that factor analysis was performed to reduce the variables (IBM SPSS 23).

Following the methodology, variables for multivariate analysis were selected by the step-down method. Significant variables after univariate analysis and interaction variables (above r=0.4) were also candidates for an adjusted logistic regression model. Interactions for all variables were tested by Spearman's rank correlation tests and a final multivariate model of non-vaccination against the flu as a dependent variable was obtained.

Qualitative analysis was performed on replies to the open-ended question of opinions on flu vaccination. Replies to an open-ended question on concerns about health care, policy and the health care system were analyzed by text analysis.

4.3 Results

The author sent 1457 questionnaires in total in 2009 and 2010 and 586 (39.2%) were returned. Eight returned questionnaires were incomplete, leaving 578 (167 in 2009, 411 in 2010) to be included in this study.

4.3.1 Goodness of fit test between two populations

As two independent data sets were collected, first the goodness of fit test was undertaken to test for differences in participant characteristics between the two groups. From the results, no differences existed in participant characteristics between the two groups including age (p=0.81), work status (p=0.16), regions where they live (p=0.32), living with family or not (p=0.59), subjective life standards (p=0.48), sports hours per week (p=0.21), immunization status (p=0.89) and self-rated health (SRH) (p=0.08) (Table 10). Given these results, the author combined the two data sets together and analyzed them as one aggregated data set.

4.3.2 Descriptive analysis results

4.3.2.1 Participant characteristics

The study had a total of 578 participants. Table 11 shows the results of descriptive analysis of participant characteristics. The participants' mean (SD) age was 73.19 (SD=4.43; 65-93 years). About sixty-two percent of participants responded they were living with their spouse and only 4.5 percent of participants responded they were living alone.

Nearly 37 percent were working and about 85 percent responded that their SRH was good. About 32 percent of the participants responded that they had contact histories of flu-like symptoms within the past two years.

<u>Medical histories</u>

Among those who reported their medical history (n=514), the most frequently reported were hypertension (28.7%), hay fever (15.7%), cancer (12.8%) and diabetes

(10.9%). The total number of medical histories for each participant was zero to two (70.1%) followed by three to five (28.2%). Only one participant reported that he had no issues in his medical history to report. Thirty-two percent of the participants had medical histories such as respiratory, cardiovascular, diabetes and gallbladder disease that meant they should be recommended to have flu vaccinations (Table 12).

For the healthy life style question, 74.9 percent of participants responded that they regularly exercised such as walking or playing sports. About 41.6 percent of the participants answered they had spent one to five hours per week for sports followed by 6 to 10 hours per week (23.8%). About 69.4 percent responded that they had taken good nutrition (Table 13). Preventive practices besides vaccinations against flu were gargling (70.1%), washing hands (67.8%), good nutrition (58.5%) and having enough sleep (56.8%) (Table 14). For knowledge about flu symptoms, they reported high fever (92.6%), exhaustion (65.9%), joint or muscle pain (65.2%), sneezing (44.8%), sore throats (22.4%) and low-grade fevers (8.3%). They responded that their knowledge of cold symptoms was sneezing (79.9%), exhaustion (73.5%), low-grade fever (66.6%), sore throats (40.3%), high fevers (31.5%) and joint or muscle pain (29.1%) (Table 15).

More than 90 percent of the participants responded that high fever was an influenza symptom. Many responded that they felt more exhausted when they caught a cold (73.5%) than the flu (65.9%); some confusion was observed such that nearly 45 percent responded sneezing as an influenza symptom when comparing the flu and colds.

4.3.2.2 Influenza vaccination status

The influenza vaccination statuses of the participants were annually (46.4%), sometimes (18.3%) and never (33.8%) (Table 11). Table 16 shows the reasons for non-vaccination against the flu. The most frequent reasons for non-vaccination were unnecessary (28.8%), ineffective (15.7%), burdensome (12.1%) and scared of side effects (10.1%).

Among those who had flu vaccinations (n=379), 91.1 percent reported they had no side effects. The most frequently reported side effects were fever (8.3%) and swelling at injection sites (3.7%); serious side effects such as the motor or neurological related side effects (1.1%) were also reported (Table 17).

4.3.2.3 HBM factors

Table 18 shows a descriptive analysis of HBM constructs. About 20 percent of the participants thought they were vulnerable to the flu or colds and about 30 percent of the participants thought flu vaccines were ineffective. For perceived severity of flu, nearly 84 percent of the participants responded that they knew the difference between the flu and ordinary colds.

For the cue to action information sources, the most frequently reported source was learning from the media (44.5%), followed by family doctor recommendations (9.5%), friend or family recommendations (2.6%), communication from local governments (5.2%) and academic journals or experts' information (4.5%). The least frequently reported was learning from booklets or brochures obtained at hospitals or in public places (1.6%).

As explained in the methodology section, barrier variables were created by combining reasons for non-vaccination and text responses to open-ended questions that were extracted by text analysis (Tables 16 & 19).

Newly created HBM barrier variables are included in Table 18. For barrier factors, the most frequently reported responses were the vaccination was unnecessary (19.7%), fear of harmful side effects (11.8%), information about vaccine scarcity (7.3%), vaccination being expensive (5.7%), concern about vaccine scarcity (5.5%) and being busy (1.6%).

4.3.2.4 Social factors

Table 11 also contains the social factors of participants. The residential area was urban (71.5%), rural-adjacent (26.1%) and rural (2.4%); more participants were living in urban areas. The reported residential prefectures of the participants were Tokyo (43%), Kanagawa (12.3%) and other prefectures in the Kanto region (18.3%) that concentrated in the Tokyo area and nearby.

About 36 percent of the participants responded that they were working and more than half responded that their subjective life standards were good or very good. This ratio demonstrates that this population was biased to better subjective life standards.

For self-rated health (SRH), as many as 85.3 percent of the participants responded with good; only 14.7 percent responded with poor.

To focus on the social network factor, those who obtained the information only through non social network factors such as learned from communication from local governments, booklets or brochures obtained in public places, academic journals or experts' information and learning from the media were aggregated. As a result about 50 percent of the participants did not rely on information sources from social networks (Table 18).

For social activities, Table 20 shows the responses to a questionnaire about groups and organizations that respondents participated in. The most frequent responses were hobby clubs (36%), followed by retiree organizations (29.8%). The average number of organizations or clubs of those who participated in any were 2.3 per respondent. Table 21 shows social activities the respondents participated in. The most frequent responses were fitness and sports activities (35.9%), followed by life and environment activities (30.3%). Those who responded none accounted for 14.5 percent.

4.3.2.5 Text analysis of open-ended question about concerns

Free text responses (n=300) to open-ended question of 'do you have any concerns over health care, policy and the health care system?' were analyzed by text analysis software (Fujitsu Trend Search 2008). Keywords extracted by text analysis and a concept mapping figure that demonstrates the relationship between these keywords are shown in Table 26 and Fig. 30.

From the results, nearly 70 percent of respondents replied that they have concerns. The top keywords were health care, hospitals, doctors and policy, but flu and flu vaccine were noticeably among their top concerns (Table 26). If we look at the concept map (Fig. 30), these keywords are connected with the keywords of scarcities, government, outbreak and others.

4.3.3 Univariate analysis results

4.3.3.1 Characteristics of participants

Table 11 also contains the results of univariate analysis for each demographic variable as non-vaccination against the flu to be the independent variable and calculated the non-adjusted ORs. From the results, participants were more significantly likely to be vaccinated against the flu if they were 75 years and older (OR=0.53;

p<0.01) and had flu-like symptoms within the past two years (OR=0.54; p=0.002) (Fig. 15). The participants who responded that they were working (OR=1.19; p=0.33) were less likely to be vaccinated but not significantly. Those who lived alone (OR=1) were likely more vaccinated, but were not significant due to the low number of participants who reported living alone (4.5%). For medical histories and non vaccination analysis, those who had histories of rheumatism, gout or arthritis were significantly less vaccinated (OR=5.28; p=0.015) and those who had any medical histories making them recommendable for flu vaccinations such as respiratory (OR=0.67; p=0.46), cardiovascular (OR=0.57; p=0.08), diabetes (OR=0.81; p=0.46) and gallbladder (OR=0.57; p=0.40) diseases were more vaccinated but not significantly. For the total number of medical histories, the Mann-Whitney U test comparing median ranges demonstrated that those who had 'a number of medical histories' were more significantly likely to have been vaccinated (p=0.015) .

Tables 13 and 14 contain univariate analysis results of the life style health and preventive practices against the flu and non-vaccination analysis respectively. Those who responded measuring blood pressure regularly (OR=0.64; p=0.013), quitting drinking or decreasing the volume (OR=0.54; p=0.009), gargling (OR=0.50; p<0.01), washing hands (OR=0.57; p<0.01) and wearing masks (OR=0.58; p<0.01) were significantly more vaccinated. Those who had more sports per week were less vaccinated (p=0.045).

4.3.3.2 HBM factors

Table 18 also includes the results of univariate analysis of HBM factors on non vaccination against seasonal influenza as a dependent variable. From the analysis, the factors of perceived vulnerability to the flu or colds (OR=0.27; $p<0.001$) (Fig. 17), perceived flu severity (OR=0.54; $p<0.01$) (Fig. 18), cues to action; recommendations from family doctors (OR=0.23; p=0.001) (Fig. 19), knowing about the vaccination subsidies (OR=0.21; $p<0.001$) (Fig. 20) and communication from local governments (OR=0.22; p=0.014) (Fig. 21) significantly decreased non vaccination risk. Perceived efficacy (OR=30.04; $p<0.01$) (Fig. 22), barrier factors such as fear of harmful side effects (OR=6.67; $p<0.001$) (Fig. 23), being busy (p=0.001) (Fig. 24) and vaccination being unnecessary ($p<0.001$) (Fig. 25) significantly increased the non vaccination risk. However, the variable of 'concern over vaccine scarcity' was shown to not be a barrier, and those concerned over vaccine scarcity were more vaccinated (Fig. 26) (OR=0.26; p=0.013).

WTP became significant and those who were willing to pay were more significantly vaccinated with the seasonal influenza vaccine ($p<0.001$) (Fig. 29).

4.3.3.3 Social factors

Table 11 also contains results of univariate analysis of social factors for non vaccination against seasonal influenza as a dependent variable. Among social factors, those who reported SRH as poor were more vaccinated than those who reported good and was significant (OR=0.51; p=0.02) (Fig. 16). From the results, those who were living in rural adjacent regions (OR=1.35; p=0.14) and those who had lower subjective life standards (OR=1.03-1.52; p=0.11-0.97) were less vaccinated, but not significantly. For social network factors of cues to action, there was no significant difference between those who obtained the information depending on social networks and those who obtained the information depending on human relationships (p=0.87).

For social activity factors, 12 responses regarding organizations and groups (Table 20) and ten responses regarding social activities (Table 21) had similarities and partially overlapped so that factor analysis was undertaken and the number of total variables was reduced to 10 (IBM SPSS 23). From the correlation results between social activity scores after factor analysis and seasonal influenza vaccination status, those who participated in a community and security, academics and learning, productivity, religion, community and elderly clubs and volunteer activities were more vaccinated and those who participated in fitness and sports, hobbies and culture, supporting the elderly and commercial activities were less vaccinated but not significantly.

4.3.4 Multivariate analysis results

As explained in the methodology section, variables for multivariate analysis were selected. Variables which showed significance and close significance after univariate analysis, and interaction variables by correlation test ($r>0.4$), were the candidate variables, but there were no interaction variables that should be considered as candidate factors in this study. As a result the candidate variables were participant age, SRH, flu-like symptoms within the past two years, a history of cardiovascular disease, rheumatism/gout or arthritis, a number of medical issues, sports hours per week, HBM factors such as perceived vulnerability to the flu or colds, perceived flu severity, perceived efficacy of influenza vaccine, cue to action factors of family doctor recommendations, knowing about vaccination subsidies, communication from local governments, barrier factor of fearing harmful side effects, the vaccination being expensive and WTP. The barrier factor of the vaccine being unnecessary was overlapped with the barrier factor of the vaccine being ineffective (r=0.74) and they were not independent of each other. The factor of concern over vaccine scarcity was not regarded as a barrier factor so that these factors were excluded from the candidates. Also the barrier factor of being busy was excluded due to the low number of only one event although the variable was significant by univariate analysis.

As a result, the selected variables for the final model were participant age, a history of cardiovascular disease, perceived vulnerability to the flu or colds, perceived vaccine efficacy, perceived barriers such as fearing harmful side effects and the vaccination being expensive, cue to action factors such as family doctor recommendations, knowing about vaccination subsidies and communication from local governments. The factor of a history of rheumatism, gout or arthritis that was excluded in a previous step was included due to additional space for a number of variables (Table 22). The results of multivariate analysis are shown in Table 23.

This shows that participants who were older (aOR=0.90; p<0.01), with a history of cardiovascular diseases (aOR=0.26; p=0.016), perceived vulnerability to the flu or colds (aOR=0.13; p<0.001), knew about the vaccination subsidies (aOR=0.21; p<0.001) and had the information from communication from local governments (aOR=0.12; p=0.024) were significantly more vaccinated. Those who thought the flu vaccine ineffective (aOR=35.10; p<0.00), with a history of rheumatism, gout or arthritis (aOR=10.90; p<0.018), feared harmful side effects (aOR=8.74; p<0.001) and thought the vaccine expensive (aOR=7.89; p=0.001) were significantly less likely to have been vaccinated. Those who had family doctor recommendations (aOR=0.39; p=0.09) were more likely to have been vaccinated but not significantly.

4.4 Discussion

4.4.1 Characteristics of participants

For the characteristics, those who were older and had flu-like symptoms in the past two years were more vaccinated after the multivariate and univariate analyses respectively. This result was concordant with previous influenza studies undertaken in Japan (138, 171). Participants with more sports hours per week were less vaccinated. For the factor of working, the odds ratio for non-vaccination of the working population was higher than those not working in this study, but not significantly. Previous studies undertaken in Japan showed that seasonal influenza vaccinations were low among the healthy and working population (171, 190). Wada *et al*. reported in their study researched in 29-69 years old population that the vaccination rate of this population was low at around 25 percent (171). The characteristics analysis from this study suggests that those who were healthier and younger, probably working and with more sports hours, were less vaccinated.

4.4.1.1 Medical histories

Those with a history of cardiovascular disease were more vaccinated after multivariate analysis. Cardiovascular disease is one of the high-risk diseases that results in recommendations that people with it have flu vaccinations. One concern revealed in this study is that this high-risk group of participants was not vaccinated significantly enough. Wang *et al*. have shown that flu vaccination is effective for risks of morbidity, hospitalization, ICU admissions and mortality in the large-scale high-risk population (175). Those with high-risk diseases may not know the effectiveness of flu vaccination for reducing these risks. This concern about this high-risk group should be studied and addressed further in the elderly population in Japan.

Participants with a medical history of rheumatism, gout or arthritis were influenced less by vaccination after multivariate analysis. This may be partially influenced by influenza vaccinations still being made from eggs, resulting in those allergic to eggs not being recommended to have the vaccination.

In addition, those who with more medical histories were significantly more vaccinated after univariate analysis. Yi *et al*. reported that those with underlying diseases were more accepting of the flu vaccination (142). This may be due to their often having the chance to communicate with family or their attending doctors urging vaccination. Participants with health issues commented as follows:

"I completely rely on my attending physician. I follow his advice to be vaccinated (78 years old)."

"I have a good accessible attending physician and there is no worry (69 years old)."

From these comments, physician recommendations may have been effective to increase seasonal influenza acceptance in this population with diseases.

