EXPERT REVIEWS

Vaccine presentation in the USA: economics of prefilled syringes versus multidose vials for influenza vaccination

Expert Rev. Vaccines 9(11), 1343–1349 (2010)

Claudia C Pereira[1] and David Bishai[†1]

[1]*Department of Population Family and Reproductive Health, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Suite 4622, Baltimore,MD 21205, USA*
[†]*Author for correspondence:*
Tel.: +1 410 955 7807
Fax: +1 410 955 2303
dbishai@jhsph.edu

In the USA, influenza vaccines are available as parenteral injections or as an intranasal preparation. Injectable influenza vaccines are available in either multidose vial (MDV), single-dose vial or prefilled syringe (PFS) presentations. PFSs have gained market share in the USA but have not yet reached the levels of uptake currently seen in Western Europe. Here, we review the topic of vaccine presentation in the USA, with a special focus on influenza vaccines. Second, we present the results of a time-motion study that measured administration costs of influenza vaccination comparing MDVs versus PFSs during the 2009/2010 influenza campaign. Vaccinating with MDVs took an average 37.3 s longer than PFSs. The cost of administering 1000 immunizations in 2009 using MDVs were US$8596 versus US$8920.21 using PFSs. In a pandemic situation where 300 million Americans would require vaccination, PFSs would save 3.12 million h in healthcare worker time, worth US$111.1 million. The higher acquisition costs of PFS vaccines compared with MDVs are offset by lower administrative costs and increased safety.

Keywords: costs • immunization • influenza vaccine • multidose vials • prefilled syringes • time motion • vaccine administration

Injectable influenza vaccination (this article focuses only on injectables; intranasal influenza vaccine [Flu-mist™] has an important role in influenza vaccination but is not considered here) in the USA is currently distributed in three main presentations: vials, which can be single or multidose (MDV), and prefilled syringes (PFSs). The USA predominantly uses MDVs, but PFSs have gained market share over the last few years [101]. We estimate that, currently, PFSs hold approximately 30% of the market for influenza vaccines. Comparing the two influenza vaccine preparations in terms of monetary acquisition, PFSs may cost slightly more per dose than MDVs, but could offer advantages in speed, disposal, wastage and patient safety owing to premeasured accurate doses that reduce dosing errors [1–3]. PFSs also reduce the risk of microbial contamination, which can occur from improper aseptic techniques. Vaccines in PFSs do not contain the preservative thimerosal, whereas MDV vaccines do. A drawback of PFSs is a requirement for more storage space as they can be heavily packaged by the manufacturer to prevent damage. Bulkier packaging can increase refrigeration costs. Production, shipment and storage of MDVs are all cheaper, but using MDVs can be more time consuming for the healthcare worker, because each dose must be drawn from the vial using a needle and an empty syringe, leading to higher administration costs. Using MDVs adds operational complexity and more potential for dosing errors and contamination.

The goal of this article is twofold. First, we provide a descriptive overview of the current literature on operational features of MDVs and PFSs. Second, we report measurements comparing the efficiency and costs associated with MDVs and PFSs for influenza vaccination during the 2009/2010 influenza campaign. Our measurements emerge from a time-motion study of the influenza vaccination process at immunization clinics. Nurses' activities related to MDVs and PFSs were observed and timed using a stop watch. All relevant usage costs associated with PFSs and MDVs were identified and compared. We also measured the amount of vaccine that remained in vials after they were deemed empty by the healthcare worker.

 10.1586/ERV.10.129 ISSN 1476-0584

What is the current status of MDV & PFS use in influenza vaccination the USA?

A variety of factors have led to a growing number of manufacturers of vaccines and other injectables offering PFS platforms for their products. Over the last decade, the US market for PFSs grew at a rate of approximately 20% per year [101]. For vaccines, efficiency and perceived safety drive the growth of PFS presentations. Despite the lack of evidence of toxic effects of thimerosal, the public perception of risk owing to this preservative has shifted many providers away from MDVs towards preservative-free PFSs. In 2004, the Institute of Medicine's Immunization Safety Review committee rejected any causal link between thimerosal and autism [4]. Despite such information, many parents and patients still exhibit concerns over the use of vaccines in general [5,6], and from MDVs in particular.

