

UNIT-DOSE DRUG DISTRIBUTION SYSTEMS: OLD-FASHIONED OR SAFER WAYS FOR PHARMACEUTICAL CARE?

Unit-dose drug dispensing is periodically subject to controversy as a result of the insufficient justification for its effectiveness in the quality of healthcare. Data in the literature, describing various assessment methods of medication errors, their clinical gravity and nosocomial drug related events, are analysed making distinction between the different organizations of the drug use process. This bibliographic review confirms that unit-dose drug distribution systems effectively improve the quality of care. Whatever assessment methods are used, unit-dose drug dispensing significantly reduces the incidence of medication errors. Strong presumptions exist that individualization of drug distribution systems reduces nosocomial adverse drug events. Appropriate comparative studies remain necessary to clarify the impact of this organizational change on the current prevalence of nosocomial adverse drug events.

Key words: Drug distribution systems; medication errors; nosocomial adverse drug events, quality assurance; systematic review

INTRODUCTION

In different countries, recurrent debates question whether unit-dose drug distribution systems provide optimal choices for organizing the drug use process in hospitals. Among many examples, one which is currently developing in Europe and the controversy which occurred during the 1980s in the USA may be cited.

The current European debate

The publication of the first European survey of hospital-based pharmacy services conducted in 1995 by the European Association of Hospital Pharmacy revealed that unit-dose drug dispensing is not widespread throughout Europe: only 6.5% of the hospitals responding used such systems [1]. The most advanced countries in this respect are Spain (57%) [2–3], the Netherlands (43.5%) and Portugal (27.3%). With the exception of Sweden (6.7%), the implementation rate of unit-dose drug distribution is less than 5% in hospitals of the other European states. These percentages can be compared with the results of successive surveys on professional practices conducted in the USA since 1967. Currently, in that country, fewer than 3% of responding hospitals remain without any bed served by unit-dose drug dispensing [4].

Analysing the causes of these differences, Delaney refers to a recent comparison of error rates between a computerized unit-dose system with automated floor stocks and the English traditional system, concluding that the unit-dose system is less favourable [5]. In this he states “*in an environment of cuts in health spending and hospital downsizing in America, some hospital pharmacists are beginning to wonder if they can continue to use a labour-intensive drug distribution system which may not provide the previously assumed benefits of safety*” [1].

In the same issue of European Hospital Pharmacy, another writer refers to the same study, wondering about the impact of unit-dose dispensing on the reduction of medication error rates and concluding that “*more data are needed to establish the role of unit-dose packaging in drug distribution*” in this field [6]. In reply to the defensive reaction of the delegate of the Sociedad Española de Farmacia Hospitalaria [2], it was held that the “*weakness of previously published studies on error rates in various drug distribution systems has been the failure to assess what the outcomes for patients were as a result of errors*” [7].

The 1985 American controversy

That was not the first time that the basic beliefs on which unit-dose drug dispensing systems are established had been queried because their organizational characteristics were not understood when pharmacists asked themselves such questions. In the USA in 1981, Barker showed that dysfunction of a centralized unit-dose system caused medication error rates closer than expected to those of traditional systems [8]. The unit-dose cart deliveries occurred twice daily in this system, having been reduced from four times a day several years before. This reduction led to a total medication error rate of 9%, excluding wrong-time errors. The rate came closer to a traditional system (from 6.7% to 20.7%) than the results expected (from 1.8% to 3.8%), according to the literature synthesis then undertaken by the authors of this study. During this consultant evaluation, it appeared that such a high medication error rate was the result of a design that differed somewhat from basic principles of the unit dose concept.

