Unit-of-Use Versus Traditional Bulk Packaging

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Abstract

Background*: The choice between unit-of-use versus traditional bulk packaging in the US has long been a continuous debate for drug manufacturers and pharmacies in order to have the most efficient and safest practices. Understanding the benefits of using unit-of-use packaging over bulk packaging by US drug manufacturers in terms of workflow efficiency, economical costs and medication safety in the pharmacy is sometimes challenging.*

Methods*: A time-saving study comparing the time saved using unit-of-use packaging versus bulk packaging, was examined. Prices between unit-of-use versus bulk packages were compared by using the Red Book: Pharmacy's Fundamental Reference. Other articles were reviewed on the topics of counterfeiting, safe labeling, and implementation of unit-of-use packaging. Lastly, a cost-saving study was reviewed showing how medication adherence, due to improved packaging, could be cost-effective for patients.*

Results*: When examining time, costs, medication adherence, and counterfeiting arguments, unit-of-use packaging proved to be beneficial for patients in all these terms.*

Introduction

Whether to use unit-of-use versus traditional bulk packaging is a continuous debate for drug manufacturers and pharmacies in order to have the most efficient and safest practices. The FDA published the bar code label requirement in February 2004 requiring manufacturers, repackers, relabelers, and private-label distributors of medications registered by the FDA to include bar codes containing at least the National Drug Code (NDC) of the product.[1] Since this rule, the use of unit-of-use packaging has increased. Many drug manufacturers and pharmacies in the United States decide not to use unit-of-use packaging mainly because of costs but overall unit-of-use packaging can be more safe and efficient, result in less counterfeiting, reduce unnecessary costs and ultimately prevent adverse effects.

There are several types of packaging utilized in pharmacies across the US. A unit-of-use package is prescription medication that contains a quantity "designed and intended to be dispensed directly to a patient for a specific use without modification except for the addition of a prescription label by a dispensing pharmacist."[2,3] Examples of unit-of-use packages are blister packs, compliance packs, course-of-therapy packs and vials containing a 30-day supply or a quantity of medication appropriate for specific disease state. In contrast and not to be confused with unit-of-use packaging, there is unit dose packaging. These are medications contained in a single unit package, readily available to be dispensed, and usually contain no more than a 24-hour supply of doses that are delivered or available to a patient-care area[4], such as in a hospital Pyxis. Only a small percentage of U.S. drug manufacturers utilize unit dose packaging, which is most often geared towards hospitals. Therefore, the difference between these two types of packaging is that unit-of-use packaging contains multiple doses while unit dose packaging contains one dose.[5] Bulk packaging contains one type of medication per package intended for multiple single doses.[6]

Realistic Example: Unit-of-Use Efficiency

Implementing more unit-of-use packaging could reduce pharmacy workload by eliminating some of the tedious dispensing tasks. Examples of these are, returning stock bottles to storage shelves, retrieving dispensing vials, and measuring dosage units.[2] A unit-of-use time savings study carried out by Lipowski et al. in a community pharmacy analyzed the time saved between dispensing unit-of-use versus bulk packaging. The authors conducted a simulation study where they compared two teams in regards to their accuracy and time spent to prepare medications according to the assigned packaging method. The first team prepared a set of 50 prescriptions using the bulk packaging method and then filled a set of 50 prescriptions using the unit-of-use packaging method. The second team prepared the same number of prescriptions but used the unit-of-use packaging method first, then used the bulk packaging method. Each team consisted of a pharmacist and a technician who prepared the prescriptions using both methods in order to minimize confounding factors and bias. When using the unit-of-use packaging method, the first and second team accomplished prescription preparation in 19.5 minutes and 20.5 minutes, respectively (see Table 1). In contrast, bulk packaging took longer to accomplish, taking the first and second team 45 minutes and 41.5 minutes, respectively. Between these two teams, the average time

saved by using unit-of-use packages, for 50 prescriptions, was 23.25 minutes or approximately 28 seconds per prescription.[2]

This study also looked at the amount of time pharmacists were involved in actual prescription assembly versus cognitive activities that could be accomplished during the simulation such as reviewing prescription orders, finding drug interactions, counseling patients, and calling health care providers. Pharmacists were involved in prescription assembly for 26% of the bulk packaged orders versus only 4% of the unit-of-use packaged orders (see Table 1).