Efficiency

Influenza vaccines have traditionally been delivered in clinical settings, but recent years have seen a shift towards more vaccines being offered in workplaces, retail centers and at schools. In all of these settings, efficiency and streamlining are extremely important [7]. Patients with wavering interest in influenza vaccination and consumers are likely to be deterred by long waiting times. Efficiency is especially important in mass vaccination settings where the goal is to deliver vaccines as quickly as possible [8]. The success of mass influenza vaccination clinics relies on the ability to offer rapid access to low-cost influenza vaccinations in a safe and organized manner. This is particularly important in the USA at present because the Advisory Committee on Immunization Practices (ACIP), which advises the CDC on vaccine use and policy, voted unanimously to recommend universal seasonal influenza vaccination for all Americans aged 6 months and older, starting in the 2010/2011 season [9].

Prior studies comparing MDVs and PFSs have been conducted in Canada, Japan and countries in Europe. A study conducted by Scheifele and colleagues in Canada concluded that PFSs could save nurses' time in mass immunization clinics. Authors noted that PFSs reduced nursing service time by 9–12 person-hours per 1000 doses, depending on the PFS packaging (individual or trays), thus reducing labor costs by 25–33% [2]. An earlier study in 1996 conducted in European hospitals compared prefilled disposable syringes with conventional vial-based systems for parenteral injections and demonstrated that PFSs led to a cost reduction of 1.5 French Francs (or 1996 GB£0.15) per injection [3]. A study conducted in a hospital in Japan demonstrated that for PFSs, the operation time during the preparation of vaccination was reduced by 31.7% in comparison with vial preparations [1]. The authors emphasized that PFSs are especially important in influenza vaccination, because vaccinations for large numbers of people are concentrated into a few months of the year. Safety and convenience become more critical with high throughput vaccination. According to the Japanese study, healthcare professionals in Japan are eager for further development of PFSs for vaccines and medications not yet available and support increased availability of the products currently available in PFSs [1]. No published studies for the USA have addressed efficiency in influenza vaccination, hence the rationale for the study presented here.

Safety

Safety is a top concern in vaccination. Paradoxically, there is idiosyncratic variation in the way vaccines are administered, reflecting peculiarities in the way a task can be performed from practice to practice. Although the CDC has issued guidelines for best practices in vaccine administration [102,103], it is left to individual practices to achieve guideline adherence. Unsafe injection-related practices may not be recognized, but when observed should be obvious and the magnitude of the consequences of unintended deviant practices may not always be understood [10]. According to research conducted at the CDC, improper handling of injectable medications can lead to infections and other severe outcomes in patients [104]. The research from the CDC presented at the Fifth Decennial International Conference on Healthcare-Associated Infections 2010 showed that nosocomial infections can result from inadequate injection safety practices, and such events could be prevented by safer practices. Some of the unsafe practices were related to hygiene and improper storage and labeling. For instance, the CDC identified as safety breaches the use of multidose medications that were accessed multiple times with nonsterile syringes and needles [105].

The National Center for Immunization and Respiratory Diseases (NCIRD) of the CDC strongly recommends that healthcare workers draw the vaccine only at the time of administration to reduce errors and ensure that the cold chain is maintained and that vaccine is not inappropriately exposed to light [106]. Problems noted by the NCIRD in regard to the practice of drawing vaccine at times other than immediately prior to patient injection (e.g., 'predrawing') include:

- Misidentification of the contents of an unlabeled syringe;
- Vaccine wastage;
- Bacterial contamination, especially of vaccines from single-dose vials that do not contain bacteriostatic agents;
- Possible reductions in potency from interaction between the plastic syringe and vaccine components;
- Inability of the person administering the dose to be sure of the composition and sterility of the product.

