### -Regular Articles-

# Impact of Community Pharmacists Advocating Immunization on Influenza Vaccination Rates among the Elderly

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This study was carried out to investigate whether the personal advocacy of influenza vaccination by community pharmacists to people aged 65 years and above affected the vaccination rate and number of influenza patients. A cluster randomized controlled trial was conducted with the cooperation of 84 community pharmacies in the wards of Suginami and Nerima, Tokyo. Participants were aged 65 years and above living in Suginami and Nerima wards, Tokyo, receiving dispensing services in their community pharmacies. The intervention was that pharmacists in the intervention pharmacy group provided information on the risk of influenza and benefits of influenza vaccination. Main outcome measures were the self-reported influenza vaccination rate in January 2004, and the number of participants with influenza, as confirmed by inspection of their prescriptions from January to May 2004. The vaccination rate in the intervention pharmacy group (81.6%) was significantly higher than that in the control pharmacy group (64.9%). The number of participants with influenza among the intervention group (2/881) was significantly lower than that among the control group (11/895). The personal advocacy of influenza vaccination by community pharmacists among people aged 65 years and above increases the vaccination rate and decreases the number of influenza patients.

Key words-----influenza; vaccination; pharmacist; elderly; advocacy

### **INTRODUCTION**

Influenza epidemics usually occur during the winter, and influenza was responsible for an average of 36 000 deaths per year in the United States from 1990 to 1999.<sup>1)</sup> Although the rate of influenza infection is the highest among children, serious illness and death following influenza are the most common in elderly people and patients at higher risk for complications.<sup>2–4)</sup> Thus, the prevention of influenza infection is an important public health activity among the elderly.

Influenza vaccination is effective in reducing influenza-related illness, pneumonia, hospitalization, and death among the elderly.<sup>5–7)</sup> In Japan, influenza vaccination of people aged 65 years and above has been recommended by the government since 2001 under the reimbursement for influenza vaccination program. Despite that recommendation, the rate of vaccination in that group was 35% in 2002–2003 season,<sup>8)</sup> which was far lower than the government target rate of 60%.<sup>9)</sup> Multiple factors contribute to the low vaccination rate, including lack of awareness of the vaccine among the general public and health care workers in Japan.<sup>10)</sup>

Several studies<sup>11-13</sup> have reported that campaigns by health care workers, including personal and mailed reminders, lead to an increase in vaccination rates. In particular, it was reported that personal reminders by physicians at clinics were more effective than reminders by letter.<sup>11)</sup> Community pharmacists have many opportunities to contribute to public health through immunization advocacy and to increase their responsibilities in the public-health realm.<sup>12,14-16)</sup> Nonetheless, personal advocacy by community pharmacists has not yet been shown to play an important role in increasing vaccine acceptance and decreasing the number of influenza patients. A cluster randomized controlled trial was therefore conducted to determine whether the personal advocacy of influenza vaccination by community pharmacists to people aged 65 years and above affected the vaccination rate and number of patients with influenza.

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# METHOD

Study Site and Population All community pharmacies in the Suginami Pharmaceutical Association and the Nerima Pharmaceutical Association were invited to participate in the study in September 2003. Thirty-nine community pharmacies in the Suginami Pharmaceutical Association and forty-five community pharmacies in the Nerima Pharmaceutical Association agreed to participate in the study. We stratified these community pharmacies into two wards based on the residence (Suginami and Nerima, Tokyo) and three levels based on the number of estimated participants reported from each pharmacy (<20 participants=small size pharmacies, 20 to 39 participants=medium size pharmacies, and 40 to 60 participants=large size pharmacies). Community pharmacies within each of the six strata were randomly assigned to either the intervention pharmacy or the control pharmacy group.

Participants were recruited from among patients who received dispensing services at the pharmacies. Inclusion criteria were aged 65 years and above and residence in one of the two wards. Exclusion criteria were admission to hospital or nursing home, history of hypersensitivity to the vaccine, and vaccination from October to December in 2003 before receiving the intervention. The study protocol was approved by the Institutional Review Board of Kitasato University School of Pharmacy, and informed consent was obtained from each participant.