The last component of the study analyzed medication errors and found four counting errors when processing bulk-packaged prescriptions, two per team, versus zero for the unit-of-use packaging. This study showed that implementing unit-of-use packaging in a retail setting significantly reduces the amount of time a pharmacist is involved in medication dispensing, allows more time for other activities, such as counseling, and decreases counting errors.[2]

Limitation: Costs

Many drug manufacturers view the cost of packaging as a limiting factor of using unit-of-use packaging over traditional bulk packaging. The U.S. Barrier Packaging study conducted in 2002, showed 85% of all medications were in bulk packaging while the other 15% were in either unit dose or unit-of-use packages used mostly for physician samples or hospital medications.[7] National surveys conducted by the NCPA in 2000 and APhA in 1985 also showed that more bulk packages were purchased due to unit-of-use packages being more expensive for consumers.[5,8] There has been no significant event that has changed the current trend of unit-of-use packaging being more expensive. The time-saving study by Lipowski et al. also estimated the actual acquisition cost (AAC) of bulk packages versus similar unit-of-use packages. Of the 50 types of prescriptions used in the Lipowski et al. study, they reported the unit-of-use packages cost $6.31 more.[2] The unit-of-use method tends to consist of more expensive packaging due to the need for an increased amount of packaging and labeling materials (see Table 2).

Average drug prices can be found in the *Red Book: Pharmacy's Fundamental Reference*, from which Table 2 is derived.[9] Table 2 shows that the alprazolam was cheaper in 2006 when bought in bulk packaging, at the expense of $59.00 for 100 tablets versus the unit-of-use packaging price of $61.67 for 100 tablets. Hydrochlorothiazide and methylprednisolone follow the same trend as alprazolam, with the unit-of-use price being slightly higher than the bulk price. In contrast, azithromycin when purchased with unit-of-use and bulk packaging had the same price of $46.66 per 18 tablets despite the types of packaging used.[9] Omeprazole shows an exception where not all medications are cheaper in bulk pricing but are less with the unit-of-use pricing. The last example presented in Table 2 is simvastatin that shows no price difference between the unit-of-use pricing and bulk pricing despite the number of units purchased.[9] Whether purchasing 30, 90, or 1,000 simvastatin tablets, the price of $5.25 per tablet remains the same. Most medication prices may vary depending on the manufacturer chosen, quantity, and type of packaging. Although this is a small medication pricing example of common medications purchased, it exhibits the general trend that unit-of-use medications are generally more expensive than bulk packaged medications.

In the case of the Lipowski et al. study, eliminating the cost of separate prescription vials, decreased counting errors, and the time saved can offset the increased cost of the unit-of-use packaging. Another study by Heaton et al. supports the Lipowski et al. study that by using unit-of-use packaging, it can decrease overall inventory costs. This is due to requiring fewer units in stock at any given time therefore, increases inventory turnover and cash flow.[2,10] A downfall of unit-of-use packaging is the increased need for storage area needed, which is limited in many pharmacies, especially in the urban setting. However, no longer needing space for prescription vials would help counteract the storage space problem for medications.

Improved Product Labeling

When labeling is provided by a drug manufacturer, unit-of-use packaging offers several labeling advantages compared to bulk packaging. First, a unit-of-use dosage form can be dispensed in its original container. This allows the counting and repackaging of dosage units in the pharmacy to be eliminated and therefore reducing human error. Patient compliance may be improved by each unit dose being labeled and more recognized when a dose is missed.[11] For example, patients can clearly see if they have missed a dose when one of their blisters is unopened in their 30-day blister packet supply. Patients maybe then more compelled to finish all 30 days of the prescription. Still, patients should be instructed on how to handle missed doses and how to avoid overdosing on medications if a dose is missed.

Counting errors in the prescription dispensing process have implications for customer relations, inventory management, and therapeutic outcomes.[2] Not receiving the correct quantity of medication, may cause patients to distrust the pharmacy and result in less than ideal patient care. Dispensing excess medication to a patient increases costs to a pharmacy and could eventually lead to adverse events for a patient. Unit-of-use packaging promotes patient safety by

improving sanitary, patient compliance, and product identification through the inclusion of bar codes, manufacturer, expiration date, and lot number on the label in the event of product recall. Unit-of-use packaging also makes drug counterfeiting more difficult because the packaging, as well as the drug, must be replicated exactly the same as the original manufacturer.[12]