One example of a medication-switch error happened in January of 2010 in Massachusetts (USA) where several staff members at an elementary school had to be taken to a hospital after being injected with insulin rather than the H1N1 vaccine [107]. In addition, during observation of the clinics for this study, numerous guidelines were not adhered to (further details of these observations are discussed in the results section). Better vaccine and medication labeling, as well as the use of antigens that cannot be predrawn in advance and left in refrigerators with no labeling, would be key factors to counter such events. Furthermore, adequate recording of lot numbers would ensure proper information

in the case of adverse events. Recording the correct lot number in the medical record and/or in the patient vaccination card is a task made easier by PFSs in comparison with MDVs because PFSs have a detachable label in the package.

The results of a qualitative survey conducted at five European hospitals showed that approximately 95% of participating hospital workers found PFSs more convenient to use and handle than vials or ampoules, and that PFSs saved time during injections. Furthermore, 67% found PFSs more convenient to discard. Other aspects of PFSs that were highlighted by healthcare professionals were: decreased risk of dosing errors, smaller risk of microorganism transmission to the patient and lower risk of injuries for nurses [3]. The study by Hirayama and Kuroyama in Japan showed that PFSs avoided wastage, made inventory control easier, lowered the risks of nurses making a mistake and also enabled quicker responses in emergency situations [1]. In summary, current literature indicates that PFSs have the potential to be safer and more efficient than vials. But there have been no studies from the USA to support a systematic comparison. This was our rationale for studying the time required to administer vaccines via vials versus PFSs.

Efficiency & costs: Baltimore study

Methods

The efficiency, costs and safety practices related to influenza vaccination were evaluated in a time-motion study. Seven practices in Baltimore (MD, USA) and the metropolitan area participated in the study. The practices included hospitals, clinics and private medical centers. The sites varied in their location; three were urban and four suburban. Five practices provided both seasonal and H1N1 influenza vaccines, whereas two only provided the seasonal influenza vaccine. We observed 31 immunization professionals (Table 1), all of whom were registered nurses with various years of experience, ranging from 3 to 39 years (mean: 18.1; SD: 11.7). The practices sampled were selected based on their willingness to participate in the study and permission was obtained from each healthcare provider to have their immunization-related activities observed and timed. Observations and data collection took place between October 2009 and March 2010.

Data collection

We collected time and cost data on all activities related to immunization with MDVs and PFSs for both seasonal and H1N1 influenza vaccines. The time spent by immunization professionals on their vaccination-related activities was recorded using a stopwatch. We observed tasks in the vaccine preparation process, from the time of removal of the vial or the syringe package from the refrigerator until the time it was ready to be administered to a patient. Often during the observations it was not possible to observe all tasks involved in one vaccine preparation process as a whole, as there was no standardized way of executing the tasks. For instance, sometimes nurses attached needles to syringes in bulk, so they were readily available when needed. That may have happened hours or days before they actually drew vaccine from a vial, so that the observer was not able to observe that step, but could observe the other steps of the sequence. We assumed that the time to actually inject the patient would be the same for both methods, so we did not measure the time it took to inject. Our time measurements end from the moment the vaccine was considered ready to inject.

Table 1. Characteristics of the sample of registered nurses observed.

Registered nurse ID	Years of experience[†]	Site[‡]	Times observed (n)[§]
1	37	2	80
2	7	2	69
3	28	2	23
4	8	2	42
5	23	2	90
6	6.5	3	1
7	5	3	2
8	7.5	3	17
9	6	3	47
10	39	3	12
11	17	3	13
12	7	3	7
13	3	3	19
14	15	3	34
15	31	3	5
16	30	3	2
17	12	3	25
18	23	3	7
19	37	3	8
20	9	4	7
21	23	4	3
22	11	1	10
23	8	1	6
24	25	1	1
25	27	1	5
26	9	1	6
27	34.5	1	3
28	30	1	2
29	10	1	4
30	31	5	4
31	3	5	1
			Total = 555

[†]Years of experience as a nurse.
[‡]Sites six and seven provided empty vials and participated in interviews about prefilled syringes and multidose vials.
[§]Number of times a nurse was observed performing multiple tasks, which could be the preparation of one or multiple vaccines to be administered.