**Interventions** Pharmacists in the intervention pharmacy group displayed two posters, provided participants with information on the risks of influenza and benefits of the vaccine in addition to the information in a leaflet and on the two posters, and physically placed the leaflet in the hands of the participants. The leaflet and two posters contained information on influenza susceptibility and severity, vaccine efficacy, cost, and sites where vaccinations were available to elderly residents of the two wards.

The personal interventions were conducted from 14 October to 20 December 2003, because influenza vaccinations are usually offered from mid-October through late December in Japan, with most people receiving them in November and early December. Each intervention pharmacist was responsible for contacting 5 to 60 participants. To minimize bias, pharmacists in the control pharmacies did not display the two posters, physically place the leaflet in the hands of the participants, and were specifically requested to avoid initiating any discussion of vaccination with participants. If, however, their participants inquired about an influenza vaccination, the pharmacists were free to discuss vaccination opportunities.

**Outcome Measures** Data were collected through a baseline survey and two follow-up surveys. After the provision of information on the purpose of the study and obtaining informed consent from participants, the baseline survey was conducted, which included questions regarding age, gender, and influenza vaccination status in the year prior to the study (2002-2003 influenza season). The baseline survey took place from 14 October to 20 December 2003 in the intervention pharmacies and from 5 to 31 January 2004 in the control pharmacies, because the provision of information on the study and obtaining informed consent in themselves might have encouraged the pharmacists in the control pharmacies to discuss vaccination opportunities with participants.

The first follow-up survey, which collected influenza vaccination status (2003–2004 season) from October to December 2003, was conducted from January 5 to 31, 2004. The second follow-up survey, which collected the number of participants who had had influenza and influenza-associated hospitalization (influenza or pneumonia hospitalization) during the 4 months from January to April 2004, was conducted in May 2004. The two follow-up surveys were conducted in person, but telephone follow-up was conducted among nonrespondents to the follow-up surveys. Data were analyzed in October 2004.

The primary outcome measures were the selfreported influenza vaccination rate by community pharmacies and the number of participants who had had influenza by community pharmacies, as confirmed by the inspection of their prescriptions. The secondary outcome measure was the self-reported influenza-associated hospitalization (influenza or pneumonia hospitalization) rate by community pharmacies from January to May 2004.

The number of participants with influenza was defined as those with prescriptions for neuraminidase inhibitor antiviral drugs (oseltamivir or zanamivir), because those agents had not been approved for prophylaxis in Japan during this study period.

Statistical Analysis It was estimated that 712

participants in the study area divided into two groups of equal size would provide at least 80% power to detect a 10% difference in the proportions of participants receiving a recommended vaccination, given the vaccination rate 30% in a control pharmacy, 40%in a intervention pharmacy,<sup>17)</sup> and  $\alpha = 0.05$ . With an anticipated dropout rate of approximately 20% and cluster design effect of 10%,<sup>18)</sup> 940 participants in the study area (total 1880 participants) were specified to provide an adequate number of evaluable participants. An intention-to-treat analysis was performed on all participants to determine the vaccination rate. To determine the number of participants who had influenza and influenza-associated hospitalization, analyses included only the 1776 participants who completed both surveys.

Baseline characteristics and follow-up data between the two groups or wards of residence were compared using the weighted t-test<sup>19)</sup> for proportions (gender, prior vaccination status, and current vaccination status), the chi-square for the other proportions (the number of influenza patients and influenza-associated hospitalization), and the t-test for the continuous variable (age).

### RESULTS

A total of 1863 participants (911 in the intervention

pharmacy group and 952 in the control pharmacy group) and 84 community pharmacies (40 in the intervention pharmacy group and 44 in the control pharmacy group) were included in this study (Fig. 1). Eighty-seven participants (4.7%) (30 in the intervention pharmacy group and 57 in the control pharmacy group) and five community pharmacies (four in the intervention pharmacy group and one in the control pharmacy group) were lost to follow-up. Age, gender, and prior vaccination status did not differ significantly between the two groups (Table 1).

The current vaccination rate in the intervention pharmacy group (81.6%) was significantly higher than that in the control pharmacy group (64.9%) (p < 0.001) (Table 2). The absolute rate difference was 16.7% (Nerima, 19.5%; Suginami, 13.7%). The mean difference in the change to vaccination uptake rate between the intervention and control pharmacy groups was 8.7% (95% CI=2.2–15.2%).

