

A B S T R A C T

Large immunization clinics are commonly held to deliver influenza vaccine to seniors and others. Vaccine is typically dispensed from multi-dose vials but pre-filled syringes are now available, offering time savings for vaccinators. To determine if the higher purchase price of such syringes is offset by savings in time and injection supplies, we did a controlled comparison of syringe and vial formats in two large, concurrent, community-based influenza vaccination clinics. Vaccine preparation and immunization times were carefully documented along with costs for vaccine purchase, storage and injection supplies. Servicing 1,000 clients required 27 nurse hours using syringes and 36 hours using vials but the savings for personnel (\$234) and supplies (\$1,190) using syringes were exceeded by higher vaccine cost (\$2,090 premium) and extra storage costs (\$260) for bulkier packaging. Depending upon product and packaging style, programs using vials are cheaper by \$709-\$926 per 100 doses delivered compared to using pre-filled syringes.

A B R É G É

Des campagnes de vaccination à grande échelle contre l'influenza sont régulièrement proposées aux personnes âgées et autres populations à risque. Le vaccin est généralement administré à partir de flacons multidoses mais des seringues préremplies sont maintenant disponibles, offrant un gain de temps aux employés réalisant les vaccinations.

Afin de déterminer si le prix d'achat plus élevé de ces seringues est compensé par des économies en temps et en matériel d'injection, nous avons réalisé une étude contrôlée comparant les seringues préremplies aux flacons multidoses lors de deux grandes campagnes simultanées de vaccination contre l'influenza. Le temps nécessaire à la préparation et à l'injection du vaccin ainsi que le prix d'achat et de stockage du vaccin et du matériel d'injection ont été documentés avec soin. L'administration du vaccin à 1 000 clients a nécessité 27 heures de temps infirmier pour le système utilisant les seringues contre 36 heures pour le système utilisant les flacons. Cependant, ce bénéfice en personnel (234\$) et en matériel (1190\$) a été absorbé par le prix plus élevé du vaccin (2090\$) et le coût supplémentaire lié au stockage d'un plus grand volume (260\$).

Selon le type de produit et d'emballage utilisé, les programmes utilisant les flacons représentent une économie de 709\$-926\$ pour 100 doses administrées par rapport aux programmes utilisant les seringues préremplies.

Evaluation of Ready-to-use and Multi-dose Influenza Vaccine Formats in Large Clinic Settings

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In Canada, influenza vaccine has routinely been supplied in multi-dose vials but pre-filled syringes are a recently available option. Multi-dose vials are economical to produce, ship and store but vaccinators must draw up each dose prior to use, supplying their own needle and syringe. Time required for dispensing can be problematic in mass clinic settings. In many countries, particularly in Europe, the use of pre-filled syringes containing influenza vaccine is gaining popularity. Once unwrapped they are virtually ready to use. However, the cost per dose is higher for pre-filled syringes than it is for multi-dose vials. Is the difference made up by the savings in time and injection supplies? Are there other important differences between the formats?

The purpose of this study was to compare multi-dose and pre-filled syringe formats for influenza vaccine, delineating their respective advantages and disadvantages in the context of mass immunization clinics. The specific objectives included capturing and comparing all relevant costs of use and documenting the dose yield and safety during use of each format.

METHODS

The physical characteristics of three vaccine products were measured at the Vaccine Evaluation Center. The products included individually packaged, single dose, pre-filled syringes from Pasteur Mérieux Connaught (Toronto, ON) and BioChem Pharma Vaccins (Québec, PQ), and individually packaged 10-dose vials of Fluviral[®] (BioChem Pharma Vaccins), prepared for the 1998-99 season. Labelled dose volume in each instance was 0.5 mL. Package weights and volumes were determined using precision instruments. Available volume of vaccine was calculated from tare weights after emptying pre-filled syringes in the normal fashion or draining vials of available contents.

Unpacking and dispensing times were observed in two large, concurrent influenza vaccination clinics held in Kamloops, BC. One clinic was assigned by coin toss to use individually wrapped, pre-filled syringes (Pasteur Mérieux Connaught) while the other used multi-dose vials. In the latter instance, vaccine was mainly dispensed in one large batch before the clinic opened. Observations continued until at least 1,000 clients were seen in each clinic. To compare the unpacking times of two types of pre-filled syringes, two lots of 100 syringes were unwrapped by one test nurse. One type was the same as used earlier while the other was packaged in trays of 10 (Pasteur Mérieux Connaught). At the end of the day-long clinics, vaccinators were asked to note any product defects and personal injuries they had encountered on an open-ended questionnaire form.

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The clinic settings for time and motion studies were similar by arrangement. Both clinics were held in large shopping malls and had ample waiting space, multiple immunization stations and an easily observed vaccine preparation area. Both involved 9-10 experienced nurses familiar with mass clinics. The client mix was documented for both clinics to assess their comparability.