Cost measurement

Healthcare professionals' salaries were obtained through the US Bureau of Labor Statistics website, statistics for the year 2009 [11]. We utilized mean wages for registered nurses in the state of Maryland, USA.

Monthly storage costs were estimated by obtaining the average market price of medical-use refrigerators of 4 cubic feet capacity, assuming a 10-year useful life and a discount rate of 5%. Consumer price inflators were used to adjust prices for inflation. The average volume for a package of five doses of PFSs was 52.6 cm^3 and of ten doses of MDVs or one vial was 5.4 cm^3.

Disposal/waste cost difference was assumed to be negligible, as we pressumed that hospitals and clinics already have a contracted waste service and the choice of MDVs or PFSs would not lead to additional waste disposal collection visits.

The prices for syringes, needles, alcohol pads and gloves for the brands and models we observed were obtained from the 2009 Red Book™ Drug Reference [12]. The prices for vaccines were obtained from the IMS MIDAS database [108].

In order to account for uncertainty and to take into account the relatively small number of practices we investigated, we performed a set of one-way sensitivity analyses, using the lowest and highest costs we identified in the 2009 Red Book for vaccines, needles, gloves and alcohol. For storage we calculated the lower bound by multiplying the smallest storage unit cost by 0.8, and likewise we multiplied the largest storage cost for PFSs by 1.2. In a similar fashion, for the lower bound of healthcare worker wages, we multiplied the national average salary of a medical assistant by 0.8. For the upper bound, we used the mean salary for a registered nurse.

Statistical analyses: time use estimation

All analyses were made using STATA SE 10 [13]. The process to prepare a vaccine for injection is composed of several individual subtasks. Some subtasks were timed individually. Most were timed as part of a continuum of sequential subtasks. Stop watch episodes commonly represented more than one single subtask, but the duration of each episode was always accompanied by data on which subtasks had occurred in the interval. In our dataset we had up to seven subtasks represented in one single time measurement. The dataset was arranged so that the length of each measured episode was attached to a list of up to seven subtasks that occurred during that interval. Getting a vaccine ready from MDVs could take up to 16 subtasks and up to ten for PFSs (Figure 1).

To estimate time per subtask we used random-effects regression models to take into account the effects of healthcare professionals. The model assumed clinic-specific and worker-specific random effects. We were able to estimate individual weighted average times for each of the 21 subtasks that could possibly be performed. From our observations and from the literature, we listed all practice steps to vaccinate using MDVs and PFSs, although sometimes none of these steps were performed by a nurse. Finally, we estimated total time required to complete all subtasks for either MDVs or PFSs. The coefficients in the models were interpreted as the incremental number of seconds required to conduct each corresponding subtask. After estimating the average time required for each of the subtasks we observed, we estimated the total time to conduct the entire sequence of subtasks (Figure 1). We conducted that separately for vial-only tasks (13 tasks), common tasks for both MDVs and PFSs (six tasks) and PFS-only tasks (five tasks).

Results

We observed a total of 555 multitasking activities performed by 31 different registered nurses. We estimated that the total time in seconds to get a vaccine ready to be administered per patient was 87 s for MDVs and 49.71 s for PFSs, a difference of 37.29 s (Figure 1).

