Acceptance of Intanza® 9 µg Intradermal Influenza Vaccine in Routine Clinical Practice in Australia and Argentina

Peter Eizenberg · Robert Booy · Nadim Naser · Glen Mason · Daniel Stambouliau · Françoise Weber

Received: April 15, 2011 / Published online: July 11, 2011
© The Author(s) 2011. This article is published with open access at Springerlink.com

ABSTRACT

Introduction: Intanza® 9 µg (Sanofi Pasteur SA, Lyon, France), a split virion trivalent influenza vaccine delivered by intradermal injection with a microinjection system, became available as a vaccination for adults aged 18 to 59 years old, as of the 2010 southern hemisphere influenza season. **Methods:** This study was designed to assess the acceptability of intradermal vaccination with Intanza 9 µg in routine clinical practice by adult vaccinees and

their prescribers. Prescribers and healthy adults 18 to 59 years old in Australia and Argentina who had elected to be vaccinated with Intanza 9 µg during the 2010 southern hemisphere influenza season were recruited to complete surveys about their opinions of influenza vaccination and acceptance of the intradermal vaccination. **Results:** 1402 vaccinees and 30 prescribers in Australia, and 264 vaccinees and 16 prescribers in Argentina responded to surveys. In both countries, 98% of vaccinees were satisfied or very satisfied with Intanza 9 µg. The main reasons for satisfaction were that the injection was considered minimally painful and that the vaccination was quickly administered. Most (95%) vaccinees reported that they would prefer to receive the same vaccination next year. Furthermore, 85% of prescribers were satisfied or very satisfied with the intradermal vaccine. **Conclusion:** Intradermal vaccination for seasonal influenza using Intanza 9 µg is well accepted both by adult vaccinees and prescribers. By providing an additional, well-accepted method, Intanza 9 µg might help increase seasonal influenza vaccination rates in adults.

Peter Eizenberg
North East Valley Division of General Practice,
Melbourne, Australia

Robert Booy
National Centre for Immunisation Research and
Surveillance of Vaccine Preventable Disease, The
Children's Hospital at Westmead, Sydney, Australia

Nadim Naser · Glen Mason
Sanofi Pasteur, Sydney, Australia

Daniel Stambouliau
Fundación del Centro de Estudios Infectológicos
(FUNCEI), Buenos Aires, Argentina

Françoise Weber (✉)
Sanofi Pasteur, 2 Avenue Pont Pasteur, 69007 Lyon,
France. Email: francoise.weber@sanofipasteur.com

Keywords: acceptability; influenza; intradermal; seasonal; trivalent inactivated; vaccine

INTRODUCTION

Seasonal influenza is a disease with a substantial clinical and economic burden,¹ and the death rate is increased 50- to 100-fold in people with underlying illnesses.² Vaccination is the most effective means of preventing seasonal influenza infections.¹ In adults, coverage rates remain low. For example, a survey of 11 European countries found that vaccine coverage during the 2007/2008 influenza season ranged from 9.5% to 28.7% in adults and 11.1% to 56.0% in chronically ill persons.³

Until now, trivalent inactivated seasonal influenza vaccines have been administered primarily by intramuscular (IM) injection. Vaccination by the intradermal (ID) route using a microinjection system has been proposed as a way of improving influenza vaccine uptake because it uses a much smaller needle than the IM needle and because it allows rapid and safe vaccination.⁴ Intanza®, the first microneedle trivalent inactivated influenza vaccine, is administered using the BD Soluvia™ microinjection system (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), which consists of a 0.5-mL glass syringe fitted with a 30-gauge, short-bevel microneedle that protrudes 1.5 mm from a depth-limiting tip.⁵ Clinical studies have shown that Intanza 9 µg is non-inferior, and has a similar safety profile, to Vaxigrip® 15 µg in adults 18 to 59 years of age.⁶ Also, in a phase 3 clinical study conducted in adults aged ≥60 years, Intanza 15 µg was superior and had a similar safety profile to Vaxigrip 15 µg.⁷ Intanza was approved first in Europe in 2009 by the European Medicines Agency for the prevention of influenza in both working-age adults (18 to 59 years; 9 µg hemagglutinin per strain) and older adults (≥60 years; 15 µg hemagglutinin per strain).^{5,8} Intanza was also approved in

Australia in 2010 and was launched in adults for the 2010 southern hemisphere influenza season. In Argentina, Intanza 9 µg was approved in late 2009 under the name Istivac ID® 9 µg.