Developed and evaluated in the years 1961–67, initial unit-dose drug dispensing systems demonstrated their ability to reduce medication error rates [9–16]. They could be distinguished from traditional drug distribution systems in three fundamental ways [8,17,18]:

1. All doses were dispensed by the pharmacy in the exact dose the physician prescribed, in final, ready-to-administer form, labelled for a particular patient, and requiring no additional measurements or manipulation before their administration to the patient.
2. Only one dose of medication was dispensed at the time the dose was to be given to the patient, no more than a few hours before the scheduled administration, in an amount not to exceed a 24-hour supply and, if a 24-hour supply was dispensed at one time, it was sub-divided into specific dosage intervals.
3. All medication records, both pharmacy and nursing, were maintained by pharmacy personnel, who also performed the initial interpretation of the physician's order, so that all medication orders were filled and administered from the original or a direct copy of the physician's prescription.

The hospital's failure to implement consultants' recommendations prevented the achievement of the goal of a 3% reduction in medication error rates: the rates were even worse after modifications [19,20].

The existence of these high medication error rates re-opened the whole issue of the credibility of unit-dose drug dispensing systems. The memorable debate which followed the publication of these counterproductive results revealed that the way in which some pharmacists had organized the drug use process in their hospitals was not according to the basic tenets of unit-dose drug dispensing [17,18,21–26]:

1. Pharmacies had no control over the maintenance of medication administration records and, in some cases, had no access to medical prescriptions;
2. Numerous dosage forms, especially oral liquids and injectable forms, were not supplied in unit dose packages;
3. The frequency of deliveries had been reduced, becoming daily in the worst cases.

The merit of Barker's audit lay in demonstrating that such compromises caused damage to quality of care. The relinquishment of basic rules, as defined by the American Society of Health-Systems Pharmacists [27,28], was interpreted as losing the cause and effect relationship between organizational methods and their effects on patients, explaining the apathy of pharmacists themselves towards the ideal of unit-dose drug distribution [25]. Once again, some commentators sought further research, calling upon “*the necessity to demonstrate the relationship between specific components of a unit dose system and error rate*”, particularly its computerization, because “*of the complexity of drug distribution and the limitations of current understanding of the unit-dose concept*” by pharmacists [23,24,26]. Only one

advocate of “*pharmacist-oriented drug distribution systems*” wondered about the appropriateness of such research, considering that it had no other purpose than postponing the implementation of unit-dose drug distribution systems [18].

Europe 1996–97 and USA 1984–85 were two similar controversies grounded on insufficient evidence of efficacy of unit-dose drug dispensing systems on quality of care, particularly from the detractors’ point of view. Is knowledge really so incomplete that nearly everything remains to be demonstrated? The bibliographic research we conducted about the drug use process in hospitals shows that many answers demanded during these debates are already available in the literature [29,30].

METHODS

Few studies allow comparison of the efficiency of different ways of organizing the hospital drug use process. Publications throughout a period of over 30 years do not even use the same terminology to describe the drug use process, whether in North America or in Europe. Being unaware of these semantic subtleties can lead to misinterpreting their results. For instance, when a system is called “traditional”, it may be a ward stock system or an individual patient prescription system. We summarize the different ways of the drug use process organization in Table 1. Their modalities vary depending on the type and importance of the drug use process functions controlled by the pharmacy: dispensing, preparing or administration of the individual prescribed doses.

Assessment of medication errors

Several methods exist for detecting medication errors in hospitals [31,32]. In order for comparison, results must be obtained by the same evaluation method, which limits the selected studies in the field of medication errors.

1. *Document comparison techniques:* The studies in question compare the different documents from patients’ medical records, in particular prescription sheets with medication administration records, and note down discrepancies, considered to be medication errors. First designed in Great Britain [33–37], comparison of medical orders with nursing administration cards has been adapted in France as an outcome indicator of the drug use process [38–42]. Among the comparative analyses of medical and nursing records, the most realistic studies relate their error rates to the number of doses having to be administered [38,39,43–48].