Additionally, the differences in participant characteristics and current-year vaccination rate between the two wards were analyzed. The characteristics of participants did not differ between the two, but the current vaccination rate in Suginami was higher than that in Nerima (7.0% in control pharmacy group and 1.2 % in intervention pharmacy group).

To determine the number of participants who had

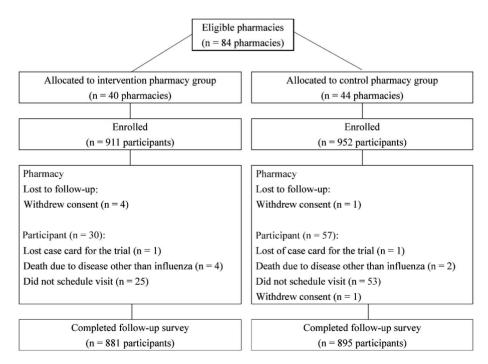


Fig. 1. Flow of Pharmacies and Participants through This Study

	Suginami		Nerima		Total	
Characteristic	Intervention ( <i>n</i> =465)	Control $(n=478)$	Intervention ( <i>n</i> =446)	Control $(n=474)$	Intervention ( <i>n</i> =911)	Control $(n=952)$
No. male (%)*	151 (32.5)	147 (30.7)	141 (31.6)	157 (33.1)	292(32.1)	304 (31.9)
Age, mean (SD), y**	76.6(6.4)	76.2(6.6)	75.9( 6.7)	74.4 ( 5.8)	76.2(6.6)	75.3(6.3)
No. vaccinated, 2002–2003 season (%)*	291 (62.6)	249 (52.1)	267 (59.9)	258 (54.4)	558(61.3)	507 (53.3)

Table 1. Characteristics of Study Participants at Baseline: Intervention vs Control Pharmacy Groups by Ward of Residence

Weighted *t*-test: \* *p*>0.05, *t*-test: \*\* *p*>0.05.

Table 2. Influenza Vaccination Status at Baseline and Follow-up: Intervention vs Control Pharmacies by Ward of Residence

Residence	Intervention				Control			
	No of	% Vaccinated, Mean (S.D.)			No of	% Vaccinated, Mean (S.D.)		
		2002–2003 season	2003–2004 season	Difference	pharmacies /participants	2002–2003 season	2003–2004 season	Difference
Total	36/911	61.3 (21.6)	81.6(18.2)	20.3 (15.3)	* 43/952	53.3(16.0)	64.9(13.1)	11.6(13.0)
Nerima	20/446	59.9(19.8)	81.0(19.2)	21.1(15.9)	22/474	54.4(12.9)	61.4(12.7)	7.0(7.6)
Suginami	16/465	62.6 (23.6)	82.2(17.6)	19.6(15.1)	**	52.1 (18.8)	68.4(13.0)	16.3 (15.6)

Between-pharmacy differences at follow-up, Weighted *t*-test: \* p < 0.001, \*\* p = 0.008.

influenza and required influenza-associated hospitalization, the 1776 participants who completed the two follow-up surveys were analyzed. The number of participants with influenza in the intervention pharmacies (2/881) was significantly lower than that in the control pharmacies (11/895) (p=0.022). The relative risk (RR) of having influenza in the intervention group compared with the control pharmacy group was 0.18 (95%CI=0.04–0.83). No participants with influenza-associated hospitalization were observed in the intervention and control pharmacy groups.

### DISCUSSION

The personal advocacy of influenza vaccination by a community pharmacist to people aged 65 years and above was effective in increasing the vaccination rate and thereby decreasing the number of patients with influenza. To the authors' knowledge, this is the first outcome study to confirm the effectiveness of personal advocacy.

The increased vaccination rate after intervention (16.7%) was higher than that reported for senior center-based reminder letters (11.2%),<sup>13)</sup> community-based reminder letters (8.8%),<sup>17)</sup> and community

pharmacy-based reminder letters (10.3%).<sup>12)</sup> Compared with interventions by mail,<sup>12,13,17)</sup> intervention that included displaying posters in pharmacies, a personal talk in addition to the display of a leaflet and posters, and handing the leaflet to the participants might have given patients a more extensive understanding of influenza vaccination. As it required about five minutes per participant to conduct the intervention, it did not disrupt the pharmacists' daily work. Thus, the intervention described here is replicable with little adaptation by other community pharmacists.