The performance and reliability of ID vaccination with Intanza was confirmed in a total of 9110 subjects enrolled in randomized clinical trials in six European countries, New Zealand, and Australia,⁵ but its acceptance in routine clinical practice has not been directly evaluated. Here, we assessed the acceptability of ID influenza vaccination with Intanza 9 µg under routine conditions of use during the 2010 southern hemisphere influenza season. The study was performed in Argentina and Australia, the two countries in which Intanza 9 µg was first marketed. In the Argentinean study, we also collected opinions of vaccinees by telephone survey 7 to 10 days after vaccination.

MATERIALS AND METHODS

Study Design and Participants

This was an uncontrolled survey of the acceptance of Intanza 9 µg in routine clinical practice by adult subjects and healthcare practitioners. The survey was carried out in Argentina and Australia during the 2010 southern hemisphere influenza season following entry of Intanza 9 µg into the market. Healthcare professionals in general practice and occupational health clinics across Victoria, New South Wales, and Queensland, Australia, and in vaccination clinics in the greater Buenos Aires area, Argentina, asked adults aged 18 to 59 years old whether they would like to be vaccinated with Intanza 9 µg in place of an IM influenza vaccine. Other than discussing the features of Intanza 9 µg, healthcare professionals provided no additional information or reading materials. Those who elected to be vaccinated with Intanza®

9 µg and were willing to complete surveys were sequentially enrolled in the survey. The survey was carried out between April 28 and June 23, 2010 in Australia and between July 12 and August 31, 2010 in Argentina. Each vaccinee was required to provide written informed consent prior to receiving the vaccine and had to be vaccinated in order to be included in the survey. Exclusion criteria included hypersensitivity to the active substances or any of the excipients. Immunization was postponed in vaccinees with febrile illness or acute infection.

Treatment and Assessments

Immediately after being vaccinated with Intanza 9 µg, vaccinees completed a self-administered questionnaire in English (Australia) or Spanish (Argentina). This questionnaire collected demographic information and asked the subjects about their perception of risk for contracting influenza, their influenza vaccination history, satisfaction with the ID vaccination, and their vaccine preference for the next year. Seven to 10 days after vaccination, vaccinees participating in the Argentinean survey were contacted by

telephone and asked again about their vaccine preference for the next year. Up to three attempts were made to contact vaccinees. At the end of the influenza season and after all patients had been vaccinated, prescribers completed a questionnaire that asked them about their satisfaction with Intanza 9 µg.

Statistical Analysis

All analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC, USA). Categorical variables were described by the percentage of each response choice, with missing data excluded in the calculation of percentage.

RESULTS

Intanza 9 µg Vaccinee Responses

Demographics

The survey in Australia included 1402 vaccinees, and the survey in Argentina included 264 vaccinees. Both studies included approximately equal numbers of men and women (Table 1). Most (70.0%) of the vaccinees

Table 1. Vaccinee demographics.

Parameter	Australia		Argentina		Overall	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Answering self-administered questionnaire	1402	100	264	100	1666	100
Answering telephone survey	-	-	208	78.9	-	-
Sex	<i>N</i> =1401		<i>N</i> =258		<i>N</i> =1659	
Male	692	49.4	126	48.8	818	49.3
Female	709	50.6	132	51.2	841	50.7
Age	<i>N</i> =1399		<i>N</i> =263		<i>N</i> =1662	
18–49 years	939	67.1	225	85.6	1164	70.0
50–59 years	412	29.4	38	14.4	450	27.1
60–74 years	48	3.4	0	0.0	48	2.9

Demographic results were from a self-administered questionnaire. Percentages were calculated as $100 \times (\text{number in each category } [n] \div \text{the total number of responses available for each question } [N])$.

were 18 to 49 years old. The remainder were mostly 50 to 59 years old, although a few vaccinees in the Australian survey ($n=48$; 3.4% in Australia; 2.9% overall) were 60 to 74 years old, which constituted an off-label use of the vaccine, although all respondents were included in the analysis.

Vaccinees' Feeling of Risk for Contracting Influenza

Most vaccinees (63.6% in Australia, 56.3% in Argentina; 62.5% overall) felt at risk for contracting seasonal influenza (Table 2). For those feeling at risk in Australia, the most common reason was “I come into contact with many people in my daily life” (71.3%), but in Argentina, this was cited less often (31.8%). Also, “I have a chronic illness” was a common reason for feeling at risk in Argentina (23.6%) but not in Australia (4.3%).