2. *Observation-based techniques:* Direct observation methods are grounded in the disguised-observation technique developed by Barker and MacConnell at the beginning of the 1960s [31,32,49]. An observer accompanies the person giving medications and witnesses the administration of each dose. The observer writes down exactly what the subject does when administering drugs and notes the consumption of the medication by the patient. The notes are then compared with the original physician order to determine whether there was compliance with the order. A medication error is counted when the subject does not carry out the order accurately. The observation is “disguised” in that the subject is unaware of the goal of the study. The observation is openly conducted, but for another reason than the acknowledged study on medication errors. Some recent studies describe the development of this method in Europe [3,5,50,51]. The medication error rates reported by disguised observation techniques are expressed as a percentage of the total opportunities for error, which means the sum of all the doses ordered plus all the unordered doses given. Two groups of results must be distinguished: those which include or which exclude wrong-time administration errors, depending on calculation of medication error rates [3,5,16,32,36,49–74].

Evaluation of adverse drug events

The contribution of drugs to nosocomial pathology is documented by numerous retrospective or prospective studies published in the international literature. In this field also, several methods are in use, but their different sensitivities must be taken into account when comparing their results according to their calculation modes:

- iatrogenic cases observed in hospitals,
- drug-related nosocomial iatrogenesis,
- adverse drug events,
- drug-related nosocomial iatrogenesis occurring during hospitalization,
- preventable adverse drug events or due to errors or negligence.

Unlike studies of medication error, no comparisons of nosocomial adverse drug events have been

undertaken according to the organization of the hospital drug use process. This criterion, ignored by most authors, constitutes one element of the context in which studies take place rather than one of the scheduled study plans. However, to us it seemed possible to deduce the organization of the drug use process from the conditions under which these prospective or retrospective clinical studies were carried out [75–92].

Estimation of medication errors' clinical gravity

Several studies, conducted in unit-dose drug distribution systems, estimate the capacity for interception of adverse drug events resulting from prescription errors by pharmaceutical interventions [79,88–90]. Other studies used pharmaceutical analysis of prescribing orders to evaluate adverse drug events caused by prescription errors, especially their clinical gravity according to similar classifications [93–99].

It is possible to analyse the connections between the drug use process organization and its effectiveness from the reported literature data. According to Donabedian's model, we successively reviewed medication errors and nosocomial drug-related illness, the first as a process indicator of drug distribution systems, the second as their outcome indicator [100].

RESULTS

Medication errors as process indicators of drug distribution systems

Taking care to compare only results arising from the same methodology, it appears that medication error rates vary significantly according to the drug use process organization.

Results from document comparison techniques: the document comparison method shows discrepancy rates between 20% and 62% of the patients' records, depending upon the authors [40–43,101,102]. Considering error rates related to the number of doses known to be administered, medication errors and prescription error rates vary from 1% to 10% in traditional systems, as detected by this method (Figure 1) [38,39,43–47].

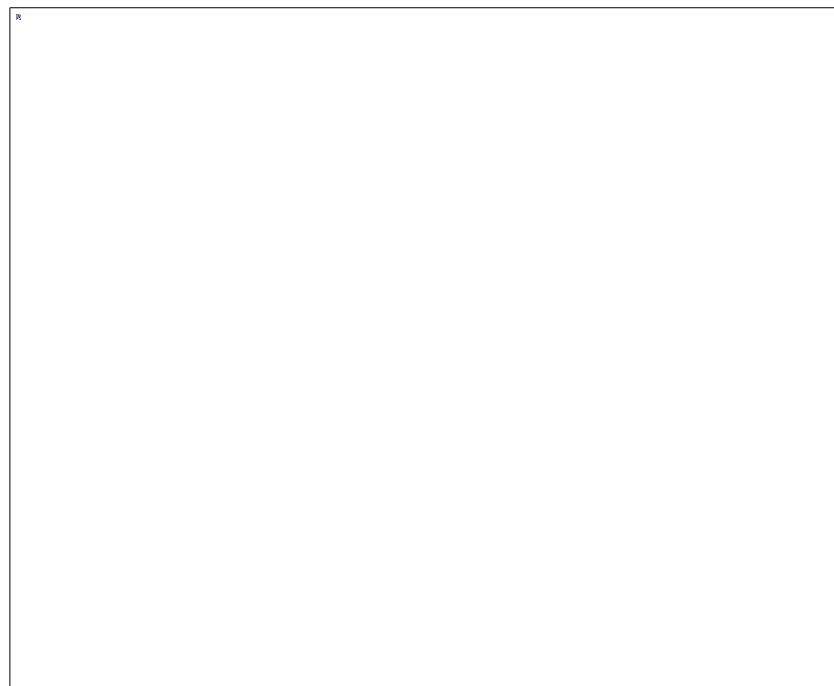


Figure 1. Medication errors rates reported by document analysis, according to some organizational modes of the drug use process (error rates related to the number of doses having to be administered).