In addition to increasing the vaccination rate, the intervention resulted in a decrease in the number of patients with influenza. However, the present study was not able to show that the increased vaccination rate resulted in fewer influenza-associated hospitalizations, because no participant with influenza-associated hospitalization was observed in the intervention pharmacy and the control pharmacy groups. Several studies<sup>12–14,20</sup> reported that campaigns by health care workers lead to an increase in vaccination rates and a corresponding decrease in the number of influenza patients and influenza-associated hospitalizations.

Grabenstein et al.14) estimated that an increase of 10.3 % in the vaccination rate due to a pharmacy-based reminder letter would prevent 1514 cases of influenza and 64 influenza-associated hospitalizations per 100 000 persons aged 65 years and above. The increased vaccination rate after the intervention in the present study (16.7%) was about 1.6-fold higher than that reported by Grabenstein et al.<sup>14)</sup> Based on these data, it is estimated that the increased vaccination rate after intervention in the present study would prevent 102 influenza-associated hospitalizations per 100 000 persons, and therefore 1.8 influenza-associated hospitalizations might be prevented among the 1776 participants who completed the two follow-up surveys. This suggests that the lack of a demonstration of influenza-associated hospitalization might be due to insufficient power of detection. Future research is required to determine whether the increasing influenza vaccination rate after intervention resulted in a decrease in influenza-associated hospitalizations.

During this study period, participants in Suginami received a reminder letter about influenza vaccination from the ward office, but participants in Nerima did not. The reminder letter contained information on influenza susceptibility, vaccine costs, and vaccination sites available to senior residents. Previous studies<sup>11–13)</sup> showed that reminder letters increase the vaccination rate. To avoid potential bias due to the Suginami reminder letter, the results were stratified by ward of residence. The effect of intervention on the influenza vaccination rate was greater in Nerima (19.6%) than in Suginami (13.7%). It is thus thought that the effect of intervention in Suginami might be underestimated due to the reminder letter. However, the intervention significantly increased the vaccination rate not only in Nerima but also in Suginami. This suggests that personal intervention by a community pharmacist may succeed in reaching elderly nonresponders better than other vaccination promotion activities (newsletter articles, media announcements, and reminder letter from the ward office) and may be an effective addition to current immunization promotion strategies.

One limitation of this study is that participants were recruited from among patients who received dispensing services from pharmacies and may have been more motivated to receive influenza vaccinations. The prior vaccination rate in our study (61.3% in the intervention pharmacy group and 53.3% in the control pharmacy group) was considerably higher than that observed among all people aged 65 years and above in the two wards (28.5% in 2002–2003 season). The high vaccination rate in this study may be attributed to greater awareness of disease prevention because of high-risk medical conditions among the senior population who use prescribed medicines than among the general senior population.<sup>12)</sup> Thus, participants may not have been representative of the senior population in general.

The second limitation is that the intervention relied on participants visiting a community pharmacy during the vaccination season. The Japanese government reported that the number of people aged 65 years and above was 24 224  $000^{21}$  in 2003 and that about onehalf visited a community pharmacy in the vaccination season.<sup>22)</sup> Thus, the present results may be generalizable to about 50% of all Japanese people aged 65 years and above. In contrast, the reminder letter from the ward office did not rely on patients making visits during the vaccination season. Accordingly, it is believed that the combination of the reminder letter from the ward office and intervention by a community pharmacist may be the best strategy for increasing the vaccination rate.

The third limitation is that vaccination status was ascertained by self-report, which may not accurately reflect vaccinations received. However, several investigators have reported good agreement between self-reported receipt of influenza vaccination and medical record audits.<sup>22–26)</sup> It is therefore thought that the self-reported influenza vaccination rate accurately reflects the true vaccinations received.

The fourth limitation is that the vaccine for the 2003–2004 season contained the influenza virus antigens A/New Caledonia/20/99 (H1N1), A/Panama/2007/99 (H3N2), and B/Shandong/7/97, which were not similar to the influenza viruses isolated during this study.<sup>27)</sup> Influenza vaccine efficacy varies depending on the similarity of the vaccine strains to the circulating strain.<sup>4,28)</sup> The decrease in the number of patients with influenza as a result of the increased vaccination rate after the intervention in this study might thus be underestimated.