4.4.1.2 Other preventive measures

People who have been vaccinated against seasonal influenza followed other preventive measures than flu vaccination such as gargling and wearing facemasks. Similarly, a previous study has shown that those who took a preventive measure against the flu used other preventive measures (191). Gargling and wearing facemasks are common customs in Asian countries. Their effectiveness for influenza prevention are still controversial but Wada *et al*. suggested that using several preventive measures including vaccination against the flu may be effective for influenza protection.

4.4.2 Participant awareness and HBM factors

Similar to the results for Study I, HBM factors became significant after multivariate analysis. Vaccination behavior analysis based on HBM factors has been demonstrated to be effective in this study, too.

4.4.2.1 Perceived risk

Risk perception is a critical factor in health behavior theory. In this study, two risk perception factors, perceived severity after univariate analysis and perceived vulnerability after multivariate analysis, are significant.

Brewer *et al*. have shown in meta-analysis (N=15,988) that perceived severity and susceptibility (vulnerability) are rigidly reliable risk perception factors that influence vaccination increases (137). The number of HBM studies is insufficient in Japan, but Yi *et al*. have suggested that perceived susceptibility significantly raised the influenza vaccination rate in the Japanese adult population (142). Iwashita *et al*. reported perceived vulnerability and severity raised maternal awareness to vaccinate children with Hib vaccine (13). From this, if risk perceptions are utilized more effectively, raising awareness and the vaccination rate in the elderly population in Japan is possible.

<u>Perceived (non) efficacy</u>

Disbelief or when people think the vaccine is ineffective significantly hinders people from having the vaccination (54, 59, 138, 139). In this study, nearly 30 percent of participants responded that seasonal flu vaccine is ineffective, believing the flu vaccine unnecessary ($r=0.74$; $p<0.001$). Ciblak *et al*. have shown in their study in Turkey that disbelief in flu vaccine effectiveness greatly decreases flu vaccine acceptance, even in high-risk groups (174). One concern revealed in this study was that those with high-risk diseases were also not sufficiently vaccinated against the flu vaccination and thought flu vaccination ineffective too. They commented as follows:

"I doubt the efficacy of flu vaccine because the influenza virus changes every year. Does it really work for prevention (67 years old, high-risk group)?"

"Flu vaccination is ineffective. I don't do anything against influenza. If I contract the flu, that will be my fate (77 years old, high-risk group)."

Seasonal influenza vaccination effectiveness has been controversial elsewhere, but many studies demonstrate the effectiveness. Previous studies have shown effectiveness in influenza vaccine, including using laboratory tests to identify the influenza virus (98, 99, 100, 153, 175). These studies also suggest that influenza vaccination maintaining effectiveness requires keeping a high vaccination rate among the total population, including the healthy population (herd immunity) (101). Nakano suggested in his paper that vaccine efficacy (VE) of influenza should be evaluated in each person but under circumstance that a level of herd immunity was kept adequately (102).

Sugaya suggests that a clear decrease in excess mortality resulted from the school-located vaccination (SLV) program when seasonal influenza vaccination was mandatory for children from 1976 to 1987 and maintaining a high vaccination rate among children provided herd immunity and protected vulnerable populations such as the elderly (179).

In this study, the healthier population was less likely to have had flu vaccinations, but maintaining an adequate vaccination rate among the healthier population is necessary and will be further addressed in the future.

<u>Cues to action</u>

In this population, among the cue to action factors of the information sources, family doctor recommendations became significant after univariate analysis and knowing about the vaccination subsidy and communication from local governments became significant after univariate and multivariate analysis. The results of this study support the results of the previous influenza study by Matsui *et al*. investigating rural communities in Japan and reporting that effective information resources for elderly people were medical facilities and town halls (138).

The factor of family doctor recommendations has almost been established as the information source for urging vaccination acceptance (44, 49, 59, 133, 135). When participants have a good family doctor, they may have good advice from their doctors. Participants commented as follows:

"I am happy to have a good family doctor. I can follow his recommendations."

"I just follow my family doctor because I don't have enough knowledge about flu vaccines."

Sometimes family doctor advice is a negative influence when doctors are negative concerning vaccinations. Singleton *et al*. reported in their influenza study of the elderly population that when doctors do not recommend influenza vaccinations even if patients visit them, their vaccination rate drops (59). In this study population, when participants' doctors have negative opinions about the influenza vaccine, participants tended to avoid vaccinations as follows:

"My doctor says the flu vaccine is ineffective (76 years old)."

"My mother died from brain damage. My physician says the cause might have been the flu vaccine (69 years old)."

These comments may suggest that informing physicians and other multiple resources will be necessary to raise awareness as well. Gargano et al. reported that multiple sources of information were effective for parents to raise vaccination rate among their adolescent children (133).

A cue to action factor of knowing about the vaccine subsidy became a significant positive factor and the barrier factor of the vaccine being expensive became a significant negative factor after multivariate analysis.

In Japan, seasonal influenza vaccination has been included in NIP since 2001 for the elderly over 65 years old and for those with high-risk diseases who are over 60 years old. A few local governments provide the vaccination for free and the elderly generally pay around 1000 to 2500 yen on average depending on the subsidy. Without subsidies, it cost around 4000 to 5000 yen, which is expensive. In this study population, about 27 percent of the participants, even in the high-risk group, not knowing about the subsidy for seasonal influenza vaccination may have hindered the vaccination rate. The factor of vaccination being expensive became a barrier. Considering many countries provide seasonal influenza vaccinations free of charge to the elderly, a policy change from subsidies to being completely free of charge is necessary.

4.4.2.2 Media

The media plays an important role in public health behavior. The media has been utilized for many public health promotions such as in California (Prop 99) for tobacco control (188).

One characteristic of the information source on the flu vaccination of the study population was that nearly 45 percent of participants responded that they rely on information sources in the media such as newspapers, televisions and the internet.

However, after univariate analysis, the factor of learning from the media did not reduce non-vaccination risk. The media is sometimes reported as a negative effect as an information source (188, 189). In a parent study, Brunson *et al.* reported that the media has sometimes played a negative role for parents for vaccination compliance of their children (62).

During the 2009 H1N1 pandemic, the media overreacted to the pandemic and became one source of confusion for rushing people to hospitals to have flu vaccinations. There were participants who criticized the media. Participants in this study commented as follows:

> "The 2009 H1N1 pandemic turmoil was awful. Everybody rushed to the hospital to get vaccinated but many could not get the vaccine. However, the actual victims were few. Excessive media reporting may have been responsible for this panic (68 years old)."
>
> "The media covers vaccination scarcity too much. This has caused people to be insecure (73 years old)."

As described above, obtaining correct information from the media alone may be difficult; several information sources would work for a better result to raise the vaccination rate.

Barrier factors

In this study, the barrier factor of fear of harmful side effects was a significant factor for non-vaccination in both adjusted and non-adjusted analysis. According to the Center for Disease Control and Prevention (CDC), the seasonal influenza vaccination is among the safest medical products. The serious side effect of Guillain-Barré syndrome (GBS) is reported one per one million doses. Many studies show the non-significance of side effects of seasonal influenza vaccine comparing the vaccinated and non-vaccinated elderly populations (55, 184, 192). However, one percent of the population in this paper reported serious side effects of motor or neurological related side effects (Table 17). This raises a discrepancy with the above studies concerning safety. Further studies to watch over the side effects of seasonal influenza vaccine are necessary. Participants commented as follows:

"I am concerned over side effects. I need correct information about the risks of side effects (73 years old)."

"I worry about side effects. I want open and reliable information about side effects such as national databases (74 years old)."

In order to reduce concerns over side effects, disseminating the merits of vaccinations and delivering correct information about the risks of side effects is necessary. Establishing open to the public databases such as the Vaccine Adverse Event Reporting System (VAERS) in the US or the Database of Adverse Event Notifications (DAEN) in Australia that we can freely refer to at anytime about side effect information is also necessary. For vaccination, presenting the merits and all information including the risks of correct vaccination are crucial.

One characteristic in this study was vaccine scarcity; participants who responded in the author's study in 2009 especially commented about the vaccine scarcity learned from the lessons in the 2009 H1N1 pandemic as follows:

"Preparing enough vaccines is the government's responsibility. They should not cut the budget for influenza vaccines (72 years old)."

"I went to the hospital to get a flu shot this year, but I could not get it due to scarcity. Does the Japanese government vaccination policy work well (72 years old)?”

Those concerned about influenza vaccine scarcity were significantly more likely to be vaccinated. There may be a non-vaccination risk among those not interested in having the flu vaccination compared to those concerned about scarcity.

4.4.3 Social factors

As described in Study I, social factors influence health behaviors including vaccination. Low socioeconomic status hinders people from accessing preventive services including immunizations (51, 52).

For influenza, Casey *et al.* reported that influenza vaccination significantly declined in the population 65 years and over living in rural places (53). Armstrong *et al.* suggested that the influenza immunization rate among the elderly 65 years old and over is low among the population with low socioeconomic status (54). In a Japanese influenza study, Wada reported that low household income is a risk factor for influenza vaccination increases among the working age population (171).

In this study, those who live in rural adjacent areas were less vaccinated than those in urban areas after univariate analysis, but not significantly. Those who live in rural areas are only 2.4 percent of the total population in this study and correct analysis could not be performed. Similarly for the subjective life standard, when we compare average and good subjective life standards, those who reported average were less vaccinated than those who reported good, but nearly 60 percent of participants reported their life standard was good. Thus for socio-economic status no significant results were obtained due to population skewing.

In this study, those with poorer SRH were more vaccinated after univariate analysis. Few studies were found that have investigated SRH and vaccination, but Andrew *et al.* reported in their Canadian study that elderly people who were 65 years and older with poorer SRH were more vaccinated against influenza than was concordant with this study (194).

For social activities and participation, Kawachi *et al.* suggest that social participation contribute to one's health status (176). Kondo *et al.* report that social activities and participation are positively related with health and those with higher education and income more actively participate in social activities (157). Supporting this, in this study population of university graduates, only 14.5 percent responded that they did not participate in any social activities and all the participants progressively participated in some activity. However, social activity and participation did not influence influenza vaccination increases. This may be because the sample population was skewed to a better subjective life standard and only 4.5 percent were living alone, who may benefit from social activities.

Those with more participation and activities had a slightly higher SRH ($r=0.11$; $p=0.007$) in this study. Social activity and participation contribute somewhat to the population's health but this needs to be studied further.

The non social network factor was studied in this study, but contrary to the maternal study, no significant differences were observed. Many studies have found that social networks are mainly a benefit for women or mothers to increase vaccination acceptance for their children (62, 63, 64, 186). This is conceivable given that this study population consisted of a male population. As mentioned above, family doctor advice is a well-known social network factor to urge vaccination across genders and racial differences. And there are various studies for other preventive behaviors such as cancer screening that suggest social network can benefit for men, too (47, 72, 187). Simpson *et al.* reported in their cholesterol screening study that married men asked more about preventive services than unmarried men over 50 years old (65). Cornwell *et al*. reported in their elderly population study that social network characteristics and emotional support are associated with hypertension diagnosis and control and that no differences existed between men and women (66). From these studies, it may be early to conclude that social networks would not benefit an elderly male population. One participant commented:

> "My son is a pharmacist. I can get much information from him and it is very helpful."

For those living alone and lower socioeconomic populations, social networks have potential and may be more effective to raise awareness among the elderly male population so that further studies with a variety of socioeconomic statuses will be necessary.

4.5 Conclusion

In this study, HBM factors could provide potential effective predictors for vaccination increases. In addition, healthier populations were less vaccinated and those in high-risk groups were not significantly enough vaccinated.

Considering the first objective of this study to decrease excessive mortality, raising awareness is necessary among elderly population. In order to do this, disseminating the effectiveness of influenza vaccination, influenza severity, correct knowledge about side effects and subsidy information through communication from local government, family and attending physicians would be necessary. Nearly 50 percent of participants relied on the media to gather information about influenza in this study population so the media could be potentially effective to raise seasonal influenza vaccination acceptance among this population.

4.6 Study limitations

This study was a cross-sectional study with higher education, a comparatively higher subjective life standard and living in urban areas. In order to generalize the results of this study, further longitudinal study covering a variety of education levels and socioeconomic statuses is necessary.

Chapter IV Tables and Figures

Tables

Figures

Table 10 Goodness of fit test to test the differences of characteristics between two groups (N=578)

Participants characteristics	2009 (n=167)	2010 (n=411)	p value	
Age (Ave..±SD)	73.10±5.10	73.21±4.18	0.81	a
65-74	128 (79.5)	241 (58.6)		
75-93	33 (20.2)	170 (41.4)		
Working Status				
Yes	54 (32.3)	158 (38.4)	0.16	
No	113 (67.7)	253 (61.6)		
Residential area				
Urban	111 (76.0)	273 (69.8)		
Rural-adjacent	32 (21.9)	108 (27.6)	0.32	b
Rural	3 (2.1)	10 (2.6)		
Subjective life standards				
Very good	23 (13.9)	77 (18.7)		
Good	71 (43.0)	172 (41.8)	0.48	b
Average	70 (42.4)	156 (38.0)		
Poor	1 (0.6)	6 (1.5)		
Self rated health				
good	128 (81.5)	343 (86.8)	0.08	
poor	29 (18.5)	52 (13.2)		
Seasonal influenza vaccination				
Every year/sometimes	109 (65.3)	271 (65.9)	0.89	
Never	58 (34.7)	140 (34.1)		
Those who lived with participants				
None	10 (6.0)	20 (4.9)	0.59	
Living with family	157 (94.0)	391 (95.1)		
Sports hours per a week				
Median	4	4		
Maximum	28	26	0.21	c
Minimum	0	0		

a. p value and 95%CI were obtained by student t test comparing two samples.
b. p values were obtained by Fisher extract test.
p values were otained by X2 test for other valuables.
Total % is not necessarily 100% due to missing values.

Table 11 Demographic characteristics of participants and seasonal influenza vaccination status (N=578)

Participants characteristics	n (%)	Seasonal influenza vaccination status: Never	Sometimes /Every year	Unadjusted OR (95%CI)	p value	
Age (Ave.±SD)	73.19±4.43	72.0±4.04	73.80±4.47	(1.06 – 2.55)	<0.01 **	a
65-74	369 (64.5)	145 (39.3)	224 (60.7)	1		
75-93	203 (35.5)	52 (25.6)	151 (74.4)	0.53 (0.36-0.78)	<0.01 **	†
Working Status						
Yes	212 (36.7)	78 (36.8)	134 (63.2)	1.19 (0.84-1.70)	0.33	†
No	366 (63.3)	120 (32.8)	246 (67.2)	1		
Residential area						
Urban	384 (71.5)	127 (33.1)	257 (66.9)	1		
Rural-adjacent	140 (26.1)	56 (40.0)	84 (60.0)	1.35 (0.91-2.01)	0.14	†
Rural	13 (2.4)	3 (23.1)	10 (76.9)	0.61 (0.16-2.25)	0.45	†
Prefecture: Tokyo (252, 43%), Kanagawa (72, 12.3%), Saitama (34, 5.8%), Chiba (58, 9.9%) Others (162, 29.0%)						
Self rated health						
good	471 (85.3)	169 (35.9)	302 (64.1)	1		
poor	81 (14.7)	18 (22.2)	63 (77.8)	0.51 (0.29-0.89)	0.02 *	†
Subjective life standard						
very good	100 (17.3)	28 (28.0)	72 (72.0)	1		
good	243 (42.1)	83 (34.2)	160 (65.8)	1.33 (0.80-2.22)	0.27	†
average	226 (39.2)	84 (37.2)	142 (62.8)	1.52 (0.91-2.54)	0.11	†
poor	7 (1.2)	2 (1.0)	5 (1.3)	1.03 (0.29-5.61)	0.97	†
Sex						
Male	568 (98.4)	196 (34.5)	372 (65.4)			
Female	5 (0.9)	1 (0.5)	4 (1.1)			
Unknown	4 (0.7)	1 (0.5)	3 (0.8)			
Seasonal influenza vaccination						
	Every year	272 (47.1)				
	Sometimes	108 (18.7)				
	Never	198 (34.2)				
Those who lived with participants						
None	26 (4.5)	6 (23.1)	20 (76.9)	1		
Spouse	359 (62.1)	121 (33.7)	238 (66.3)	1.70 (0.66-4.33)	0.27	†
Spouse and children	141 (24.4)	53 (37.6)	88 (62.4)	2.00 (0.76-5.32)	0.16	†
Spouse, children, grar	19 (3.3)	7 (36.8)	12 (63.2)	1.94 (0.53-7.17)	0.32	†
Others	26 (4.5)	7 (26.9)	19 (73.1)	1.23 (0.35-4.32)	0.75	†
Temporary living alon	7 (1.2)	4 (2.0)	3 (0.8)	4.44 (0.77-25.65)	0.10	†
Flu-like symptoms within recent two years						
	179 (32.2)	45 (25.1)	134 (74.9)	0.54 (0.36-0.80)	0.002 **	†
	377 (67.8)	145 (38.5)	232 (61.5)	1		

†Unadjusted ORs were obtained from univariate logistic regression analysis of dependent variable as non vaccination of seasonal influenza.

a. p value and 95%CI were obtained by student t test for participants' age.

b.p value was obtained by Mann-Whitney U test.