Less than half of vaccinees (36.4% in Australia, 43.7% in Argentina; 37.5% overall) did not feel at risk for contracting seasonal influenza. The most common reasons for not feeling at risk in either Argentina or Australia were “I ensure a healthy lifestyle,” and “I have no chronic illness to consider myself at risk for flu.” “I rely on the strength of my natural defenses” was one of the most common reasons for not feeling at risk in Australia (26.8%) but was less important in Argentina (13.9%).

Frequency of Vaccination

More than half (55.1%) of vaccinees in Australia reported being vaccinated against seasonal influenza every year, while approximately one-third (29.9%) said that it was their first time (Table 2). In Argentina, in contrast, the majority (70.5%) reported that it was their first time to be vaccinated for seasonal influenza, and fewer than one in five (18.6%) reported that they were vaccinated every year.

Main Reasons for Being Vaccinated

The main reasons for being vaccinated during this study differed between the two countries (Table 2). In Australia, the most common reason for being vaccinated was “my own belief of the importance of flu vaccination” against seasonal influenza (43.5%), and only 15.1% of vaccinees mentioned “physician/GP advice” as the main reason for being vaccinated. In Argentina, the most common reason for being vaccinated was “physician/GP advice” (76.1%), and “my own belief of the importance of flu vaccination” against seasonal influenza was cited by only 9.5% of vaccinees.

Main Reasons for Missing Previous Vaccinations

For vaccinees who reported missing previous influenza vaccinations, the main reason reported was “I didn’t feel I was at risk of getting flu” (69.5% in Argentina and 43.3% in Australia) (Table 2). In Australia, another major reason (32.4%) for missing previous vaccinations was “I was not encouraged to be vaccinated.” “I have a fear of injections/needle size” and “I was afraid of side effects/contracting flu from the vaccine” were infrequently reported as reasons for not being vaccinated in both Australia (9.7% and 13.7%, respectively) and Argentina (1.0% and 4.1%, respectively).

Vaccinee Satisfaction with Intanza 9 μ g

Vaccinees’ satisfaction with Intanza 9 μ g was high and quite similar in the two countries. When asked immediately after the vaccination, 98% of vaccinees in both countries reported being “very satisfied” or “satisfied” with the immunization, and only 0.4% to 0.5% reported being “unsatisfied” (Figure 1A). The two main reasons for satisfaction in both countries were “the injection was minimally painful” and “the administration process was quick” (Figure 1B).

Table 2. Vaccinees' opinions and history of vaccination for seasonal influenza.