In conclusion, the personal advocacy of influenza vaccination by a community pharmacist to people aged 65 years and above is effective in increasing the influenza vaccination rate and thereby decreasing the number of influenza patients. Acknowledgments This study would not have been possible without the generous contributions of many people, including the members of the Suginami Pharmaceutical Association and the Nerima Pharmaceutical Association.

## REFERENCES

- Thompson W. W., Shay D. K., Weintraub E., Brammer L., Cox N., Anderson L. J., Fukuda K., *JAMA*, 289, 179–186 (2003).
- Ministry of Health, Labour and Welfare, Vital Statistics of Japan 2003. Vol. 1, pp. 222–223.
- Barker W. H., Mulloly P. H., Am. J. Epidemiol., 112, 798-811 (1980).
- Centers for Disease Control and Prevention, MMWR, 53, 1-40 (2004).
- Deguchi Y., Takasugi Y., Takara K., J. Med. Microbiol., 49, 553-556 (2000).
- Govaert T. M., Thijs C. T., Masurel N., Sprenger M. J., Dinant G. J., Knottnerus J. A., JAMA, 272, 1661–1665 (1994).
- Nichol K. L., Margolis K. L., Wuorenma J., N. Engl. J. Med., 331, 778–784 (1994).
- 9) Ministry of Health, Labour and Welfare: <a href="http://www.mhlw.go.jp/topics/bcg/tp1107-1g">http://www.mhlw.go.jp/topics/bcg/tp1107-1g</a>. html
   html</li
- 10) Hirota Y., Fedson D. S., Kaji M., Nature, 380, 18 (1996).
- 11) Mcdowell I., Newell C., Rosser W., CMAJ, 135, 991–997 (1986).
- Grabenstein J. D., Hartzema A. G., Guess H. A., Johnston W. P., Rittenhouse B. E., *Int. J. Pharm. Pract.*, 2, 5–10 (1993).
- 13) Krieger J. W., Castorina J. S., Walls M. L., Weaver M. R., Ciske S., Am. J. Prev. Med., 18, 123–131 (2000).

- Grabenstein J. D., Hartzema A. G., Guess H.
  A., Johnston W. P., Rittenhouse B. E., *Med. Care*, 30, 503-513 (1992).
- Modrzejewski K. A., Provost G. P., Am. J. Health Syst. Pharm., 60, 1724–1728, (2003).
- American Society of Health System Pharmacists Council on Professional Affairs, Am. J. Health Syst. Pharm., 60, 1371–1377 (2003).
- 17) Mullooly J. P., Am. J. Public Health, 77, 626–627 (1987).
- 18) Kerry S. M., Bland J. M., *Fam Pract*, 15, 84– 87 (1998).
- 19) Bland J. M., Kerry S. M., *BMJ*, 316, 129 (1998).
- Weaver M., Krieger J., Castorina J., Walls M., Ciske S., Arch. Int. Med., 161, 111-120 (2001).
- 21) Ministry of Health, Labour and Welfare. *Vital Statistics of Japan 2003*, Vol. 1, p. 471.
- 22) Ministry of Health, Labour and Welfare. Survey of Medical Care Activities Covered by Public Health Insurance, 2003.
- Buchner D. M., Carter W. B., Inui T. S., Med. Care, 23, 771–779 (1985).
- Larson E. B., Olsen E., Cole W., Shortell S., J. Fam. Pract., 8, 1207–1211 (1979).
- 25) Nichol K. L., Korn J. E., Baum P., Am. J.
  Prev. Med., 7, 199–203 (1991).
- 26) Hutchison B. G., Can. J. Public Health, 80, 271–275 (1989).
- 27) National Institute of Infectious Diseases: <a href="http://idsc.nih.go.jp/iasr/25/297/dj2971">http://idsc.nih.go.jp/iasr/25/297/dj2971</a>. <a href="http://idsc.nih.go.jp/iasr/25/297/dj2971">http://idsc.nih.go.jp/iasr/25/297/dj2971</a>. <a href="http://idsc.nih.go.jp/iasr/25/297/dj2971">http://idsc.nih.go.jp/iasr/25/297/dj2971</a>.
- 28) Centers for Diseases Control and Prevention. "Epidemiology and Prevention of Vaccinepreventable Diseases," 7th ed. Atlanta: U.S. Department of Health and Human Services; 2002.