** denote significance of p value is less than 0.01.* denote significance of p value is less than 0.05.

Total % is not necessarily 100 % due to missing values.

Table 12 Participants' current and past medical histories (multiple choice) (N=578)

Current and past medical histories (n=878)	n (%)	Seasonal influenza vaccination status Never	Sometimes /Every year	Unadjusted OR (95%CI)	p value	
Stroke	14 (2.4)	5 (35.7)	9 (64.3)	1.06 (0.35–3.22)	0.91	†
	564 (97.6)	193 (34.2)	371 (65.8)	1		
Hypertension	166 (28.7)	50 (30.1)	116 (69.9)	0.77 (0.52–1.13)	0.18	†
	412 (71.3)	148 (35.9)	264 (64.1)	1		
Cardiovascular disease	55 (9.5)	13 (23.6)	42 (76.4)	0.57 (0.23–1.08)	0.08	†
	523 (90.5)	185 (35.4)	338 (64.6)	1		
Liver disease	34 (5.9)	14 (41.2)	20 (58.8)	1.37 (0.67–2.77)	0.39	†
	544 (94.1)	184 (33.8)	360 (66.2)	1		
Gallbladder disease	30 (5.2)	12 (40.0)	18 (60.0)	1.30 (0.61–2.75)	0.50	†
	548 (94.8)	186 (33.9)	362 (66.1)	1		
Diabetes	63 (10.9)	19 (30.2)	44 (69.8)	0.81 (0.46–1.43)	0.46	†
	515 (89.1)	179 (34.8)	336 (65.2)	1		
Gastroduodenal disease	58 (10.0)	18 (31.0)	40 (69.0)	0.85 (0.47–1.53)	0.59	†
	520(90.0)	180 (34.6)	340 (65.4)	1		
Tuberculosis	34 (5.9)	12 (35.3)	22 (64.7)	1.05 (0.51–2.16)	0.90	†
	544 (94.1)	186 (34.3)	358 (65.8)	1		
Asthma	24 (4.2)	5 (20.8)	19 (79.2)	0.67 (0.24–1.90)	0.46	†
/Chronic bronchitis	554 (95.8)	193 (34.8)	361 (65.2)	1		
Anemia	10 (1.7)	4 (40.0)	6 (60.0)	1.29 (0.36–4.61)	0.70	†
	568 (98.3)	194 (34.2)	374 (65.8)	1		
Rheumatism /gout	11 (1.9)	8 (72.7)	3 (27.3)	5.28 (1.38–2.10)	0.015 *	†
/Arthritis	567 (98.1)	190 (33.5)	377 (66.5)	1		
Cancer	74 (12.8)	27 (36.5)	47 (63.5)	1.12 (0.67–1.86)	0.67	†
	504 (87.2)	171 (33.9)	333 (66.1)	1		
Appendicitis	71 (12.3)	18 (24.5)	53 (74.6)	0.62 (0.35–1.09)	0.09	†
	507 (87.7)	180 (35.5)	327 (64.5)	1		
Bone fracture	42 (7.3)	15 (35.7)	27 (64.3)	1.07 (0.56–2.01)	0.84	†
	536 (92.7)	183 (34.1)	353 (65.9)	1		
Pneumonia	28 (4.8)	9 (32.1)	19 (67.9)	0.90 (0.40–2.03)	0.80	†
	549 (95.1)	189 (34.4)	361 (65.6)	1		
Hay fever	91 (15.7)	28 (30.8)	63 (69.2)	0.83 (0.51–1.34)	0.45	†
	487 (84.3)	170 (34.9)	317 (65.1)	1		
Other allergies	18 (3.1)	7 (38.9)	11 (61.1)	1.23 (0.47–3.22)	0.67	†
	560 (96.9)	191 (34.1)	369 (65.9)	1		
Others (52)						
Low back pain (9), Prostatomegaly (8), Glaucoma (3), Colon polyp (4), Ureteral calculi (2), Rupture of Achilles tendon (1), prostatitis (1), Asperger's syndrome(1), Meniere disease(1), Hypercholesterolemia (1), Colon diverticulitis (1), Sinusitis (1), Retinal hemorrhages (1), Abnormal lipido metabolism (1), Empyema (1), Parkinson's disease (1), Sleep apenea syndrome (1), Fundus hemorrhage (1), Chronic gastroenteritis (1), Thrombocythemia (1), Pancreatitis (1),						
Number of histories						
0–2	405 (70.1)	146 (36.0)	259 (64.0)			
3–5	163 (28.2)	51 (31.3)	112 (68.7)		0.015*	a
6–9	10 (1.7)	1 (10)	9 (90)			

a. .p value was obtained by Mann–Whitney U test.

† Unadjusted ORs were obtained from univariate logistic regression analysis of dependent variable as non vaccination of seasonal influenza.

** denote significance of p value is less than 0.01.* denote significance of p value is less than 0.05.

Table 13 Healthy lifestyle and influenza vaccination status (multiple choice) (N=578)

Do you practice any healthy habits to keep your health?

Healthy habits	Total n (%)	Seasonal influenza vaccination status: Never	Sometimes /Every year	Unadjusted OR (95%CI)	p value	
Exercise or walking regularly	433 (74.9)	154 (35.6)	279 (64.4)	1.27 (0.85-1.90)	0.25	†
	145 (25.1)	44 (30.3)	101 (69.7)	1		
Sports hours/week					0.045*	a
0 hour	150 (26.7)	47 (31.3)	103 (68.7)			
1-5 hours	234 (41.6)	71 (37.2)	163 (43.9)			
6-10 hours	134 (23.8)	50 (37.3)	84 (62.7)			
11-15 hours	32 (5.7)	16 (50)	16 (50)			
16-28 hours	12 (2.1)	7 (3.7)	5 (1.3)			
Measuring weight regularly	293 (50.7)	93 (31.7)	200 (68.3)	0.80 (0.57-1.13)	0.2	†
	285 (49.3)	105 (36.8)	180 (63.2)	1		
Measuring blood pressure regularly	255 (44.2)	73 (28.6)	182 (71.4)	0.64 (0.45-0.91)	0.013*	†
	322 (55.8)	124 (38.5)	198 (61.5)	1		
Quit smoking or decrease number of a cigarrettes per a day						
	192 (33.2)	72 (37.5)	120 (62.5)	1.24 (0.86-1.78)	0.25	†
	386 (66.8)	126 (32.6)	260 (67.4)	1		
Taking rest regularly	177 (30.7)	54 (30.5)	123 (69.5)	0.79 (0.54-1.15)	0.22	†
	400 (69.3)	143 (35.8)	257 (64.3)	1		
Quit alchol drinking or decrease drinking volume						
	121 (21.0)	29 (24.0)	92 (76.0)	0.54 (0.34-0.85)	0.009**	†
	456 (79.0)	168 (36.8)	288 (63.2)	1		
Relieving stress	101 (17.5)	27 (26.7)	74 (73.3)	0.66 (0.41-1.06)	0.09	
	476 (82.5)	170 (35.7)	306 (64.3)	1		†

†Unadjusted ORs were obtained from univariate logistic regression analysis

a. .p value was obtained by Mann-Whitney U test.

Note: Totals are not necessarily match because of missing values.

** denote significance of p value is less than 0.01.* denote significance of p value is less than 0.05.

Table 14 Preventive practices besides vaccination and seasonal influenza vaccination status (multiple choice) (N=578)

Practices	Total n (%)	Seasonal influenza vaccination status Never	Sometimes /Every year	Unadjusted OR (95%CI)	p value	
Taking good nutrition	338 (58.5)	111 (32.8)	227 (67.2)	0.86 (0.61–1.22)	0.39	†
	240 (41.5)	87 (36.3)	153 (63.7)	1		
Having enough sleep	328 (56.8)	112 (34.1)	216 (65.9)	1.00 (0.71–1.42)	0.998	†
	249 (43.2)	85 (34.1)	164 (65.9)	1		
Washing hands	391 (67.8)	117 (29.9)	274 (70.1)	0.57 (0.39–0.81)	<0.01**	†
	186 (32.2)	80 (43.0)	106 (57.0)	1		
Gargling	405 (70.1)	119 (29.4)	286 (70.6)	0.50 (0.43–0.72)	<0.01**	†
	173 (29.9)	79 (39.9)	94 (24.7)	1		
Wearing masks	148 (25.6)	38 (19.2)	110 (74.3)	0.58 (0.38–0.89)	0.01*	†
in public places	430 (74.4)	160 (80.8)	270 (71.1)	1		
Avoid crowded places	146 (25.3)	46 (31.5)	100 (68.5)	0.85 (0.56–1.27)	0.42	†
	432 (74.7)	152 (35.2)	280 (64.8)	1		
Humidify rooms	92 (15.9)	27 (13.6)	65 (17.1)	0.77 (0.47–1.24)	0.28	†
	486 (84.1)	171 (35.2)	315 (64.8)	1		

† Unadjusted ORs were obtained from univariate logistic regression analysis of dependent variable as non vaccination of seasonal influenza.
Total values are not necessarily match by calculation due to missing values.
** denote significance of p value is less than 0.01.* denote significance of p value is less than 0.05.

Table 15 Knowledge about symptoms when contracted to flu or cold (multiple choice) (N=578)

Expected symptoms	Flu	Cold
High fever	535 (92.6)	182 (31.5)
Low-grade fever	48 (8.3)	384 (66.6)
Joint or muscle pain	377 (65.2)	168 (29.1)
Feel exhausted	380 (65.9)	425 (73.5)
Sore throat	129 (22.4)	233 (40.3)
Sneeze	259 (44.8)	461 (79.9)
Total	1728	1853

Total % is not 100% due to multiple choice question.

Table 16 Reasons for non-vaccination of seasonal influenza vaccine (Multiple choice)
(N=578、n=198)

Reason for non-vaccination	n	%
The vaccine is unnecessary	57	28.8
The vaccine is not effective	31	15.7
The vaccine is bothersome	24	12.1
Fear of harmful side effects	20	10.1
The shot is expensive	5	2.5
Being busy	4	2.0
Others;	11	5.6
I am healthy (3), I took pneumococcus vaccine (1), Government administration failure (1), I distrust vaccination (1), Other preventive measures are important (1), I will contract flu if I take vaccine (1), I hate hospital (1), I try not to contract flu (1), I have no knowledge about vaccine (1)		
Total	162	

Total % is not 100% due to multiple choice question.

Table 17 Reported side effects experiences among participants who had seasonal influenza vaccinations (n=379)

Reported side effects	n (%)
Swelling/Pain at injection site	14 (3.7)
Fever/Chilling	13 (8.3)
Movement disorder/Disturbance in consciousness	4 (1.1)
Allergic reactions	2 (0.4)
Other (unknown)	1 (0.3)
None	335 (91.1)

Note: Total values are not necessarily match due to missing values

Table 18 Health Belief Model factors and seasonal influenza vaccination status (N=578)

HBM factors	n (%)	Seasonal influenza vaccination status: Never	Sometimes /Every year	Unadjusted OR (95%CI)	p value	
Perceived vulnerability to flu or cold						
Do you think you are vulnerable to flu or cold?						
Yes	114 (20.1)	17 (14.9)	97 (85.1)	0.27 (0.16-0.48)	<0.001 **	†
No	454 (79.9)	117 (39.0)	277 (61.0)	1		
Perceived efficacy of seasonal infuenza vaccine						
Do you think influenza vaccine is effective?						
Yes	406 (70.2)	56 (28.3)	350 (92.1)	1		
No	172 (29.8)	142 (82.6)	30 (17.4)	30.04 (18.48-48.82)	<0.01 **	†
Perceived severity of influenza						
Do you have a correct knowledge of symptoms and differences between flu from cold?						
Yes	484 (84.3)	156 (32.2)	328 (67.8)	0.54 (0.35-0.86)	<0.01 **	†
No	90 (15.7)	42 (46.7)	48 (53.3)	1		
Cue to the action						
Recommendation from family doctor						
Yes	55 (9.5)	8 (14.5)	47 (85.5)	0.30 (0.14-0.65)	0.002 **	†
No	523 (90.5)	190 (36.3)	333 (63.7)	1		
Knowing subsidy to the vaccine						
Yes	415 (73.1)	101 (24.3)	314 (75.7)	0.21 (0.14-0.31)	<0.001 **	†
No	153 (26.9)	93 (60.8)	60 (39.2)	1		
Friends' or family's recommendations						
Yes	15 (2.6)	5 (33.3)	10 (66.7)	0.96 (0.32-2.84)	0.94	†
No	563 (97.4)	193 (34.3)	370 (65.7)	1		
Communication from local governments						
Yes	30 (5.2)	4 (13.3)	26 (86.7)	0.28 (0.10-0.82)	0.016 *	†
No	548 (94.8)	194 (35.4)	354 (64.6)	1		
Academic journals or experts' information						
Yes	26 (4.5)	8 (30.8)	18 (69.2)	0.85 (0.36-1.98)	0.70	†
No	552 (95.5)	190 (34.4)	362 (65.6)	1		
Learning from booklets or brochures obtained at hospitals or public places						
Yes	9 (1.6)	1 (11.1)	8 (88.9)	0.24 (0.03-1.90)	0.18	†
No	569 (98.4)	197 (34.6)	372 (65.4)	1		
Learning from the media (TV, internet, magazines)						
Yes	257 (44.5)	90 (35.0)	167 (65.0)	1.06 (0.75-1.50)	0.73	†
No	321 (55.5)	108 (33.6)	213 (66.4)	1		
Only through non social network information sources						
Yes	283 (49.0)	96 (33.9)	187 (66.1)	0.97 (0.69-1.37)	0.87	†
No	295 (51.0)	102 (34.6)	193 (65.4)	1		

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		n (%)	Never	Sometimes /Every year	Unadjusted OR (95%CI)	p value	
			Seasonal influenza vaccination				
Perceived barriers							
Fear of harmful side effects							
	Yes	68 (11.8)	48 (70.6)	20 (29.4)	6.67 (3.71-12.00)	<0.001 **	†
	No	510 (88.2)	150 (29.4)	362 (70.6)	1		
Information is scarce							
	Yes	42 (7.3)	16 (38.1)	26 (61.9)	1.20 (0.63-2.29)	0.59	†
	No	536 (92.7)	182 (34.0)	354 (66.0)	1		
The vaccination is expensive							
	Yes	33 (5.7)	16 (48.5)	17 (51.5)	1.88 (0.93-3.81)	0.08	†
	No	545 (94.3)	182 (33.4)	363 (66.6)	1		
Concern over vaccine scarcity							
	Yes	32 (5.5)	4 (12.5)	28 (87.5)	0.26 (0.90-0.75)	0.013 *	†
	No	546 (94.5)	194 (35.5)	352 (64.5)	1		
Being busy							
	Yes	9 (1.6)	8 (88.9)	1 (11.1)		0.001 **	a
	No	569 (98.4)	190 (33.4)	379 (66.6)			
The vaccination is Unnecessary							
	Yes	114 (19.7)	108 (94.7)	6 (5.3)	75.4 (32.12-177.20)	<0.001 **	†
	No	464 (80.3)	90 (19.4)	374 (80.6)	1		
WTP (Yen)							
1000		157 (33.4)	54 (42.9)	103 (65.6)			
5000		292 (62.1)	70 (24.0)	222 (64.5)			
10000		17 (3.6)	1 (5.9)	16 (94.1)		<0.001 **	b
20000		1 (0.2)	0 (0.0)	1 (0.3)			
>20000		3 (0.6)	1 (33.3)	2 (66.7)			

†Unadjusted ORs were obtained from univariate logistic regression analysis of dependent variable as non vaccination of flu.
a. p value was obtained by Fisher Exact Test due to assumption for χ 2 test was unmet.
b.p value was obtained by Mann-Whitney U test.
** denote significance of p value is less than 0.01.
* denote significance of p value is less than 0.05.