Patient prescription drug distribution systems reduce medication error rates much more effectively than the combination of the ward stock and individual patient prescription systems. In comparison with traditional floor stock systems, medication error rates are respectively brought down to 71% and 11%. The mixed ward stock and individual patient prescription system has no effect on prescribing errors and even worsens distribution errors. The 18% increase of distribution errors seems to be due to the fact that, putting numerous medication doses at nurses' disposal, the mixed ward stock and individual patient prescription drug distribution system increases, by this proportion, the total number of opportunities of error [44]. The comparison of documents also showed that individual patient prescription only for dispensing particular drugs does not improve the safety of the distribution in comparison with the traditional floor stock system [103].

In traditional floor stock systems, transcription errors concern 2% to 7% of the number of doses being administered [46]. In the United Kingdom, the daily updating of the medication administration card was discontinued when it was demonstrated that this action alone lowered transcription error rates by 47% and overall medication error rates by 59% to 76% [36]. In this country, drugs are administered in response to medical drug orders but the ward stock distribution system still remains [5,104–109]. As assessed by document comparison techniques, computerizing drug orders gives additional safety to the drug use process. In fact, the reduction in transcription error rates following computerization (from -63% to -65%) is greater than that following the suppression of the nursing medication administration card [39,44,110,111]. However, the correction of prescription errors is only possible if the typing of medication orders is under pharmaceutical supervision: nurses' typing of drug orders modifies very slightly the medication error rate.

Results from observation-based techniques: The medication error studies using observation-based techniques provide a solid basis for comparison between the different organizations of the hospital drug use process. We present the graphical expression of medication errors, excluding wrong-time errors, according to drug distribution systems in Figure 2 [3,5,16,32,36,49–74]. Most of the comparative studies between traditional floor stock systems and unit-dose drug distribution systems reveal a decrease in medication error rates, symbolized by negative-sloping sections in Figure 2. When results include wrong-time errors, the individualization of the drug use process decreases medication error rates by 40% to 60% in comparison with floor stock systems and by 50% in comparison with the mixed ward stock and individual patient prescription drug distribution system [3,5,16,32,36,49–52,54,55,58,59,62–66,69,70,74].



- ^b Improved prescription and administration documents in a ward stock system.
- ^c Ward stock + individual patient prescription system (computerized or not).
- ^d Individual patient prescription system (IPPS) or patient prescription distribution system (PPDS).
- ^e Manual unit-dose drug distribution systems.
- ^f Automated unit-dose drug distribution systems.
- ^g Unit-dose drug distribution system with administration technicians

Figure 2. Medication error rates excluding wrong-time errors assessed by observation-based studies.

The improvement of the drug use process reduces medication error rates, excluding wrong-time errors, by between 50% and 80% in comparison with ward stock systems and mixed drug distribution systems, that is to say a reduction of the drug-related risk of more than two-thirds (Figure 2). These studies allow one to conclude that the computerized unit-dose drug distribution system is the safest hospital drug distribution system, avoiding most of the medication errors arising from an insufficient organization of the drug use process. The comparisons between drug distribution systems are particularly accurate when the studies are conducted by the same research team, using the same methodology. Despite a bias due to lack of observation, Hynniman's multicentric study allowed the comparison of different traditional drug distribution systems. As a result, the mixed ward stock and individual patient prescription drug distribution system was shown to provoke many more medication errors than the traditional ward stock system (+80%), providing confirmation of the results obtained 3 years earlier in the United Kingdom by Hill & Wigmore (+19.6%) [36,56]. Designed and tested by Latiolais, a total control of the drug use process, including the administration of drugs, is the most effective with the lowest medication error rates, but this system is unusual in the USA and inconceivable in Europe [57,66].