Costs involved in the clinics were determined using the actual costs of refrigerator rental and purchase of disposable needles and syringes. Minor supplies costs (alcohol wipes, bandaids, disposal containers) were not included. Nursing costs were based on the salary rate for nurses with 6 or more years of experience, as specified by the BC Nurses Union, consistent with the level of experience of participating staff. Purchase price of multi-dose vials of vaccine was based on the provincial contract price for 1998-99 while prices for pre-filled syringes were based on purchases of 200 doses or more, in 1998-99 (personal communication, Order Desk, Pasteur Mérieux Connaught) (personal communication, Marketing Department, BioChem Pharma).

RESULTS

The physical measurements of vaccine packages are summarized in Table I. Shipping weights per 10 doses of vaccine were 7.0-10.3 fold greater with the pre-filled syringes than with multi-dose vials because the syringes are glass and require abundant protective packaging (less than 5% of package weight resulted from vaccine). Similarly, the packaged syringes were 20.4-27.5 times more voluminous per 10 doses than packaged vials, necessitating much larger volumes of refrigerated space for transportation and storage.

Pre-filled syringes were slightly over-filled, yielding a mean of 0.54 mL for one product and 0.55 mL for the other (Table I). Multi-dose vials were also over-filled, with an average of 5.8 mL (range 5.0-6.3 mL).

Pre-filled syringes were shorter than plastic disposable syringes, necessitating somewhat different hand positioning for vaccination. Pre-filled syringes had

Measure	Multi-dose Vials-BCP*	Singly Packaged Syringes-BCP*	Singly Packaged Syringes-PMC†
Units examined	13	75	40
Weight of unopened units (gm)			
1 dose	2.18	15.31	22.4
10 doses	21.82	153.1	224.4
Packaging materials weight (gm)			
1 dose	1.58	14.66	21.72
10 doses	15.82	146.6	217.2
Package volume (cc), unopened units 10 doses	51.41	1050	1415
Average volume of dispensable vaccine, per dose (mL)	0.58	0.53	0.55
Standard Deviation per dose (mL)	0.05	0.014	0.018

* BCP - BioChem Pharma
 † PMC - Pasteur Mérieux Connaught

attached needles, with double needle caps that were more difficult to remove than the single caps of plastic-hub disposable needles and that precluded the option to choose needle size. The syringes from BioChem Pharma contained a large air bubble that had to be removed prior to use whereas those from Pasteur Mérieux Connaught were ready to use. The syringe barrel of the former product lacked graduations, precluding dose volume reductions for children. Most personnel considered the packaging of individual pre-filled syringes difficult to open and a few reported abrasions or paper cuts in doing so whereas the packaging of vials was easily removed.

Preparations for the clinic utilizing pre-filled syringes included rental of a refrigerator to provide the extra space required. For the individually packaged syringes, 1,000 doses required about 142L or 4 cubic feet of storage space. Several coolers were required to transport vaccine to the clinic site.

The teams of nurses who staffed the clinics had an average of 15.4 and 17.6 years of nursing experience. The client mix was similar between the clinics: persons ≥65 years of age accounted for 85% in each instance; females represented 51.4-52.3%; 5.5-7.0% were first-time recipients of influenza vaccine; 2.2-4.5% had impaired mobility; and <0.5% were children.

Both clinics processed 1,000 or more clients in about 4 hours after starting, the period during which time and motion observations were made by research staff. Waiting lines existed for most of this time at both clinics, motivating staff to work quickly.

Using individually packaged, pre-filled syringes, the amount of nursing time required to unpack and prepare syringes and to immunize 1,005 clients was 27.0 person hours. Preparation time averaged 24.1 minutes per 100 doses, based on observations of 560 units unwrapped by 9 nurses. Using pre-filled syringes packaged in trays of 10, preparation time was reduced to 4.75 minutes per 100 doses in the hands of the one test nurse, who required 19.25 minutes to unwrap 100 individually packaged, pre-filled syringes. Only 2 syringes were unusable because of product defects. Actual immunizing time was 1,378 minutes per 1,005 clients or 1.4 minutes per person and included greeting the client, preparing the skin, uncapping the syringe and administering the vaccine.

Using 10-dose vials, the amount of nursing time required to dispense vaccine and immunize 1,011 clients was 36.0 person hours. Preparation time averaged 57.8 minutes per 100 doses, and included unwrapping and opening vials, unwrapping syringes and withdrawing vaccine into syringes. Vaccine dispensing time per se was observed for 17 vials and 10 nurses

TABLE II
Comparison of Costs to Immunize 1,000 Clients with Influenza Vaccine

Cost Item	Costs Observed		Costs Estimated*	
	Multi-dose Vials	Individually Packaged Syringes (PMC)	Individually Packaged Syringes (BCP)	Trays of 10 Syringes (PMC)
Refrigerator rental	NA	\$260	\$260	\$260
Nursing services†	\$935.28 (36.0 hr)	\$701.46 (27.0 hr)	\$774.20 (29.8 hr)*	\$623.52 (24.0 hr)*
Injection supplies	\$1,190	NA	NA	NA
Vaccine cost	\$1,880	\$3,970	\$3,680	\$3,970
TOTAL	\$4,005.28	\$4,931.46	\$4,714.20	\$4,853.52

* See text for assumptions
† Salary rate \$25.98/hr

and averaged 3.9 minutes per 10-dose vial (range 2.1 to 4.8 minutes). Actual immunizing time, defined as above, was 1,575 minutes for 1,011 clients or 1.6 minutes each.