Table 19 Barrier keywords extracted from open-ended question about free opinion about influenza vaccination by Text Analysis (N=578, n=324)

Categories	n	%
Vaccine Policy (problem, bad, etc.)	59	10.1
Efficacy (not effective, doubtful, etc.)	52	8.9
Information (scarce, scarcity, etc.)	43	7.3
Vaccine Scarcity (scarce, not enough,	33	5.6
Expensive, Subsidy (need, etc.)	32	5.5
Accessibility (late, problem, etc.)	30	5.1
Pandemic, Outbreak (worry, scary, etc	27	4.6
Side effect, Safety (worry, scary, etc.)	26	4.4
Media (mess, panic, etc.)	24	4.1
Priority (problem, bad, etc.)	13	2.2
Cost effective (wonder, doubt, etc)	7	1.2
Facility, Hospital (far, worry, etc.)	6	1
Total	352	

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Table 20 Groups and organizations respondents participated in (Multiple choice) (N=578)

Organization/Group	n (%)
Elderly clubs	42 (7.3)
Neighborhood associatior	127 (22.0)
Women's associations	1 (0.2)
Hobby clubs	208 (36.0)
Fitness or sports related	154 (26.7)
Study or culture clubs	120 (20.8)
Civic activity clubs	13 (2.2)
Religious organizations	25 (4.3)
Volunteer organizations	90 (15.6)
Commerce and industry a	41 (7.1)
Retiree organizations	172 (29.8)
Employment center servi	17 (2.9)
None	132 (22.9)
Total	1010

Total % is not 100% due to multiple choice question.

Table 21 Social activities respondents participated in (N=578)

Activities	n (%)
Fitness and sports	207 (35.9)
Hobbies (culture)	158 (27.4)
Academic activities (research or art)	110 (19.1)
Community activities	54 (9.4)
Productive work (gardening or dispatched woı	34 (5.9)
Neigborhood security activities	12 (2.1)
Home care support for the elderly	12 (2.1)
Life and environment activities	10 (30.3)
Support activities for the elderly (driving etc)	6 (1.0)
Support activities for schools or children	8 (1.4)
None	84 (14.5)
Total	695

Table 22 Multivariate analysis variable selection by step-down method using step-wise likelihood analysis

Variables in the equations

		B	SD	Wald	df	p value	Exp(B)	EXP(B) 95% CI Lower	Upper
Step 1a	Flulike history 2 years	.993	.806	1.516	1	.218	2.699	.556	13.107
	Perceived vulnerability to flu	-2.297	.590	15.137	1	.000	.101	.032	.320
	Perceived severity	-.476	.437	1.188	1	.276	.621	.264	1.462
	Perceived efficacy	3.650	.386	89.531	1	.000	38.480	18.066	81.960
	Barrier expensive	2.067	.674	9.393	1	.002	7.898	2.106	29.611
	Willing To Pay	.023	.269	.007	1	.931	1.024	.604	1.736
	Age	-.095	.039	5.991	1	.014	.909	.843	.981
	Number of medical histories	-.035	.143	.059	1	.808	.966	.730	1.277
	Self Rated Health	-.341	.550	.384	1	.535	.711	.242	2.090
	Rheumatism/gout/arthritis	1.728	1.242	1.934	1	.164	5.627	.493	64.216
	Cardiovascular disease	-1.313	.739	3.154	1	.076	.269	.063	1.146
	Sports hours per a week	.033	.038	.779	1	.377	1.034	.960	1.113
	Barrier side effect	1.681	.515	10.666	1	.001	5.373	1.959	14.737
	Family doctor's recommendation	-1.203	.630	3.652	1	.056	.300	.087	1.031
	Communication from local govt	-1.649	.954	2.985	1	.084	.192	.030	1.248
	Knowing subsidy	-1.538	.372	17.071	1	.000	.215	.104	.446
	Constant	6.298	2.940	4.589	1	.032	543.454		
Step 2a	Flulike history 2 years	.996	.805	1.532	1	.216	2.708	.559	13.117
	Perceived vulnerability to flu	-2.295	.590	15.138	1	.000	.101	.032	.320
	Perceived severity	-.478	.436	1.202	1	.273	.620	.264	1.457
	Perceived efficacy	3.647	.383	90.446	1	.000	38.344	18.085	81.298
	Barrier expensive	2.058	.667	9.510	1	.002	7.832	2.117	28.975
	Age	-.095	.039	6.043	1	.014	.909	.843	.981
	Number of medical histories	-.035	.143	.059	1	.808	.966	.730	1.278
	Self Rated Health	-.338	.549	.379	1	.538	.713	.243	2.091
	rheumatism/gout/arthritis	1.722	1.240	1.927	1	.165	5.595	.492	63.629
	Cardiovascular disease	-1.310	.739	3.144	1	.076	.270	.063	1.148
	Sports hours per a week	.033	.037	.771	1	.380	1.033	.960	1.112
	Barrier side effect	1.681	.514	10.678	1	.001	5.370	1.960	14.717
	Family doctor's recommendation	-1.202	.630	3.647	1	.056	.300	.087	1.032
	Communication from local govt	-1.626	.914	3.161	1	.075	.197	.033	1.181
	Knowing subsidy	-1.537	.372	17.061	1	.000	.215	.104	.446
	Constant	6.355	2.865	4.922	1	.027	575.532		
Step 3a (cont'd)	Flulike history 2 years	1.006	.805	1.563	1	.211	2.735	.565	13.236
	Perceived vulnerability to flu	-2.317	.584	15.755	1	.000	.099	.031	.310
	Perceived severity	-.486	.435	1.246	1	.264	.615	.262	1.444
	Perceived efficacy	3.643	.383	90.388	1	.000	38.190	18.023	80.924
	Barrier expensive	2.043	.664	9.476	1	.002	7.717	2.101	28.346

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		B	SD	Wald	df	p value	Exp (B)	EXP (B) 95% CI	
								Lower	Upper
Step 3a (cont'd)	Age	-.095	.039	6.053	1	.014	.909	.843	.981
	Self Rated Health	-.361	.541	.446	1	.504	.697	.242	2.011
	Rheumatism/gout/arthritis	1.725	1.242	1.930	1	.165	5.614	.492	64.020
	Cardiovascular disease	-1.346	.723	3.469	1	.063	.260	.063	1.073
	Sports hours per a week	.033	.037	.767	1	.381	1.033	.960	1.112
	Barrier side effect	1.682	.514	10.706	1	.001	5.379	1.963	14.735
	Family doctor's recommendation	-1.221	.623	3.839	1	.050	.295	.087	1.000
	Communication from local govt	-1.634	.914	3.199	1	.074	.195	.033	1.170
	Knowing subsidy	-1.540	.372	17.158	1	.000	.214	.103	.444
	Constant	6.301	2.849	4.891	1	.027	545.259		
Step 4a	Flulike history 2 years	.989	.810	1.492	1	.222	2.689	.550	13.144
	Perceived vulnerability to flu	-2.328	.581	16.046	1	.000	.098	.031	.305
	Perceived severity	-.461	.434	1.127	1	.288	.631	.270	1.477
	Perceived efficacy	3.653	.383	90.741	1	.000	38.596	18.202	81.842
	Barrier expensive	2.028	.657	9.528	1	.002	7.598	2.097	27.534
	Age	-.098	.038	6.473	1	.011	.907	.841	.978
	Rheumatism/gout/arthritis	1.756	1.249	1.977	1	.160	5.789	.501	66.955
	Cardiovascular disease	-1.430	.702	4.145	1	.042	.239	.060	.948
	Sports hours per a week	.034	.037	.859	1	.354	1.035	.962	1.113
	Barrier side effect	1.664	.510	10.653	1	.001	5.281	1.944	14.343
	Family doctor's recommendation	-1.249	.628	3.953	1	.047	.287	.084	.982
	Communication from local govt	-1.622	.914	3.150	1	.076	.197	.033	1.184
	Knowing subsidy	-1.547	.371	17.365	1	.000	.213	.103	.441
	Constant	6.449	2.845	5.138	1	.023	631.816		
Step 5a	Flulike history 2 years	.939	.807	1.353	1	.245	2.556	.526	12.428
	Perceived vulnerability to flu	-2.316	.578	16.079	1	.000	.099	.032	.306
	Perceived severity	-.457	.433	1.114	1	.291	.633	.271	1.479
	Perceived efficacy	3.667	.384	91.392	1	.000	39.117	18.446	82.951
	Barrier expensive	2.052	.649	9.992	1	.002	7.782	2.181	27.771
	Age	-.101	.038	6.968	1	.008	.904	.839	.974
	Rheumatism/gout/arthritis	1.679	1.265	1.762	1	.184	5.361	.449	63.984
	Cardiovascular disease	-1.477	.700	4.452	1	.035	.228	.058	.900
	Barrier side effect	1.623	.508	10.218	1	.001	5.070	1.874	13.719
	Family doctor's recommendation	-1.170	.620	3.569	1	.059	.310	.092	1.045
	Communication from local govt	-1.514	.902	2.818	1	.093	.220	.038	1.289
	Knowing subsidy	-1.533	.371	17.081	1	.000	.216	.104	.447
	Constant	6.815	2.810	5.881	1	.015	911.733		

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		B	SD	Wald	df	p value	Exp(B)	EXP(B) 95% CI Lower	Upper
Step 6a	Flulike history 2 years	1.024	.791	1.679	1	.195	2.785	.591	13.118
	Perceived vulnerability to flu	-2.252	.568	15.715	1	.000	.105	.035	.320
	Perceived efficacy	3.707	.383	93.900	1	.000	40.744	19.249	86.241
	Barrier expensive	2.057	.651	9.971	1	.002	7.824	2.182	28.051
	Age	-.099	.038	6.929	1	.008	.905	.841	.975
	Rheumatism/gout/arthritis	1.621	1.260	1.654	1	.198	5.057	.428	59.767
	Cardiovascular disease	-1.549	.703	4.855	1	.028	.213	.054	.843
	Barrier side effect	1.627	.509	10.238	1	.001	5.091	1.879	13.795
	Family doctor's recommendation	-1.165	.617	3.566	1	.059	.312	.093	1.045
	Communication from local govt	-1.581	.907	3.037	1	.081	.206	.035	1.218
	Knowing subsidy	-1.532	.371	17.091	1	.000	.216	.104	.447
	Constant	6.304	2.737	5.305	1	.021	546.735		
Step 7a	Perceived vulnerability to flu	-2.087	.541	14.880	1	.000	.124	.043	.358
	Perceived efficacy	3.684	.380	93.973	1	.000	39.821	18.906	83.874
	Barrier expensive	2.019	.650	9.648	1	.002	7.533	2.107	26.937
	Age	-.104	.037	7.686	1	.006	.902	.838	.970
	Rheumatism/gout/arthritis	1.577	1.255	1.579	1	.209	4.843	.413	56.719
	Cardiovascular disease	-1.560	.700	4.962	1	.026	.210	.053	.829
	Barrier side effect	1.563	.504	9.629	1	.002	4.774	1.779	12.813
	Family doctor's recommendation	-1.044	.607	2.957	1	.086	.352	.107	1.157
	Communication from local govt	-1.579	.912	2.995	1	.084	.206	.035	1.233
	Knowing subsidy	-1.524	.369	17.029	1	.000	.218	.106	.449
	Constant	6.641	2.708	6.014	1	.014	765.499		
Step 8a	Perceived vulnerability to flu	-2.081	.534	15.170	1	.000	.125	.044	.356
	Perceived efficacy	3.679	.378	94.906	1	.000	39.606	18.894	83.026
	Barrier expensive	1.990	.648	9.425	1	.002	7.319	2.054	26.082
	Age	-.105	.037	7.885	1	.005	.900	.837	.969
	Cardiovascular disease	-1.588	.700	5.143	1	.023	.204	.052	.806
	Barrier side effect	1.643	.500	10.787	1	.001	5.172	1.940	13.787
	Family doctor's recommendation	-1.019	.602	2.860	1	.091	.361	.111	1.176
	Communication from local govt	-1.603	.912	3.094	1	.079	.201	.034	1.201
	Knowing subsidy	-1.512	.366	17.103	1	.000	.221	.108	.451
	Constant	6.751	2.707	6.217	1	.013	854.833		

a. Step 1: Candidate variables; Flulike history 2 years, Perceived vulnerability to flu, Perceived severity, Perceived efficacy, Barrier expensive, Willing To Pay, Age, Number of medical histories, SRH, Rheumatism/gout/arthritis, Cardiovascular disease, Sports hours per a week, Barrier side effect, Family doctor's recommendation, Communication from local govt, Knowing subsidy.

Table 23 Multivariate analysis findings for predicting non immunization of seasonal influenza vaccine (N=578)

	Adjusted OR (95%CI)	p value
Age	0.90 (0.84–0.96)	0.01*
History of cardiovascular diseases	0.26 (0.09–0.78)	0.016*
History of rheumatism/gout/arthritis	10.90 (1.51–78.77)	0.018*
Perceived vulnerability to flu or cold	0.13 (0.05–0.31)	<0.001**
Perceived efficacy of seasonal infuenza vaccine		
The vaccine is not effective	35.10 (19.56–66.37)	<0.001**
Cue to the action		
Recommendations from family doctors	0.39 (0.13–1.19)	0.09
Knowing subsidy to the vaccine	0.21 (0.11–0.39)	<0.001**
Communication from local government	0.12 (0.02– 0.76)	0.024*
Perceived barriers		
The vaccine is expensive	7.89 (2.41–25.80)	0.001**
Fear of harmful side effects	8.74 (3.62–21.11)	<0.001**

** denote p value is less than 0.01

* denote p value is less than 0.05

Adjusted ORs were obtained from multivariate analysis of dependent variable as non vaccination of flu.