Questions/answers	Australia		Argentina		Overall	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Do you feel at risk of getting flu?	<i>N</i> =1400		<i>N</i> =263		<i>N</i> =1663	
Yes	891	63.6	148	56.3	1039	62.5
No	509	36.4	115	43.7	624	37.5
Reason for feeling at risk	<i>N</i> =888		<i>N</i> =148		<i>N</i> =1036	
I come into contact with many people in my daily life	633	71.3	47	31.8	680	65.6
I have previously experienced flu	157	17.7	10	6.8	167	16.1
I am at risk because of my older age	58	6.5	2	1.4	60	5.8
I have a chronic illness	38	4.3	35	23.6	73	7.0
Other	2	0.2	54	36.5	56	5.4
Reason for not feeling at risk	<i>N</i> =504		<i>N</i> =115		<i>N</i> =619	
I ensure a healthy lifestyle	164	32.5	28	24.3	192	31.0
I have no chronic illness to consider myself at risk for flu	150	29.8	24	20.9	174	28.1
Relying on natural defenses	135	26.8	16	13.9	151	24.4
I am too young to be at risk for flu	28	5.6	7	6.1	35	5.7
I try to avoid crowded environments	27	5.4	12	10.4	39	6.3
Other	0	0.0	28	24.3	28	4.5
How often do you receive a flu vaccine?	<i>N</i> =1396		<i>N</i> =264		<i>N</i> =1660	
Every year	769	55.1	49	18.6	818	49.3
Have not in the past - this is my first time	418	29.9	186	70.5	604	36.4
Every two years	101	7.2	8	3.0	109	6.6
Less than every two years	108	7.7	21	8.0	129	7.8
Main reason for missing previous vaccinations	<i>N</i> =578		<i>N</i> =197		<i>N</i> =775	
I didn't feel I was at risk of getting flu	250	43.3	137	69.5	387	49.9
I was not encouraged to be vaccinated	187	32.4	5	2.5	192	24.8
I was afraid of side effects/contracting flu from the vaccine	79	13.7	8	4.1	87	11.2
I have a fear of injections/needle size	56	9.7	2	1.0	58	7.5
Other	6	1.0	45	22.8	51	6.6
What / who prompted you to receive your flu vaccine today?	<i>N</i> =1394		<i>N</i> =264		<i>N</i> =1658	
My own belief of the importance of flu vaccination	607	43.5	25	9.5	632	38.1
Family, friend or colleague	452	32.4	14	5.3	466	28.1
Physician/GP advice	210	15.1	201	76.1	411	24.8
Physician's office assistant/practice nurse advice	63	4.5	1	0.4	64	3.9
Poster/communication in waiting room or pharmacy	39	2.8	2	0.8	41	2.5
Other	23	1.6	21	8.0	44	2.7
Which of the following would be most effective in reminding you of future flu vaccination?	<i>N</i> =1392		<i>N</i> =263		<i>N</i> =1655	
Postcard/email/SMS alert sent by your nurse/physician's assistant/GP clinic	521	37.4	57	21.7	578	34.9
Advice from your physician/GP	351	25.2	129	49.0	480	29.0
Advice/reminder from family or friend	170	12.2	10	3.8	180	10.9
Articles in the media	144	10.3	51	19.4	195	11.8
Other or none	206	14.8	16	6.1	222	13.4

Results were from a self-administered questionnaire. Percentages were calculated as $100 \times (\text{number in each category } [n] \div \text{the total number of responses available for each question } [N])$.

Figure 1. Vaccinees' satisfaction with Intanza® influenza vaccination and preferences for the following year. (A) Immediately after vaccination, vaccinees were asked "how satisfied are you with the vaccine you received today?" Possible responses were "very satisfied," "satisfied," "somewhat satisfied," and "not satisfied." Results were from the self-administered questionnaire completed just after vaccination. (B) Vaccinees responding "very satisfied," "satisfied," or "somewhat satisfied" to "how satisfied are you with the vaccine you received today?" were asked "what is the main reason for your satisfaction?" Possible responses were "the injection was minimally painful," "I was reassured by the microneedle (short and thin needle)," "the administration process was quick," and "other (specify reason...)." (C) Vaccinees were asked "for next year's flu season, would you consider the following?" Possible responses were "to be vaccinated with the same vaccine as today," "to be vaccinated with IM vaccine," and "no vaccination." The day of vaccination results were from the self-administered questionnaire completed immediately after vaccination, and the results for 7 to 10 days after vaccination were obtained by telephone survey. Percentages were calculated as $100 \times (\text{number in each category } [n] \div \text{the total number of responses available for each question } [N])$.

When asked immediately after vaccination about their vaccine preference for the following year, most vaccinees (96.7% in Australia, 87.0% in Argentina; 95.2% overall) answered “same as today” (Figure 1C). In Argentina, the response was the same (86.5%) when the vaccinees were asked a second time, 7 to 10 days after vaccination.

Vaccinees’ Opinions of the Most Effective Reminder to be Vaccinated

In Australia, vaccinees reported that an email or text message would be the best way to remind them about future influenza vaccinations, followed by advice from a physician or GP (Table 2). In Argentina, these two methods were also cited most often as effective reminders, although “advice of a physician” was mentioned first and an “email or text message” as the second most effective reminder.

Prescriber Responses

Demographics

Thirty prescribers in Australia and 16 in Argentina answered survey questions about their perceptions of vaccination with Intanza 9 µg. In Argentina, all prescribers were in the greater Buenos Aires area, and therefore in urban settings. In Australia, nearly all (29/30; 96.7%) practiced in an urban setting, and only one (3.3%) practiced in a peri-urban setting.

Prescriber Satisfaction with Intanza 9 µg

Most (76.7%) of the prescribers in Australia and all 16 (100%) in Argentina indicated that they were “satisfied” or “very satisfied” with the ID vaccine (Figure 2). Only two prescribers (4.3%, both in Australia) were “unsatisfied” with the ID vaccine. Most prescribers/vaccinators reported preferring ID over IM vaccination (70.0% [21/30] in Australia, 83.3% [10/12; 4 surveys unanswered] in Argentina; 73.8% [31/42] overall).