Counterfeiting is a significant problem in the field of pharmaceuticals worldwide, causing an increase in costs and, worst of all, a threat to patient safety. The World Health Organization (WHO) is working with the International Criminal Police Organization (Interpol) to help decrease the billions of dollars lost due to this illegal trade. In 2009, Interpol seized approximately 20 million pills, bottles and sachets of counterfeit and illegal medicines in a five month operation in China and nearby Asian countries. Asia has the largest amount of counterfeit medications but these illegal acts can be found worldwide.[13] Attaining accurate estimations of the money lost in counterfeit medications is difficult since there is a large number of sources and information that contribute to these scandals. This problem has vastly expanded due to Internet sales. The WHO reports that over 50% of the counterfeit cases are due to illegal medication Internet sites.[13] Not only are large amounts of money lost but also lives. In 2008, for example, 150 people in Singapore were hospitalized for having severe hypoglycemia. Several deaths occurred and others suffered severe brain damage due to taking counterfeit medications that were supposed to treat erectile dysfunction but instead contained large doses of glyburide, a medication used for diabetes.[13] The cost of implementing safety programs is minimal compared to the loss of a life or lives because of counterfeit medications. Increasing unit-of-use packaging can help decrease the act of medication counterfeiting because of the arduous method needed to duplicate both individual medication packages and medications. Although unit-of-use packaging would initially increase costs for drug manufacturers, the long-term effect would greatly triumph this by decreasing the number of adverse effects and possible deaths.

Cost-Saving Example from Stroke Prevention

Unit-of-use packaging has been shown to increase medication adherence amongst patients, because of the ease of taking medications and ease of recognition when a dose has been missed. Taking a look at an idealistic example of the cost effectiveness due to medication adherence of a hypertensive medication shows its impact of decreasing long-term costs by preventing patient adverse events.

One study by Cherry et al. looked at the clinical and economic burden of non-adherence with antihypertensive and lipid-lowering therapy in hypertensive patients. They determined lifetime costs, morbidity, and mortality associated with three types of medication adherences: no treatment, ideal adherence, and real-world adherence. The study simulated patients' characteristics matching those of the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm and event probabilities were calculated with the Framingham Heart Study risk equations.[14] For the purpose of this article, only the arm of the primary stroke patients will be reviewed in regards to the effect of medication adherence on costs.

This study estimated the cost difference, consisting of hospitalizations, physician costs, and annual institutional care, between varying adherence scenarios. Of the three types of adherence scenarios, the ideal adherence was used in this study as the gold standard. Cherry et al. found patients with no treatment accrued treatment costs of $12,800, with increased patient lives by 14.73 months and had 0.74 more cardiac events (see Table 3). In comparison, real-world adherence accrued costs of $23,300, increased patient lives by 15.07 months and resulted in 0.61 more cardiac events while ideal adherence accrued costs of $32,500 increased patient lives by 15.49 months, and resulted in 0.44 more cardiac events. When compared with no treatment, real-world adherence patients had a longer life expectancy while ideal adherence patients had an even longer life expectancy in regards to patients adhering to taking their anti-hypertensive therapy. While it may seem that no treatment would have less direct medical costs per patient due to not taking any medications, this study found that patients with ideal adherence saved $22,000 per life-year gained which cancels out the low costs of no treatment and highlights the burden of more cardiac events. Patients with real-world adherence saved $31,000 per life-year gained. Cherry et al. also applied their findings prospectively to a larger population model. In a population of 10,000 patients, 6100 lifetime stroke events would be expected as real-world adherence. With ideal adherence, 1700 (28%) of the 6100 events would be avoided.[14]

Although the Cherry et al. article attempted to avoid any biases, there were some limitations related to assumptions on adherence rates and effectiveness of the anti-hypertensive therapy. They noted that these costs may not be as relevant to date because of amlodipine losing patent protection in the United States in 2007 and can now be acquired at lower costs. However, amlodipine was one of the three anti-hypertensive medications used in the model and

the impact of this price would have not changed the average daily WAC significantly.

Overall, in patients with hypertension and cardiovascular risk factors lost more than half of the potential benefits from anti-hypertensives due to poor adherence. Anti-hypertensives are cost-effective at real-world adherences and even more so at ideal adherences. Cherry et al. supported an intervention, depending on costs of implementation, to improve adherence as means to increase the cost effectiveness of health care.[14] Patients have multiple reasons to be non-compliant such as financial constraints, denial, mistrust, and intolerable side effects. In specific, utilizing more unit-of-use medication packaging, can be one intervention to help compliance of patients.