Hosmer Lemshaw test, ROC analysis, R2=0.32

Table 24 Main extracted keywords of open-ended question about "concerns" (N=300)

Categories	n
Health Care	76
Hospitals	64
Doctor	59
Policy	40
Government	40
Scarcities	28
Co-payment	28
Health Care Program for the Elderly Aged 75 Years and Over	28
Increase	23
Access	21
Flu	21
Expensive	20
Vaccine	19
Local Health Care	19
Support	18
Burden	18
Excessive	18
Prevention	16
Diseases	15
System	13
Primary Care Doctor	13
Quality	13
Infectious Diseases	12
Medical Expense	12
Society, Health System	11
Others	55
Total	994

Morphological analysis、keyword associator (Fujitsu Trend Search 2008)

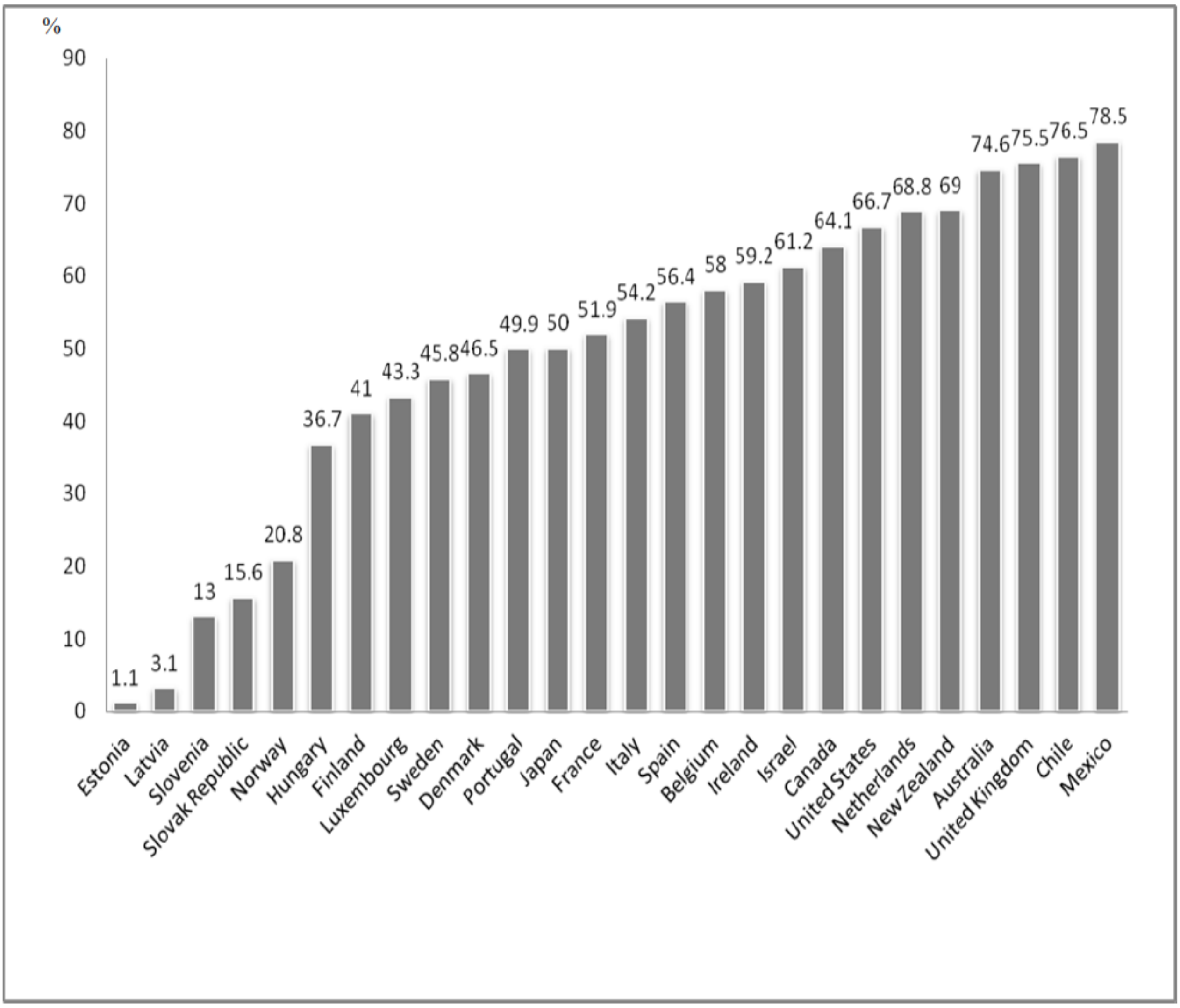


Figure 14 Influenza vaccination rates among elderly population 65 years and older by OECD countries (Countries data not available are not included in this graph. Author created the graph based on Health care use, OECD Data 2015, https://data.oecd.org/healthcare/influenza-vaccination-rates.htm (Accessed March 01, 2016)

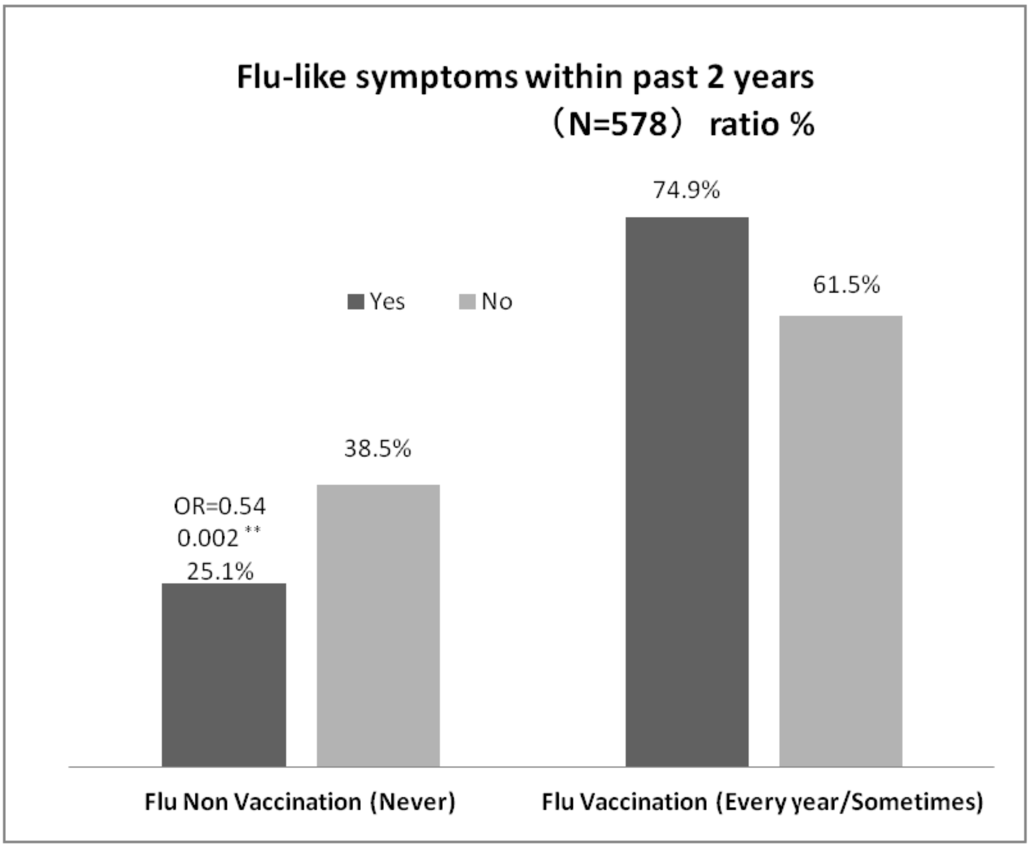


Figure 15 Univariate analysis result of seasonal influenza study: Flu-like symptoms within recent 2 years (N=578)

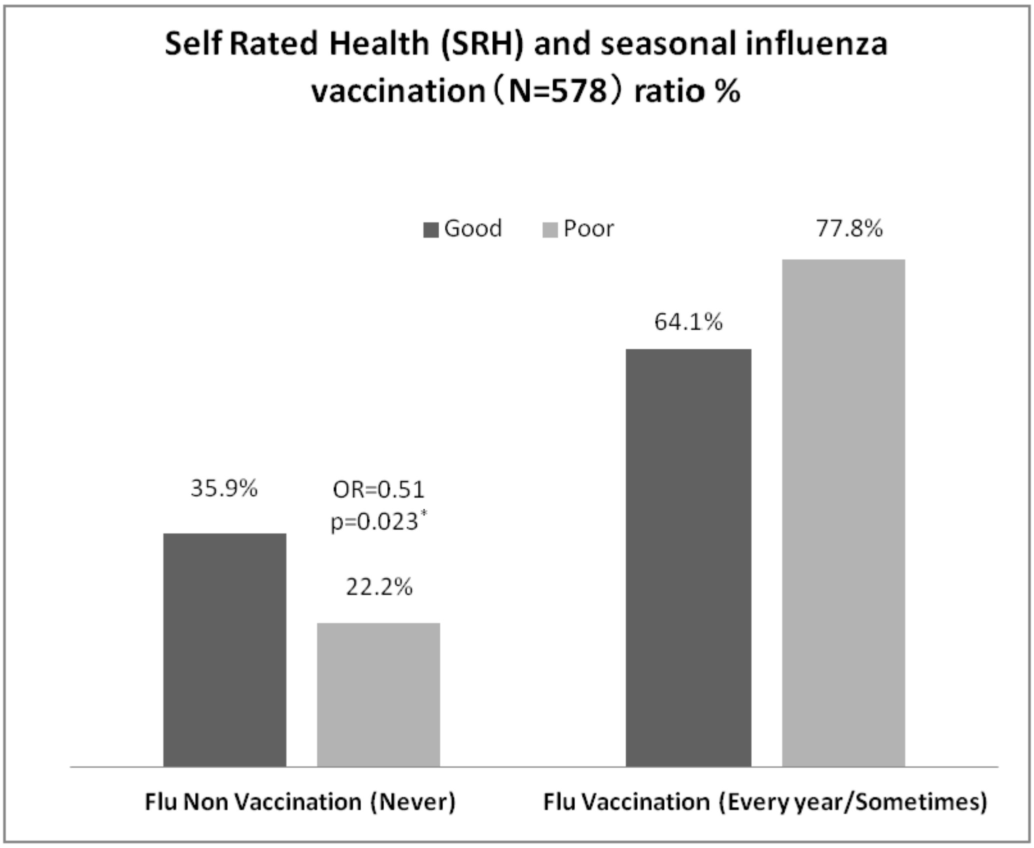


Figure 16 Univariate analysis result of seasonal influenza study: Self Rated Health and seasonal influenza vaccination (N=578)

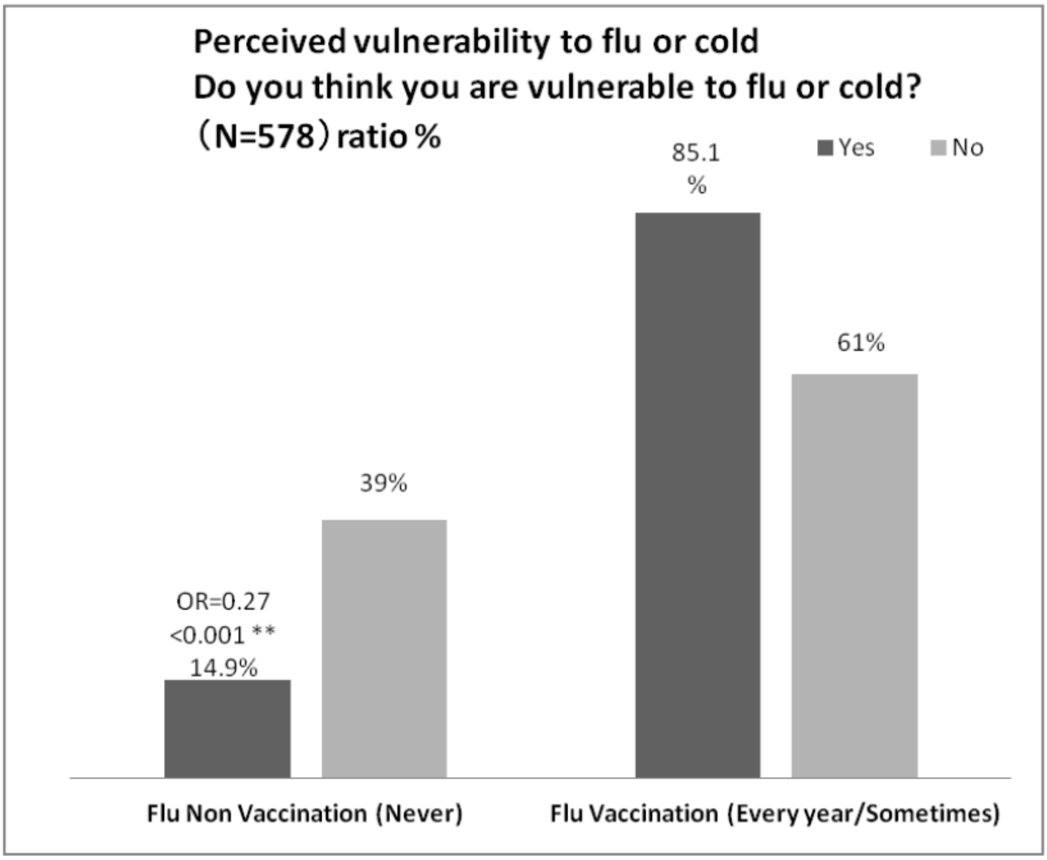


Figure 17 Univariate analysis result of seasonal influenza study: Perceived vulnerability to flu or cold (N=578)

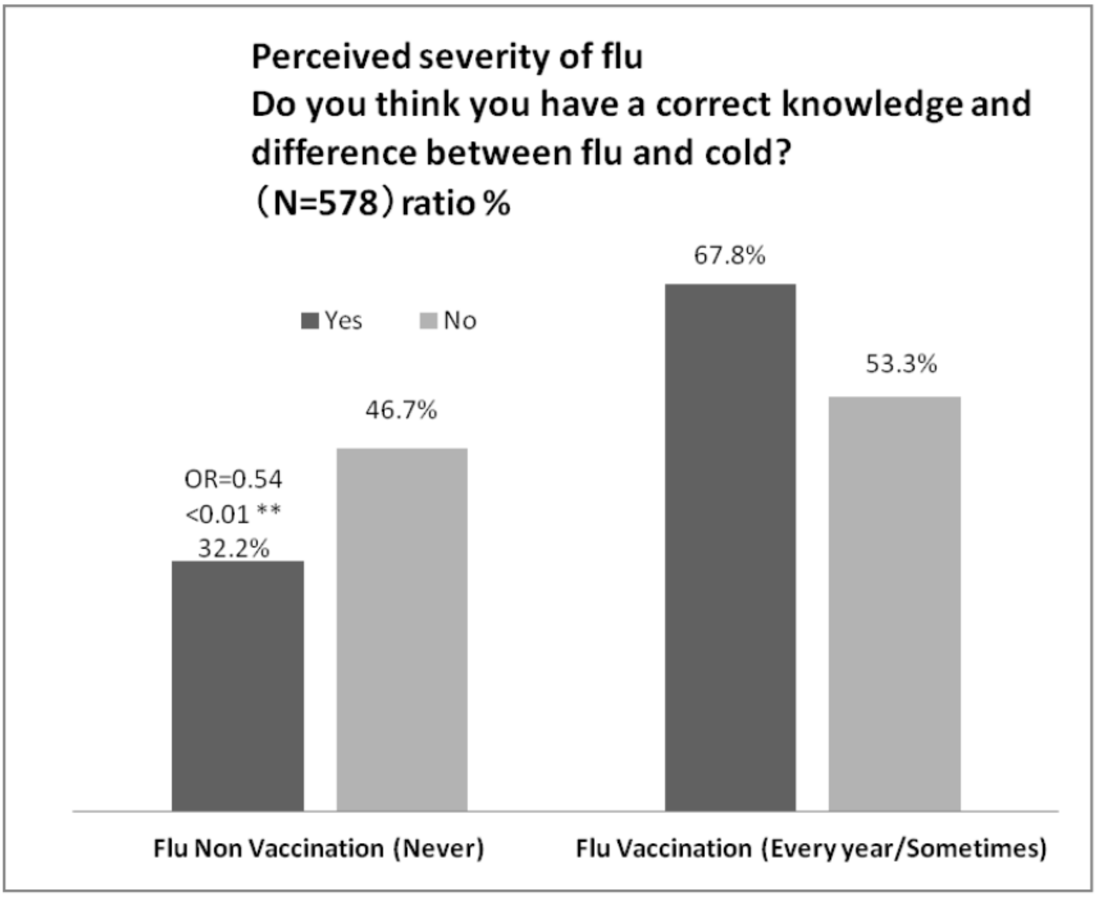


Figure 18 Univariate analysis result of seasonal influenza study: Perceived severity of flu (N=578)