DISCUSSION

This survey evaluated the acceptance in routine clinical practice of the first ID influenza vaccine, Intanza 9 µg, by both adult vaccinees and their prescribers. This study included a total of 1666 vaccinees and 46 prescribers in Australia and Argentina, who were surveyed during the 2010 southern hemisphere influenza season. The survey showed a high rate of acceptance of ID vaccination with Intanza 9 µg by both vaccinees and prescribers. Although randomized clinical studies in adults 18 to 59 years have shown that Intanza 9 µg is non-inferior, has a similar safety profile, and a similar acceptance to Vaxigrip 15 µg,^{5,6} this was the first study to establish the acceptance of Intanza 9 µg in routine clinical practice.

Nearly all vaccinees (98% in both Australia and Argentina) considered Intanza 9 µg satisfactory or very satisfactory when asked immediately after vaccination. Also, when asked immediately after the vaccination, most vaccinees (97% in Australia, 87% in Argentina; 95% overall) reported that they would choose to receive the same vaccination the following year. In the Argentinean study, the percentage did not change when the subjects were asked again 7 to 10 days after the vaccination (86.5% vs. 87% when first asked). This suggests that local and systemic reactions occurring within 1 week of vaccination did not affect acceptability, although this study did not directly assess the impact or perceptions of local or systemic reactivity. These results agree with those of patient-reported outcomes obtained from phase 3 clinical trials of Intanza, in which 96% of both adult and elderly subjects reported being satisfied with the injection system, and 96% to 97% considered the injection to be “very” to “totally” acceptable.⁹ Although other novel routes of administration exist or are being developed for

Figure 2. Prescribers' satisfaction with the Intanza® vaccination. Prescribers were asked "how satisfied are you with the ID vaccine?" Possible responses were "very satisfied," "satisfied," "somewhat satisfied," and "not satisfied." Results were from a self-administered questionnaire. Percentages were calculated as $100 \times (\text{number in each category } [n] \div \text{the total number of responses available for each question } [N])$.

influenza vaccination,^{10–12} vaccinee satisfaction rates have not been reported for these.

For the vaccinees who reported being satisfied with Intanza 9 µg, the most common reasons for satisfaction were that they considered the injection to be minimally painful and rapidly administered. Fear of needles appears not to have played an important role for most vaccinees, as only 14% in Australia and 5% in Argentina reported that they preferred ID vaccination with Intanza 9 µg because they were reassured by the microneedle. Likewise, fear of injections or needle size was reported by only 10% of vaccinees in Australia and 1% in Argentina as a reason for missing previous vaccinations.

Professional opinion in favor of ID influenza vaccination with Intanza 9 µg was also high. Most (85%) of the prescribers surveyed indicated that they were satisfied or very satisfied with Intanza 9 µg.

Although acceptance of Intanza 9 µg by vaccinees was similar in Australia and Argentina, their attitudes toward seasonal influenza vaccination differed. Fewer vaccinees

in Argentina (20%) than in Australia (55%) reported being vaccinated every year for seasonal influenza. The main reason for not being vaccinated was a lack of education about influenza, as shown by many responding that they were not vaccinated because they did not "feel at risk of contracting the flu," and by relatively few being vaccinated because of their "own belief in the importance of vaccination." Not feeling at risk for contracting influenza was also the most common reason reported for not being vaccinated in a study of patients with coronary heart disease in the United States,¹³ and a study in Poland and Sweden in the 2003/2004 and 2004/2005 influenza seasons found that belief in being resistant to influenza was a main barrier to vaccination.¹⁴ In this context, advice from a doctor seems to be the most effective way of reminding people to be vaccinated in Argentina, whereas a specific reminder, such as an email or text message from the doctor's office, seems to be the best reminder in Australia.

The results of this survey should be interpreted in light of certain aspects of the

study design. Firstly, only subjects electing to receive ID vaccination with Intanza 9 µg were included in the survey, so we could not directly compare the acceptability of IM and ID influenza vaccination. Including only those electing to receive ID vaccination might also have biased the results in favor of ID vaccination. However, the results were nearly the same as those found in phase 3 clinical trials that also assessed satisfaction with Intanza.⁹ Another consideration is that the survey was performed primarily in urban Australian and Argentinean clinics, and that different results might be obtained in other countries or more rural settings. However, satisfaction rates were similar in Argentina and Australia, suggesting that Intanza 9 µg is well accepted by adult vaccinees and prescribers, irrespective of the country.