After adding all relevant administration costs, which included nurses' time, syringes for MDVs only, needles, storage, alcohol and gloves per 1000 injections, the total administration costs

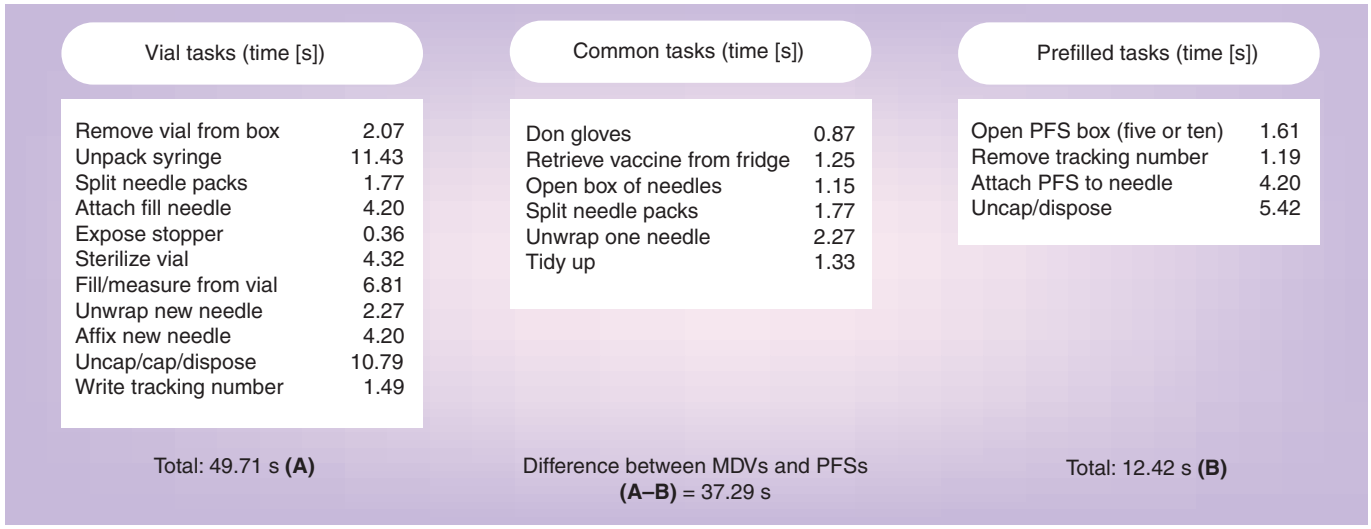

Figure 1. Estimated time in seconds for tasks associated with multidose vial and prefilled syringe use.
MDV: Multidose vial; PFS: Prefilled syringe.

Table 2. Costs associated with vaccination using multidose vials and prefilled syringes in 2009 in the USA.

Resources for 1000 doses	MDVs			PFSs		
	Units	*Price (US$)*	*Total (US$)*	*Units*	*Price (US$)*	*Total (US$)*
Staff time (person h)	13.81	14.16/h[†]	195.55	3.45	14.16/h[†]	48.85
Syringe[‡]	1000	0.39/unit	390.00	NA	NA	NA
Needles[‡]	2000	0.31/unit	310.00	1000	0.31/unit	310.00
Alcohol[‡]	1000	0.03/unit	30.00	1000	0.03/unit	30.00
Gloves[‡]	1000	0.08/unit	80.00	1000	0.08/unit	80.00
Vaccine[‡]	1000	7.59/dose[§]	7590.00	1000	8.44/dose[§]	8440.00
Storage[‡]	1000 doses/month	0.00045/unit	0.45	1000 doses/month	0.0114/unit	11.36
Total[¶]			**8596.00**			**8920.21**

[†]From the US Bureau of Labor Statistics for wages of a medical assistant [11].
[‡]From the 2009 Red Book™ [12].
[§]Average price – IMS MIDAS – Price differential is individually negotiated by distributors and dynamically changing in time.
[¶]The differences between PFSs and MDVs (per 1000 doses) is 324.21.
MDV: Multidose vial; NA: Not available; PFS: Prefilled syringe.

in 2009 were US$8596 for MDVs and US$8920.21 for PFSs, a difference of US$324.21 (Table 2) or US$0.32 per dose administered. These numbers exclude the acquisition cost of the vaccine. Our estimates thus suggest a 'breakeven' PFS price differential of US$0.32. At this price, the savings in vaccination administration costs would exactly offset the higher PFS purchase price.