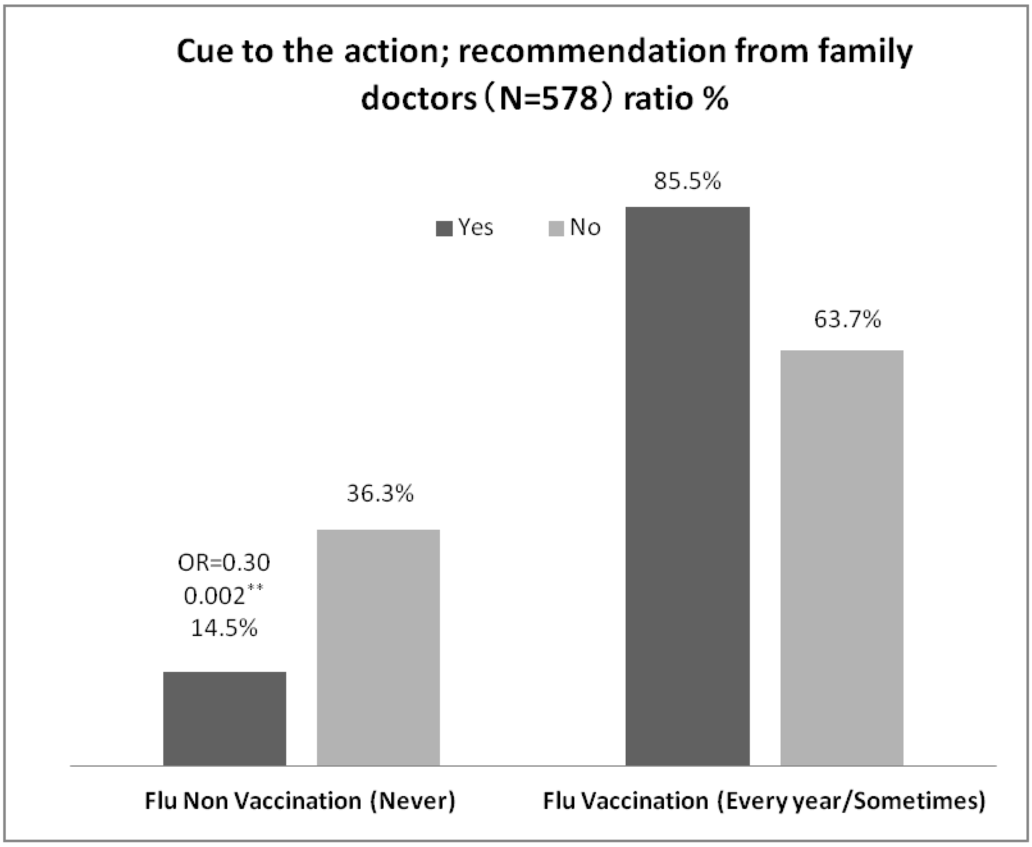


Figure 19 Univariate analysis result of seasonal influenza study: Cue to the action; recommendation from family doctors (N=578)

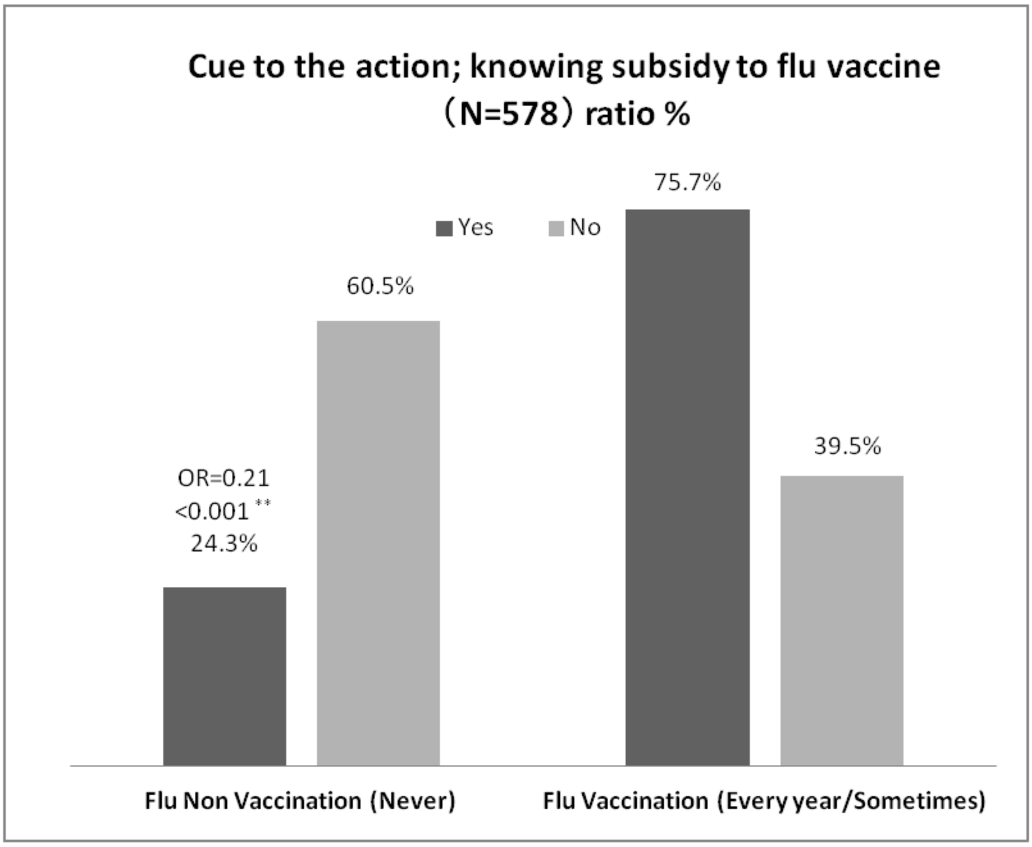


Figure 20 Univariate analysis result of seasonal influenza study: Cue to the action; knowing the subsidy to the vaccine (N=578)

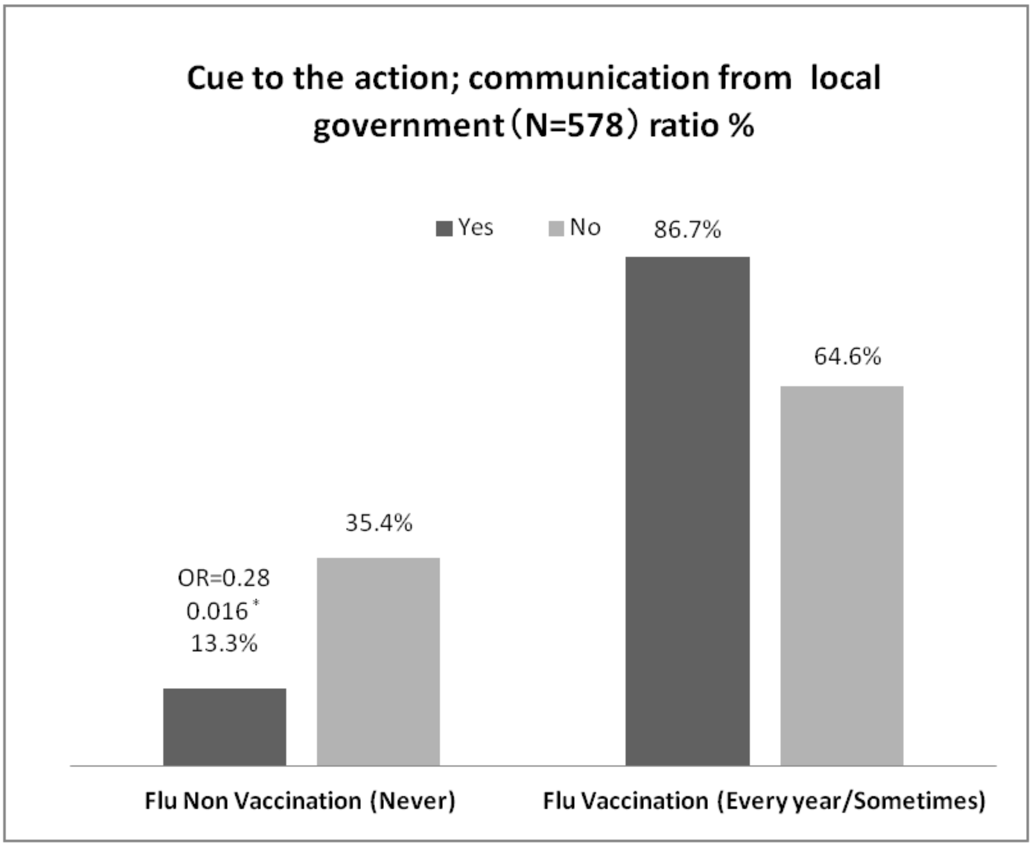


Figure 21 Univariate analysis result of seasonal influenza study: Cue to the action; communication from local government (N=578)

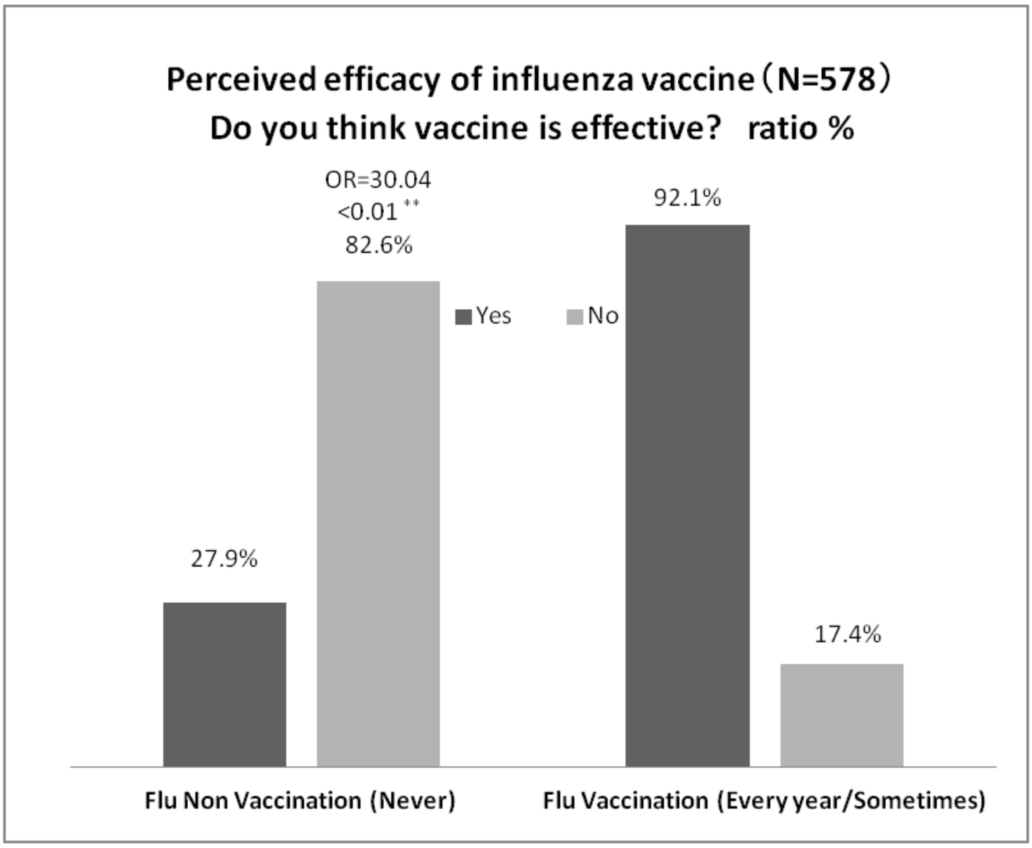


Figure 22 Univariate analysis result of seasonal influenza study: Perceived efficacy of seasonal influenza vaccine (N=578)

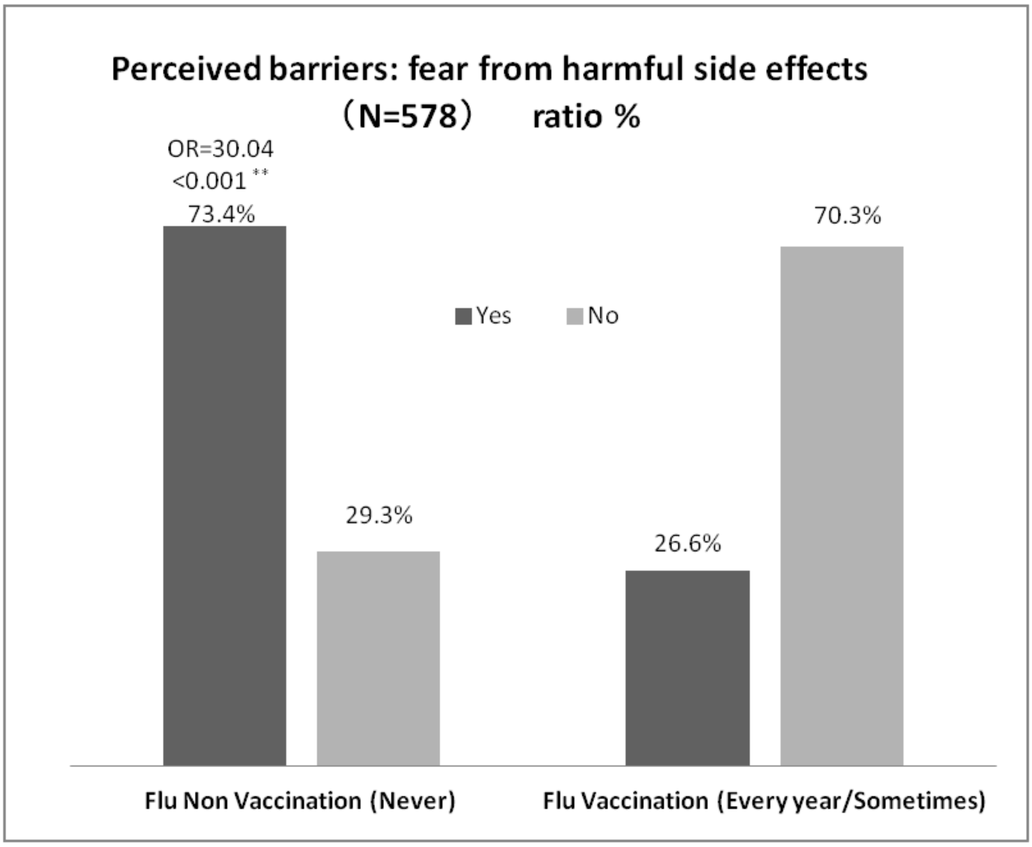


Figure 23 Univariate analysis result of seasonal influenza study: Perceived barriers: fear from harmful side effects (N=578)