In conclusion, this study showed that Intanza 9 µg was well accepted by adult vaccinees and vaccine prescribers in routine clinical practice. As such, Intanza 9 µg might have the additional benefit of increasing vaccination rates against seasonal influenza in adults by offering an alternative vaccine with a smaller needle and rapid administration. Finally, the study suggests that the most effective approaches for improving influenza vaccination coverage differ between countries.

ACKNOWLEDGMENTS

This study was funded by Sanofi Pasteur. Medical writing assistance in the preparation of this manuscript was provided by Dr. Phillip Leventhal (4Clinics, Paris, France). Financial support for this assistance was provided by Sanofi Pasteur. Potential conflicts of interest are as follows: Nadim Naser, Glen Mason, and Françoise Weber are employees of Sanofi Pasteur; Peter Eizenberg is, and has been, an advisor for vaccines for the government, industry, and

academic and research organizations, and has received financial compensation or expense reimbursement from Sanofi Pasteur in relation to presentations, consultancy, and participation in advisory panels; Robert Booy has received financial compensation (paid to The Children's Hospital at Westmead) from Sanofi Pasteur to attend and present at scientific meetings; Daniel Stambouliau received financial compensation as advisory board members for Sanofi Pasteur. Françoise Weber is the guarantor for this article, and takes responsibility for the integrity of the work as a whole. The authors thank Dr. Pablo Bonhevi of the Infectious Diseases Unit, Centro de Educación Médica e Investigaciones Clínicas, Buenos Aires, Argentina for his contributions to and review of this manuscript.

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

REFERENCES

1. Toshi PK, Jacobson RM, Poland GA. Influenza vaccines: from surveillance through production to protection. *Mayo Clin Proc.* 2010;85:257-273.
2. Barker WH, Mullooly JP. Pneumonia and influenza deaths during epidemics: implications for prevention. *Arch Intern Med.* 1982;142:85-89.
3. Blank PR, Schwenkglenks M, Szucs TD. Vaccination coverage rates in eleven European countries during two consecutive influenza seasons. *J Infect.* 2009;58:446-458.
4. Prausnitz MR, Mikszta JA, Cormier M, et al. Microneedle-based vaccines. *Curr Top Microbiol Immunol.* 2009;333:369-393.
5. Laurent PE, Bonnet S, Alchas P, et al. Evaluation of the clinical performance of a new intradermal vaccine administration technique and associated delivery system. *Vaccine.* 2007;25:8833-8842.

6. Atmar RL, Patel SM, Keitel WA. Intanza®: a new intradermal vaccine for seasonal influenza. *Expert Rev Vaccines*. 2010;9:1399-1409.
7. Arnou R, Icardi G, De Decker M, et al. Intradermal influenza vaccine for older adults: a randomized controlled multicenter phase III study. *Vaccine*. 2009;27:7304-7312.
8. European Medicines Agency. Assessment report for Intanza®. In. London: European Medicines Agency; 2009.
9. Reygrobellet C, Viala-Danten M, Meunier J, et al. Perception and acceptance of intradermal influenza vaccination: patient reported outcomes from phase 3 clinical trials. *Hum Vaccin*. 2010;6:336-345.
10. Jabbal-Gill I. Nasal vaccine innovation. *J Drug Target*. 2010;18:771-786.
11. Kweon MN. Sublingual mucosa: a new vaccination route for systemic and mucosal immunity. *Cytokine*. 2011;54:1-5.
12. Nicolas JF, Guy B. Intradermal, epidermal and transcutaneous vaccination: from immunology to clinical practice. *Expert Rev Vaccines*. 2008;7:1201-1214.
13. Madjid M, Alfred A, Sahai A, et al. Factors contributing to suboptimal vaccination against influenza: results of a nationwide telephone survey of persons with cardiovascular disease. *Tex Heart Inst J*. 2009;36:546-552.
14. Kroneman MW, van Essen GA. Stagnating influenza vaccine coverage rates among high-risk groups in Poland and Sweden in 2003/4 and 2004/5. *Euro Surveill*. 2007;12:E1-2.