We conducted a series of univariate sensitivity analyses to explore the impact of varying all costs that were common to MDVs and PFSs (Figure 2). Our results indicate that vaccine acquisition price is the main source of uncertainty in the analyses. The total administration costs varied from US$7456 to US$10,010 in 2009 dollars.

A number of clinical practice adaptations during vaccine preparation were observed and documented. At times, for instance, the same alcohol swab was repeatedly used to sterilize the vial, without being exchanged or receiving more alcohol. This was especially true when nurses were predrawing a batch of vaccines at once in preparation for a big influenza clinic day, so they had to act quickly. The observer noted instances where nurses pooled vaccine remainders from multiple spent vials in order to assemble a full dose, which does not adhere to safe injection practices.

In many clinics, vaccines were predrawn many hours in advance to expedite the vaccination process, especially in influenza clinics that need to minimize patient waiting time. With predrawing there was potential confusion about vaccine lot number, since there was no place on the syringe to write the lot number. In instances of predrawing, we frequently observed incorrect forecasts of the number of vaccines that would be needed. Leftover vaccines that were predrawn from vials would remain in the plastic syringe for the following day.

When vaccines were predrawn, nurses often relied on memory for entering vaccine lot numbers in patient records. A very common practice was to memorize one relevant lot number for a day or session and enter the memorized number on the patient's paperwork, without referencing the original packaging. Some nurses wrote the vial lot numbers on pieces of paper that they could later refer to and some even wrote the number on their skin, as a way of being able to refer to it at any time. During one session the lot number had changed between the syringes for that session and a nurse was still writing the previous lot number.

Discussion

Although MDVs require less cold storage and may have lower acquisition costs, their use imposes higher staff time burdens and higher task complexity. Practices related to predrawing vaccine into unmarked plastic syringes were observed that could impact patient safety and reduce vaccine potency. PFS packaging makes them bulkier to store but none of the clinics observed

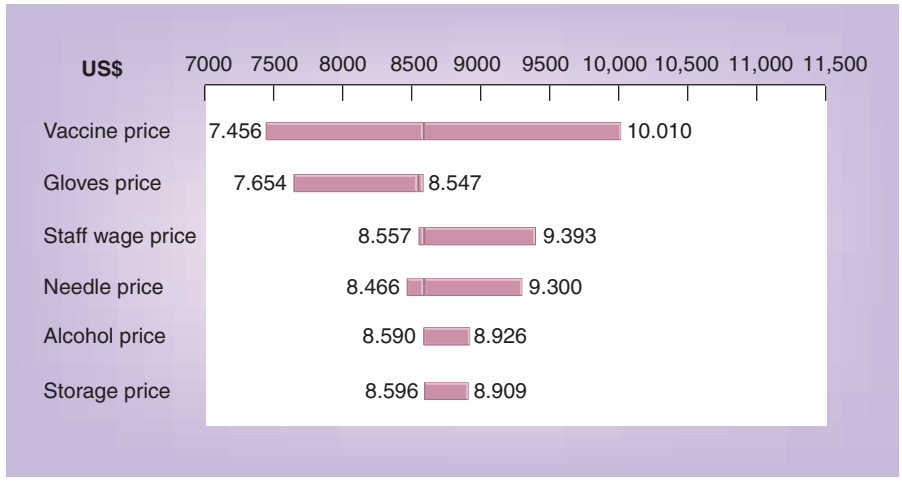

Figure 2. Tornado diagram of univariate analyses. This tornado diagram shows the degree to which uncertainty in prices affects estimates.

had cold storage constraints that would impede their ability to use PFSs. By the same token, none of the clinics were at a point where they could reduce total clinic staff if they could save 37.29 s per patient vaccinated based on the patient volumes the days we observed.