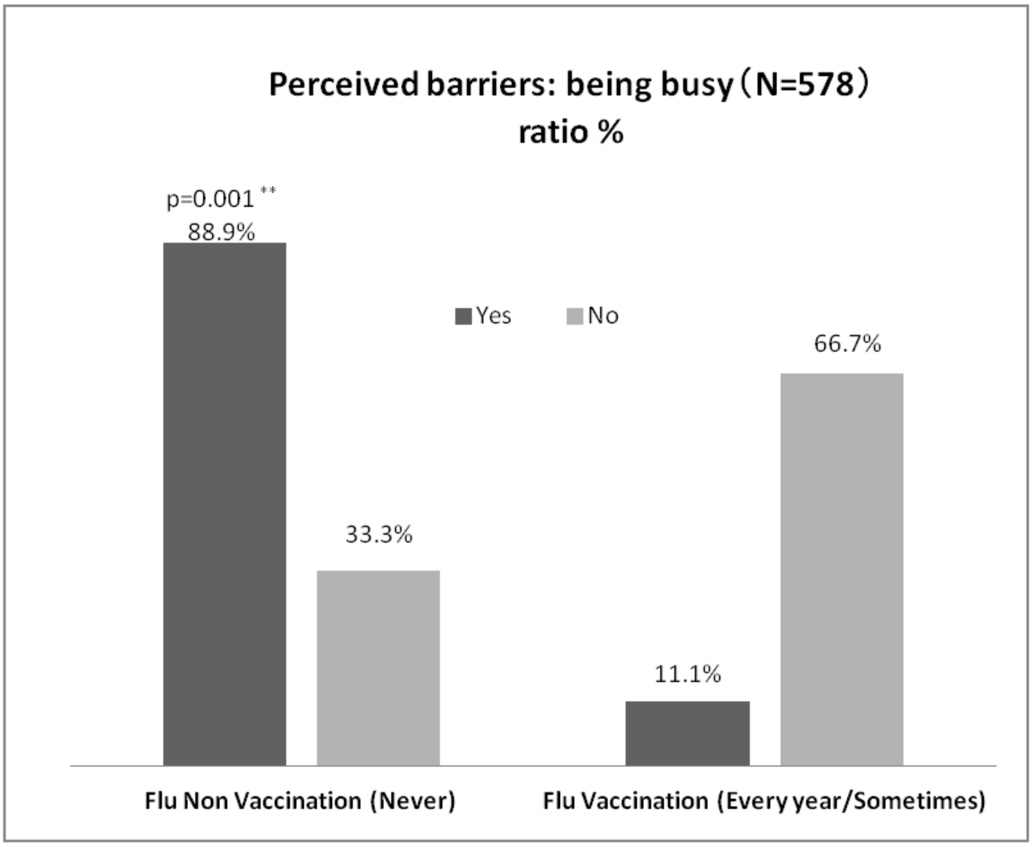


Figure 24 Univariate analysis result of seasonal influenza study: Perceived barriers: being busy (N=578)

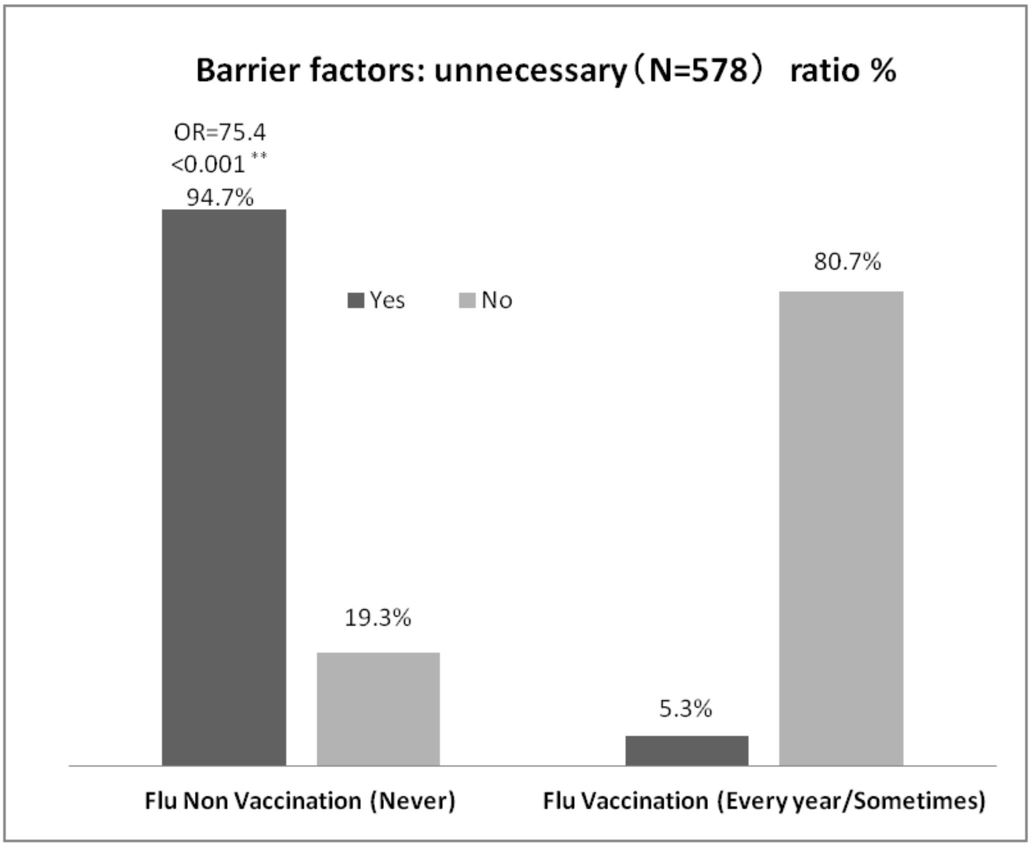


Figure 25 Univariate analysis result of seasonal influenza study: Perceived barriers: unnecessary (N=578)

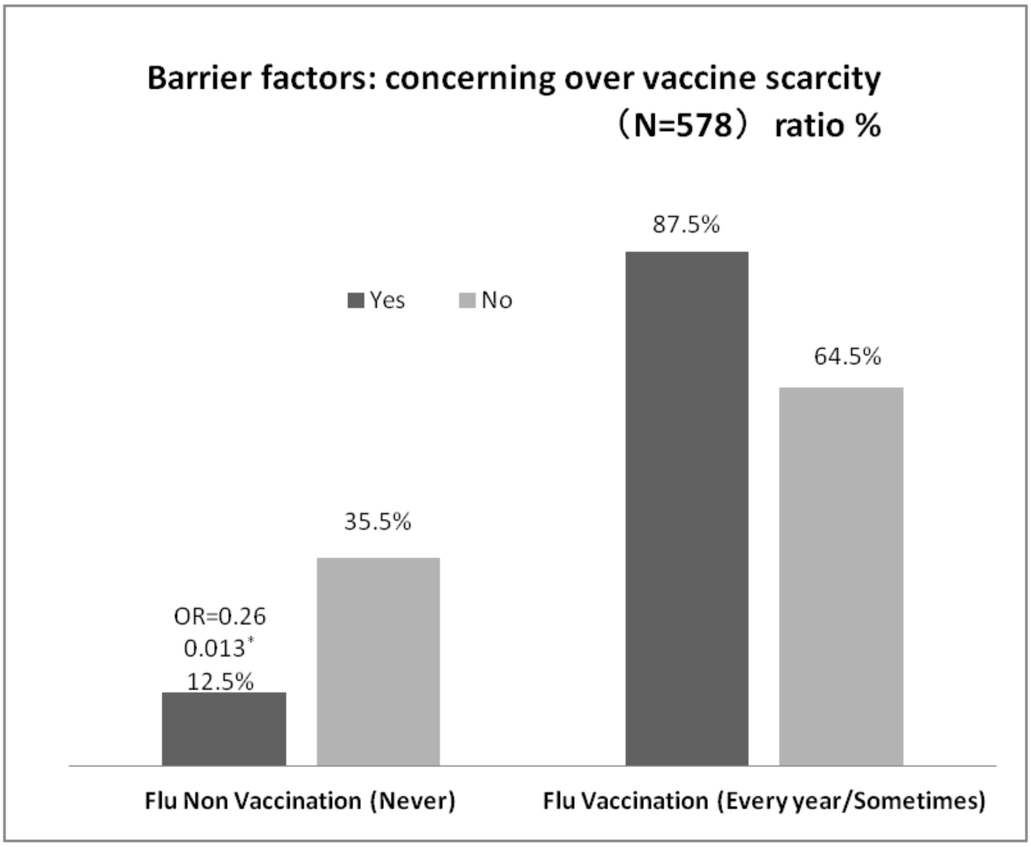


Figure 26 Univariate analysis result: Concerning over vaccine scarcity (N=578)

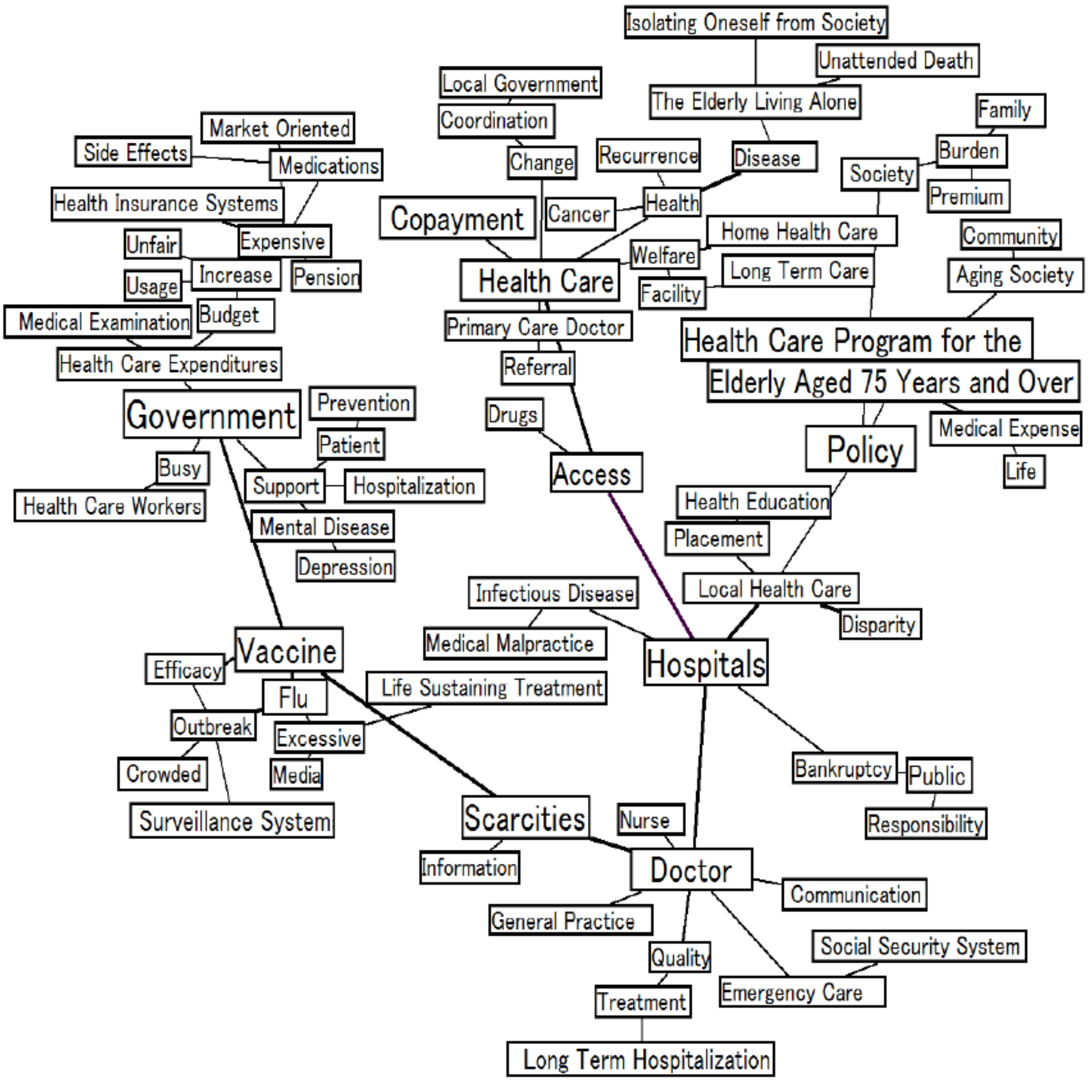


Figure 27 Concept mapping of main extracted keywords of open-ended question about "concerns" (N=300)

(Fujitsu Trend Search 2008 Concept Mapping: After default layout process, author realigns the keywords)

Chapter V

General Discussion

In the studies in this dissertation, the author focuses on two important and prioritized immunization related public health issues and explores factors based on methodologies and the Health Belief Model that have not been sufficiently examined in Japanese studies. The author is able to demonstrate expectable solutions for potentialities for both the studies in this dissertation. The implications and insights obtained through Studies I and II are described in the section below.

5.1 Methodology

One objective of the studies in this paper was to better evaluate the collected data for better results in limited situations. Even though many questionnaires were sent to potential participants, the number of questionnaires recovered was smaller than expected with 226 in Study I and 586 in Study II.

Given this limited situation and to maximize data evaluation, the triangulation method was adopted in both Studies I and II. The method uses qualitative and quantitative methods together by concurrently collecting data and integrating them into one study. This enabled more deliberate consideration, focusing on participant opinions, even if they were small in number and using the quantitative method alone would have neglected them. For example, in Study I, a few mothers among the university-graduated mothers believed that contracting mumps was better for acquiring immunity than having vaccinations.

The quantitative analysis in this paper also used a selection method to find variables for multivariate analysis. Conventional automated selection methods were not used and variables were widely selected by increasing the threshold values of selections. In this selection, both significant variables after univariate analysis and variables close to significant levels were considered as candidates, contrary to conventional selection methods. But in Study I, due to limited sample size (N= 224) and to avoid over-fitting the multivariate model, this method could not be applicable.

In Study II, in this selection process though, two variables noticeably showed significance after multivariate analysis, even though they were not significant after univariate analysis. The results are summarized in Summary Table 1; the two variables are enclosed in a square in the table. We tend to pay attention to variables that have shown statistical significance in univariate analysis, not to non-significant variables. Among these variables are those affected by correlations between variables; they became significant after adjusted multivariate analysis. The two variables in the square in the table fall into this category. This study result supports the rational described in Section 2.2.3 in Chapter II in this paper.

5.2 HBM factors

Another main objective of this paper was to organize and evaluate studies based on HBM. From both Studies I and II, HBM factors were shown to be potential effective predictors for immunizations as one preventive behavior. HBM factors that have shown significance in these studies and referenced studies in Japan and abroad that support the results of the studies in this paper are summarized in Summary Table 2. Due to different immunization characteristics investigated in the two studies, the HBM constructs included in the two questionnaires were different. This complicated comparing the two studies in this paper, but across different ages, genders and characteristics in the populations in Studies I and II, several common findings were observed. The first common findings were perceived effectiveness and the belief that the vaccine was ineffective hindering the vaccination acceptance behavior in both Studies I and II. The number of immunization behavior studies based on HBM is still few in Japan. But these results in this paper can support many studies abroad and in Japan, as mentioned in the Introduction in Chapter I. Similarly, perceived severity backed up by the results of meta-analysis elsewhere became significant in both studies in this paper after univariate analysis. The lack of significance after multivariate analysis in both studies may have been caused by the questionnaire constructs having been too simple to find differences. Further studies are necessary. The next main common finding was about the HBM barrier factor of fear of side effects that became significant after adjusted multivariate analysis in both studies. Among the maternal and parental studies abroad in Summary Table 2, Cheung *et al.* suggested that fear of side effects was stronger in parents with higher education (134). Related to this suggestion, one influenza study in the elderly population in the table of Singleton *et al.* reported that fear of side effects was a major reason for influenza vaccination rejection in a large scale Medicare population in the US. From these results, fear of side effects may be a universal cause for vaccination refusal.