The observed yield of vaccine from multi-dose vials was 1,011 doses from 102 vials, 0.9% short of the nominal yield of 1,020 doses. The observed figure included recovery of partial doses remaining in vials, the time requirement for which was captured in the total preparation time observation. No defects were reported with vials or syringes.

No needle stick injuries were reported with either format. Occasional minor complaints included sore thumbs among staff dispensing vaccine from vials and paper cuts among those unwrapping pre-filled syringes.

To compare the costs involved in immunizing 1,000 clients (Table II), the nursing salary rate used was \$25.98 per hour. For cost calculations, preparation time for pre-filled syringes packaged in trays of 10 was increased to 6.0 minutes per 100 because the one nurse observed was uncommonly proficient. We assumed that immunization time would be the same as with individually wrapped syringes from the same company. Extra storage space would still be required for trays of 10 syringes since the volume of each package is 869 cc, 17 times greater than for 10-dose vials (Table I). Costs for a clinic using pre-filled syringes from BioChem Pharma could only be estimated (Table II) as they were not available for the field study. Research nurses determined that unwrapping and uncapping these individually packaged syringes required approximately the same amount of time as the other such product. We pro-

jected that vaccine preparation times would be comparable in a clinic setting but added 10 seconds per dose of the BioChem product for removal of the large air bubble regularly present in the vaccine compartment.

DISCUSSION

This study clearly demonstrated that pre-filled syringes can save nursing time in mass immunization clinics. Individually packaged, pre-filled syringes took longer to unwrap than pre-filled syringes packaged in trays but compared with multi-dose vials they reduced nursing service time by 9 and 12 person-hours per 1,000 doses, respectively, reducing labour costs by 25%-33% (Table II). The data for pre-filled syringes packaged in trays are estimates based on experience with 100 syringes but unwrapping time was dramatically reduced with this format. Using pre-filled syringes avoids the separate purchase costs of needles and syringes, which actually exceed nursing service costs (Table II).

The main disadvantages of pre-filled syringes are greater cost per dose and much greater storage bulk. The latter would likely necessitate short-term rental of a refrigerator to hold vaccine for large clinics, as few health departments in this province have much excess storage capacity (unpublished data). Greater weight and bulk increase the cost of shipping pre-filled syringes, from the factory as well as within the province. At current prices (Table II), pre-filled syringes do not offer net cost savings over multi-dose vials. The break-even cost would be \$3.12 per dose for syringes packaged in trays of 10 and \$3.04 for the individually packaged syringes that we

assessed more fully. At program cost equivalence, the proportion of costs borne by the central vaccine purchaser shift from 47% (with vials) to 88% (with syringe trays), with end-users benefitting from reduced labour and injection supplies costs.

Both formats delivered the expected number of vaccine doses from packaged materials. Very few pre-filled syringes had manufacturing defects precluding their use (2 among 1,205 doses observed). No vials were defective. Vials were over-filled to allow for losses in dispensing but removal of partial doses remaining in vials was necessary to achieve 99% recovery of the expected number of doses. Syringes were also over-filled, delivering 8%-10% more than the nominal dose (Table I) but the extra quantity of vaccine is unlikely to influence immune responses.¹

Vaccinators had to adjust to the smaller size of pre-filled syringes, which requires use of both hands for proper syringe operation. Attached 5/8" needles are short for reliable IM administration.² Apart from that, the construction of these devices posed no particular hazards or difficulties.

Clients would have noticed no difference between the clinics resulting from the vaccine format used. Nurses using vials spent an hour dispensing vaccine before opening the clinic but then progressed very quickly. Immunizing time was 12 seconds slower per dose than with pre-filled syringes, possibly because nurses took a moment to check and adjust the dose volume.

Where pre-filled syringes were used, staff had to use more coolers to transport vaccine to clinic and had to deal with a larger volume of refuse afterward. Biohazardous waste volumes were similar between clinics. No costs were assigned to these aspects of the clinics.

We conclude that in large clinic settings, use of multidose vials offers the best value at current prices. Using pre-filled syringes reduces nursing time requirements, especially when syringes are packaged in trays, and would offer a means to reduce clinic staffing where this is a priority. Wider use of the syringe format might result in price reductions, approaching cost neutrality with the vial format. Different considera-

tions may apply to the office use of vaccines and were not assessed.

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