Nevertheless, in the broad scheme of things, the 37.29-s gap between MDVs and PFSs may have important implications. Considering the American birth cohort of 4 million infants, with each infant typically encountering approximately 15 shots before 1 year of age, the use of PFSs would save 621,500 person-hours worth US$22.2 million in healthcare worker time in 1 year of infant vaccination. In a pandemic situation where 300 million Americans would require vaccination, PFSs would save 3.12 million h, worth US$111.1 million in healthcare worker time. The economic decision rests on whether there are better uses for the precious resource of healthcare worker time, especially of nurses.

Conclusion

This work shows that the costs of vaccine administration using PFSs are lower than using MDVs. These costs primarily reflect the longer average time required to prepare a dose of vaccine from a MDV.

Given the current US scenario and system of reimbursement from health plans, the small price gap between MDVs and PFSs and storage requirements are likely to be the main reasons that practices have not yet completely switched to PFSs in the case of influenza vaccines. Furthermore, from the perspective of the clinics, those that receive most of their supplies through the Vaccines for Children Program would benefit the most from the time and convenience of PFSs compared with MDVs, as they are not incurring the expense of the vaccines. Mass vaccination clinics would need to weigh the relative convenience of PFSs in relation to MDVs, versus the full cost of both.

There are strong indications that the growth of PFS penetration into the market for vaccines will continue as American consumers and providers become more familiar with the advantages of these products.

Expert commentary & five-year view

Influenza vaccination in the USA still predominantly uses MDVs, but PFSs offer many advantages over MDVs in terms of efficiency and safety, especially considering the many opportunities for errors and contamination that the use of MDVs creates in vaccination.

Although there are unknown issues surrounding policy and market strategy related to influenza vaccines, we expect to continue to see growth in the market share of PFSs for influenza vaccines in the USA. We anticipate that this market will grow from the current 30% to 80–85% in the next 5 years. Our projection is based on interviews with important stakeholders from this industry and from our understanding of the market dynamics over the last few years. As the demand for PFSs increases, manufacturers are expected to increase production capacity and drive costs down. This has already been seen to a certain extent in the past decade. We expect to see the price gap between PFSs and MDVs diminish over the next 5 years.

Acknowledgments

The authors would like to thank the practices and nurses who kindly allowed us to observe their work and routine. They also acknowledge the helpful comments received from Brian Lynch, Nuphar Rozen-Adler, Justin Wright and Jennifer Zolot.

Financial & competing interests disclosure

The study was funded by a grant from Becton, Dickinson & Company. The authors have received a grant from Becton, Dickinson and Company. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

The authors state that the study received IRB exempt status from the Johns Hopkins Bloomberg School of Public Health Internal Review Board. Even though the IRB declared the study to be exempt, the investigators obtained consent from each participant.

Key issues

- Prefilled syringes (PFSs) have gained market share in the USA, growing at approximately 20% a year, but have not yet reached levels of uptake currently seen in Western Europe.
- In influenza vaccination, PFSs may cost more per dose than multidose vials (MDVs), but could offer advantages in speed, disposal, wastage and patient safety owing to premeasured accurate doses that reduce dosing errors.
- Efficiency and safety are the two key aspects for different stakeholders in influenza vaccination.
- A time-motion study conducted in Baltimore, MD, USA during the 2009/2010 influenza vaccination campaign estimated that the total time to get a vaccine ready to be administered per patient was 87 s for MDVs and 49.71 s for PFSs, a difference of 37.29 s.
- The total administration costs for MDVs in 2009 were US$8596 and US$8920.21 for PFSs, a difference of US$324.21 per 1000 doses or US$0.32 per each dose administered. These numbers exclude the acquisition cost of vaccination.
- MDVs require less cold storage and may have lower acquisition costs, but their use imposes higher staff time burdens and higher task complexity. Practices related to predrawing the vaccine into unmarked plastic syringes were observed that could impact patient safety and reduce vaccine potency.
- If we consider the American birth cohort of 4 million infants, with each infant typically encountering approximately 15 shots before 1 year of age, the use of PFSs would save 621,500 person-hours, worth US$22.2 million in healthcare worker time in 1 year of infant vaccination.
- In a pandemic situation, where 300 million Americans would require vaccination, PFSs would save 3.12 million h, worth US$111.1 million, in healthcare worker time.