Contrary to the above common findings, different findings between Studies I and II for HBM factors were the cue to action factors. The most significant cue to action factor in the influenza study in the elderly population was communication from local government. The most predictable cue to action factor in the mumps study in the maternal population was a family doctor recommendation, which was followed by social network factors. This may be partially explained by the vaccination being NIP or not. Generally, local governments send vaccination notifications if the vaccines are included in NIP. For this reason, communication from local government became the most effective method for seasonal influenza vaccination acceptance among the elderly population. This was because the vaccination has been included in NIP for the elderly aged 65 years old and older. To the contrary, as already mentioned in the discussion section in Studies I and II, social networks better predict parental, especially maternal, choice of vaccination, and messages transmitted by interpersonal networks strongly influence motivation to obtain vaccinations. Social networks would mainly be a benefit for mothers to raise vaccination acceptance for their children (62, 63, 64).

Different findings were obtained in the studies in this paper; the elderly significantly relied on media for vaccination information. In Study II nearly half of the participants relied on the media as their vaccination information source. Considering the above-mentioned common and different characteristics of HBM factors, raising vaccination awareness among these populations is possible. However, HBM is a behavioral model only at the individual level.

5.3 Implication and approach proposed from the studies

Healthy behaviors are thought to be maximized when environments and policies support healthful choices, and when individuals are motivated and educated to make those choices (Ottawa Charter for Health Promotion, 1986). Glantz *et al.* suggest, “Health education includes not only instructional activities and other strategies to change individual health behavior but also organizational efforts, policy directives, economic supports, environmental activities, mass media, and community-level programs” (164). Green et al. suggest health promotion as the combination of educational and environmental supports for actions and conditions of living conducive of health (145).

Here I discuss the implications and proposals through both Studies I and II.

As described elsewhere, both study I and II were cross-sectional observational studies. In addition, participants were educated and their subjective life-standards were comparatively well so that generalization to common population is unknown. But through the two studies, many issues and factors affecting immunization acceptance have been suggested, including vaccination programs, policies, facility access, costs including subsidies, disbelief in vaccines, safety, vaccine scarcity, lack of information resources, social networks, knowledge dissemination including side effects and the media.

An implication obtained from Study I; mumps vaccine has to be included in NIP to reduce cost barrier and to feel that they were unnecessary. Also, more knowledge dissemination about the severity of complications when children contracted to natural mumps and how the vaccine could prevent them would be necessary. For mothers, message dissemination complied with HBM factors especially through family doctors or social networks would be sufficient. Also, fear of side effects and safety issues remains so that safety of current vaccines has to review again.

From study II, to achieve the first objective to reduce excess mortality during influenza seasons, suppose adverse event incidence of current seasonal flu vaccines are small, knowledge dissemination to lessen the fear of side effects and disbelief, to know correctly about the subsidy to lift a burden of cost. And correct information about herd immunity to protect vulnerable populations would be a benefit. For this population of the study, message dissemination based on HBM factors especially through local government communications and through media would work well.

However, if we remind that immunizations evolve continuously, and new vaccines are introduced, we always have to consider safety issues.

Given this, personal level interventions alone will not work well enough to raise the vaccination rate.

As described elsewhere in this paper, HBM is a model at the individual level. Considering the special nature of characteristics that accompany immunization and to address the unsolved public health goals and problems presented in this paper, a more multi-level approach is necessary. More concretely, a more integrated and wider range of approaches such as an ecological model for health promotion at intra-personal levels as well as considering the natural environment, social cultural environment, information environment and especially the policy environment would be appropriate.

The ecological model was first frame-worked by Kurt *et al.*, focusing on the environment outside the person, and has been further developed. Kenneth McLeroy and others proposed an ecological model for health promotion and defined six sources of influence on health behaviors: 1) intrapersonal factors, 2) social and cultural environment, 3) interpersonal processes and primary groups, 4) institutional factors, 5) community factors and 6) public policy (32). Nagata J et al. reported in their systematic review of seasonal influenza vaccination uptake in the elderly population that structural, intermediate, and healthcare-related social determinants that influenced on the health system, provider and individual levels (56).

Ecological models have been widely used in many health promotions such as the Colorectal Cancer Control Program (CRCCP) by the Centers for Disease Control and Prevention (CDC) (193). To the current author's knowledge, no established ecological model exists for vaccination. The author thus decided to create and propose an ecological model for immunization from insights obtained through the studies in this dissertation.

The six sources in immunization activities through the studies in this paper show as first defined source and factors found from the studies in this dissertation, 1) intrapersonal factors of demographics such as gender, age (Study I and II), income and cost (Study II); family situations such as living abroad (Study I) and living alone; biological factors such as cardiovascular diseases in medical histories (Study II); psychological factors such as fear of side effects (Study I and II), self-rated health (Study II), perceived severity (Study I and II), perceived vulnerability (Study II) and perceived efficacy (Study I and II). Second defined source and factors found in the studies are; 2) social and cultural environment of the society and culture that each agent belong to; historical backgrounds such as immunization program development including withdrawal from SLV of seasonal influenza vaccine (Study II) and side effect incidence history such as MMR withdrawal due to high incidence of side effects (Study I); presumably immunization rejections and religions. The third and forth sources and factors obtained in the studies are; 3) interpersonal processes and primary groups of social support such as social networks, family, friends (Study I), counseling from medical professionals (Study I and II), presumably social activities and organizations, and exercise and healthy life style (Study II) and 4) institutional factors of health insurance, health care services, health care facilities for immunizations that can facilitate traveling to access immunization for mothers (Study I) and other immunization providing facilities that are open on weekends (Study I). The fifth sources and factors suggested from the studies are; 5) community factors of living places and work place environments, research implementation regarding immunizations focusing on factors of non immunization (Study I and II), community based organizations that can support working mothers and mothers with many children (Study I), counseling service facilities that provide correct knowledge and information source (Study I and II), facility access, transportation to help mothers living in rural region or elderly people to vaccination facilities (Study I and II), media that can provide correct information (Study II), information environment (Study I and II), local government communication including subsidy information (Study II) and public spaces where information about immunizations is provided (Study I and II). And the last sixth sources and insights obtained from the studies are; 6) public policies of implementing national and local laws of immunizations such as the national immunization program (Study I), subsidies for immunization (Study I and II), safety review and evaluation (Study I and II), guideline provisions, safety database streamlining and publishing (Study I and II). The author aligned these resource factors and constituents in an ecological model in Fig. 32.

5.4 Future work

The studies in this paper demonstrate the potentiality of HBM factor analysis in immunization behavior for the Japanese population. As they were cross sectional studies, continuing same kinds of studies is necessary to further generalize the conclusions.

In addition, as described in the study limitations, the sample populations in both studies were comparatively higher educated and well off with presumably better social capital. The social capital were out of focus in the studies in this paper, but the problems and issues proposed in this paper such as excess mortality during influenza seasons due to insufficient immunization and mumps complications due to the spread of the disease may be worse in populations deprived of social capital such as the homeless, those living alone, those with lower socioeconomic status and people living in temporary housing or evacuation housing due to earthquakes. Further studies focusing on social factors and social capital are necessary to research these underprivileged populations.

Lastly, for ecological model presented in the proposal section, each constituent for the six sources would be necessary to evaluate and validate along with relationship of constituents and each sources. This process would need on site investigations and more studies in future.

Chapter V Tables and figures

Table

Summary Table 1	Methodology Comparing analytical results: Study II seasonal influenza vaccination study in elderly population
Summary Table 2	HBM factors The results of analysis in the studies in this paper and referenced papers that support the results

Figure

Summary Figure 32	Ecology model proposal for the immunization studies in this paper

Summary Table 1 Comparing analytical results: Study II Seasonal influenza vaccination study in elderly population

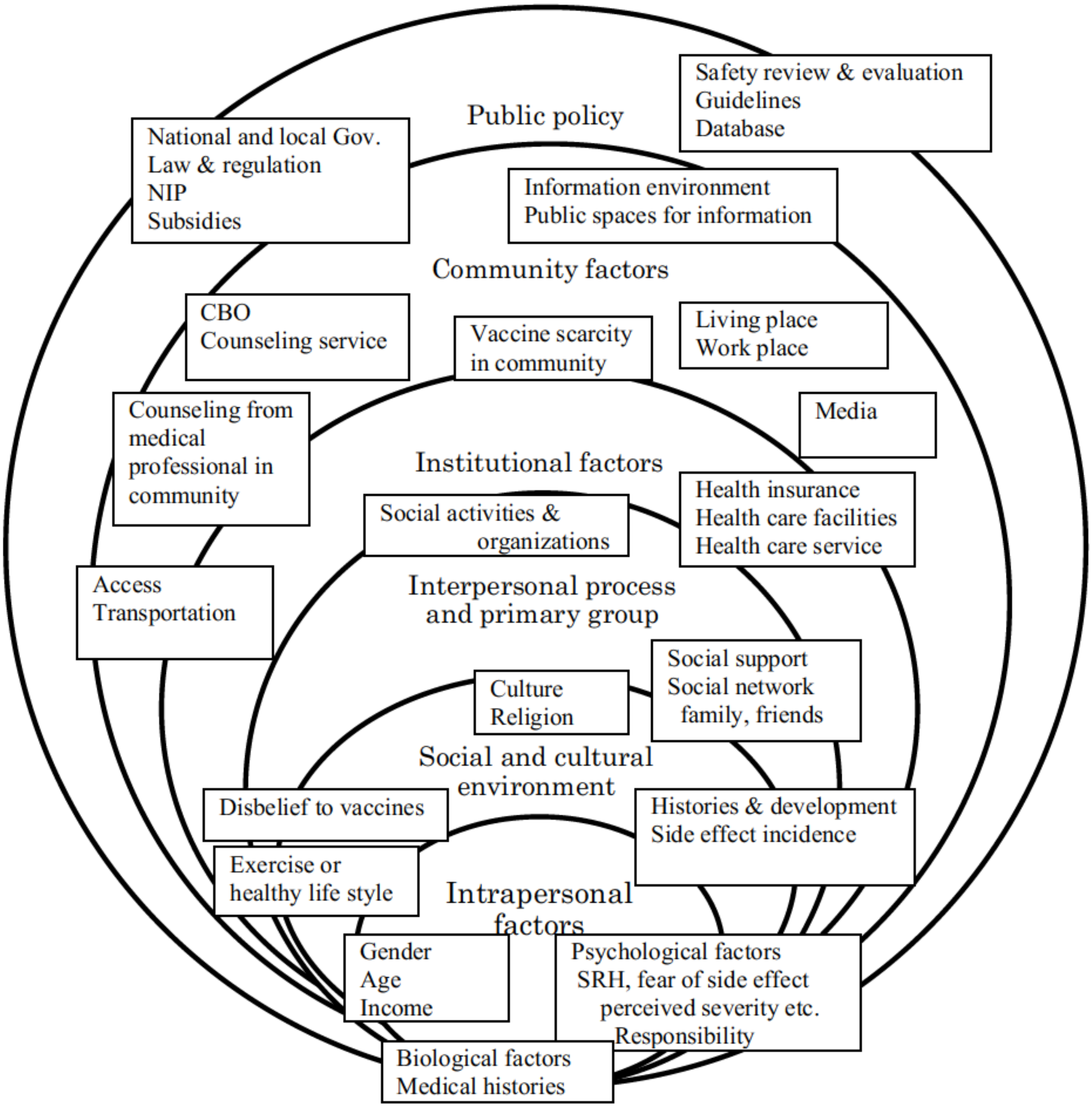
Selected variables for multivariate analysis	Univariate analysis		Multivariate analysis	
Candidate variables	OR	p value	aOR	p value
Age	0.53	<0.01**	0.90	0.01*
SRH	0.51	0.02*		
Sports hours per a week	NA	0.045*		
History: cardiobascular diseases	0.57	0.08	0.26	0.016*
Flu-like symptoms within recent two years	0.54	0.002**		
History: rheumatisum/gout/arthritis	5.28	0.015*	10.90	0.018*
Number of medical histories	NA	0.015*		
HBM factors				
Perceived vulnerability to flu or cold	0.27	<0.001**	0.13	<0.001**
Perceived severity of flu	0.54	<0.01**		
Perceived (non) efficacy of flu vaccine	30.04	<0.01**	35.10	<0.001**
Cue to the action				
Recommendations from family doctors	0.30	0.002**	0.39	0.09
Knowing subsidy to the vaccine	0.21	<0.001**	0.21	<0.0001**
Communication from local government	0.28	0.016*	0.12	0.024*
Perceived barrier				
The vaccine is expensive	1.88	0.08	7.89	0.001**
Concern over vaccine scarcity †	0.26	0.013*		
Fear of harmful side effects	6.67	<0.001**	8.74	<0.001**
Being busy †	NA	0.001**		
WTP	NA	<0.001**		

** denote significance of p value is less than 0.01.* denote significance of p value is less than 0.05.
†The variables were excluded from candidates variables by reasons specified in the paper.
WTP=Willing to pay SRH=Self rated health

Summary Table 2 HBM factors: The results of analysis in the studies in this paper and referenced papers that support the results

HBM variables	Study I Mumps (mother) study		Study II Seasonal influenza (elderly) study		Referenced papers that support the results: Japanese population		Referenced papers that support the results: poplation in abroad	
	Multi	Uni	Multi	Uni	Mother (Parent) study	Influenza (elderly) study	Mother (parent) study	Influenza (elderly) study
Perceived efficacy	Significant		Significant		Iwashita Y	Matsui D*	Wu A／Cheung S	Armstrong K /Singleton A/Ciblak A
Perceived severity	NS	Sig.	NS	Sig.	Iwashita Y/Endo H	Matsui D*	**Brewer T (meta-analysis N=15988)**	Maurer J*
Perceived vulnerability (susceptibility)	NA		Significant		Iwashta Y	Yi S*/Matsui D*	**Brewer T (meta-analysis N=15988)** Brown S/Wu A /Cheung S	
Past influenza history	NA		NS	Sig.	NA	Wada K*/Yi S*	NA	Maurer J*/Seale H*
Knowing subsidy	NS		Significant		Endo H			
Comm from local gov	NS		Significant			Matsui D*		
Recomendation from family dctor	Significant		NS	Sig.	Ono M/Endo H /Nobuhara H		Bonanni P/Gargano M /Brown K/Wu A/	Singleton A
Through social network	NS	Sig.	NS				Brunson K/Marsh A	
Being busy	Significant		NS	Sig.				
Vaccine expensive	NS		Sig.	NS		Yi S*		
Fear of side effect	Significant		Significant			Matsui D*	Merav N／Cheung S /Brown S/Brown K	Singleton A/Maurer J* /Seale H*
Not mandatory	Significant		NA		Tsuchiya Y		Bonanni P	
Willing to pay (WTP)	NS		NS	Sig.	Iwashita Y		Brown S	

NS=Not significant NA=Not applicable Multi=Multivariate analysis Uni=Univariate analysis
* Studies include eldery population.



Summary figure 32 Ecological model of proposal for the immunization studies in this paper (Author created the graph as a proposal model)

Acknowledgments

I have finally finished this dissertation. I was only able to complete this difficult dissertation thanks to everyone's support. I could not have completed it otherwise.

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Note: Journal abbreviations were complied with National Center for Biotechnology Information (NCBI) database.