Implementing Unit-of-Use Packaging

Most developed countries have implemented unit-of-use packaging, including Canada, Australia, New Zealand, and other countries in Europe and South America.[5] Implementing unit-of-use packaging may be difficult in the United States, requiring substantial changes in manufacturing, dispensing, and storage of medications. Not only would the physical processes of producing medications need to change, but also prescribing practices and therefore governing policies of prescribing. In order to increase unit-of-use packaging, there would have to be multiple negotiations made between manufacturers, prescribers, pharmacists, government agencies, and consumers.

The main area of conflict between unit-of-use and traditional bulk packaging lies in the retail market. Many health care providers see unit-of-use packaging as an opportunity for pharmacists and technicians to save time and therefore money, by reducing the processes of counting pills, filling, and labeling.[2,10] In time, health care providers will need to perform precise return-of-investment analyses on how their products are packaged and marketed to consumers. If the increased expense of unit-of-use packaging can be justified by the high return-on-investment, then soon the slow trend toward utilizing unit-of-use packaging will turn into a race amongst health care providers.[13]

Statistics show the number of outpatient prescriptions processed in the US is constantly increasing, since there is a larger aging generation needing more medications.[2] However, the number of pharmacies remains constant in the retail setting. This imbalance between the number of pharmacies and growing number of prescriptions warrants serious consideration of the changing retail pharmacy practice and efficiency improvements in prescription dispensing.[2] Increasing unit-of-use packaging in the retail market can decrease the amount of time pharmacists are needed for dispensing and allow more time for reviewing patients' medication profiles, especially with the increasing number of prescriptions and related counseling of patients, including medication therapy management.

Although buying bulk packaging is cheaper and more suitable for pharmacy automation systems, looking at the expenses of unit-of-use versus traditional bulk packaging can ultimately lead to a more efficient process and safer practice in medication dispensing. Choosing the correct medication packaging method is important to drug manufacturers and will continue to grow in the future. The continual innovation and development of material packaging was not mentioned in this article but is crucial to drug manufacturers when meeting demands of storing and delivering medications to patients. There are now many advanced ways of storing medications in unit-of-use packaging that cannot be accomplished by bulk packaging such as orally disintegrating dosage forms.[7] Utilizing more unit-of-use packaging can be beneficial from a multitude of perspectives in the pharmaceutical industry. Whether analyzing cost, compliance, or counterfeiting, the safety of patients should be the ultimate motivation to use unit-of-use packaging.

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Table 1. Lipowski Study: Unit-of-Use Method versus Bulk Method[2]

	Unit-of-Use Method (50 Prescriptions)	**Bulk Method** (50 Prescriptions)
Team 1	19.5 minutes	45 minutes
Team 2	20.5 minutes	41.5 minutes
Usage of Pharmacists in Rx Assembly	4%	26%
Number of Errors	0	4

Table 2. Comparing Red Book Unit-of-Use vs. Bulk Prices[8]

Drug	Manufacturer	Dosage	# of pills/ bottle	Unit-of-Use Price/ bottle ($)	Unit-of-Use Price/ pill ($)	Bulk Price/ bottle ($)	Bulk Price/ pill ($)
Alprazolam	Greenstone	0.25 mg	100	61.67	0.62		
	Cardinal Pharm	0.25 mg	100			59.00	0.59
Azithromycin	Pliva, Inc.	250 mg	18	139.99	7.78	-	-
			30			233.33	7.78
Hydrochlorothiazide	GSMS	25 mg	90	11.55	0.13	-	-
	Heartland	25 mg	30	2.81	0.09	-	-
			90	9.42	0.09		
	PCA, LLC	25 mg	30	-	-	2.00	0.07
			90	-	-	4.00	0.04
Methylprednisolone	Breckenridge Pharm	4 mg	21	11.00	0.52	-	-
	Qualitest	4 mg	21	10.65	0.51	-	-
			100			48.40	0.48
Omeprazole	UDL	20 mg	100	390.00	3.90	-	-
	Teva	20 mg	100	-	-	415.15	4.15
	Apotex	20 mg	100	-	-	415.14	4.15
Simvastatin	Merck	40 mg	30	157.45	5.25	-	-
			90	472.37	5.25	-	-
			1000	-	-	5249	5.25

Table 3. Cost-effectiveness over Lifetime[14]

Adherence scenario	Costs	Patient-years	Events	Savings
▪ No treatment	12,800	14.73	0.74	—
▪ Real-world	23,300	15.07	0.61	31,000
▪ Ideal	32,500	15.49	0.44	22,000