References

Papers of special note have been highlighted as:
• of interest

1 Hirayama T, Kuroyama M. Study on usefulness of pre-filled syringe containing influenza vaccine preparations. *Japan Pharmacol. Ther.* 37(9), 737–744 (2009).

• **Estimates costs and compares prefilled syringes with multidose vials.**

2 Scheifele DW, Skowronski D, King A *et al.*. Evaluation of ready-to-use and multi-dose influenza vaccine formats in large clinical settings. *Can. J. Public Health* 91(5), 329–332 (2000).

• **Estimates costs and compares prefilled syringes with multidose vials.**

3 Detournay B, Aden G, Fabregas Z, Lattarulo M, Lebouvier G. Prefilled disposable syringes vs conventional injection systems: European medicoeconomic analysis. *Eur. Hosp. Pharm.* 4(4), 109–112 (1998).

• **Estimates costs and compares prefilled syringes with multidose vials.**

4 Institute of Medicine of National Academies. Immunization Safety Review Committee, Board on Health Promotion and Disease Prevention. *Immunization Safety Review: Vaccines and Autism*. The National Academies Press, Washington, DC, USA, 214 (2004).

5 Shetty P. Experts concerned about vaccination backlash. *Lancet* 375, 970–971 (2010).

6 Kimmel SR. Adolescent vaccination: physician challenges and solutions. *J. Adolesc. Health* 46, S16–S23 (2010).

7 Glazner JE, Beaty B, Berman S. Costs of vaccine administration among pediatric practices. *Pediatrics*. 124(5 Suppl.), S492–S498 (2009).

8 Fontanesi J, Hill L, Olson R, Bennett NM, Kopald D. Mass vaccination clinics versus appointments. *J. Med. Pract. Manage.* 21(5), 288–94 (2006).

9 Poland GA, Morse D. Improving the public health: the U.S. recommendation for universal influenza immunization. *Vaccine* 28, 2799–2800 (2010).

10 US Agency for International Development. *Immunization Essentials: a Practical Field Guide*. US Agency for International Development, Washington, DC, USA (2003).

11 US Department of Labor, Bureau of Labor Statistics. *Occupational Outlook Handbook.* US Department of Labor, Bureau of of Labor Statistics, Washington, DC, USA (2010).

12 Physicians Desk Reference. *2009 Red Book™ Drug References.* Thomson Reuters Healthcare, IL, USA (2009).

13 STATACorp. STATA Statistical Software: Release 10. College Station, STATACorp LP, TX, USA (2007).

Websites

101 Polin JB. The ins and outs of prefilled syringes www.pmpnews.com/article/ins-and-outs-prefilled-syringes

102 National Center for Immunization and Respiratory Diseases (NCIRD). Influenza 2008–2009: ACIP recommendations www2a.cdc.gov/podcasts/player.asp?f=11041#transcript

103 Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases www.cdc.gov/vaccines/ed/epivac/default.htm

104 Hitt E. Improper handling of injectable medications can lead to severe infections. Medscape medical news www.medscape.com/viewarticle/718928_print

105 Hitt E. Improper handling of injectable medications can lead to severe infections. Medscape Medical News www.medscape.com/viewarticle/718928_print

106 Centers for Disease Control and Prevention. Vaccine storage and handling toolkit www2a.cdc.gov/vaccines/ed/shtoolkit/pages/prep_disposal.pdf

107 Associated Press. School staff get insulin instead of swine flu shot http://abcnews.go.com/Health/SwineFluNews/school-staffers-insulin-swine-flu-shot/story?id=9606504&page=2

108 IMS MIDAS Data. August 2010 www.imshealth.com