Some studies report medication error rates lower than 4% or 5% in ward stock systems, results appearing very far from the values usually reported by other studies of traditional systems. The British method of removing re-transcriptions from the ward stock system seems to improve the quality of drug distribution from 50% to 70% in comparison with the traditional ward stock drug distribution system [5,63,71–73]. With performances similar to the computerized unit-dose drug distribution system, the only improvement of prescription and administration documents seems to be that it is more effective than the individual delivery of drugs or manual unit-dose drug distribution system...

In fact, the quality of observation-based studies depends upon their design and how they are explained to the subjects. A study conducted in Great Britain shows how the direct observation technique can be rendered invalid by observers' interventions to prevent medication errors during observation [5]. In that case, the results could not be accepted because the observers induced an important bias by modifying nurse's behaviour during the administration of doses. With 27 interventions among 84 errors, 32% of the errors were avoided in this way. Therefore, the comparison in disfavour of a computerized unit dose distribution system with daily drug cart exchanges (half-hourly deliveries of newly ordered medication and automated ward dispensing devices such as Medstation[®] from Pyxis) cannot be admitted. The conclusions of this study remain to be confirmed by other researchers but they have so disturbed European hospital pharmacists that some of them already question the efficiency of unit dose drug distribution systems [1,6].

Prevention of prescription errors by pharmaceutical analysis of medication orders

As demonstrated by numerous articles, the existence of medication errors has been put forward as justification for pharmaceutical interventions into the drug use process [93,94,98,99,112–120]. The pharmaceutical analysis of medication orders is used in evaluating the type and the clinical gravity of adverse drug events arising from prescribing errors. The biases of this detection method do not permit the use of incident report techniques: for the most part, only errors not resulting in patient harm have been reported in this way [121–123]. Clinical severity estimations of prescribing errors in studies of potential adverse drug events report the reality only partially [93–96,98,99,116,118,124,125]. In fact, they only concern errors intercepted during the pharmaceutical control of medication orders within a unit-dose drug distribution system or errors detected by document comparison techniques.

In traditional systems, prescription error rates detected by such methods are high, as revealed by a recent study conducted in a French university hospital [98]. It has been shown that the computerized mixed system combining ward stock and individual patient prescriptions significantly reduces the prescription error rates by almost one-third in comparison with the floor stock system: from 22.8% to 15.5%, which represents a decrease of 32% ($p < 0.05$). According to this study, however, prescription error rates are not modified by the intensity of the pharmaceutical presence on the hospital wards. In the floor stock drug distribution system, the only certainty is that prescription errors cannot be corrected by the pharmaceutical control of medication orders: in this case, the risk of adverse drug events arising from prescription errors is increased by the prescription errors the pharmacists do not intercept.

In unit-dose drug distribution systems, and according to Bates's studies, the interception rates of preventable adverse drug events by pharmaceutical control of medication orders varies from 31% to 77% [79,88–90]. During this process, pharmacists can suggest improvements to the drug therapy. The quality in transmitting therapeutic information is also improved: Comer observes that, if 38% of the clinical pharmacy activity are devoted to prevent transcription errors, only 3.4% of the pharmaceutical interventions concern prescription errors [114].

Nosocomial adverse drug events as outcome indicators of the drug use process

The relationship between the hospital drug use process and adverse drug reactions is seldom established. When considering drug therapy, adverse drug reactions, events or misadventures can happen solely because of the patient's response to the medication, as well as because of the circumstances of their use [126,127]. The former is rather the concern of pharmacology while the latter

calls into question organization and quality of the drug use process. Depending on ones point of view, drug-related hazards and risks are subject to various definitions. Vague distinctions between numerous terms are a source of confusion in describing nosocomial adverse drug events [128,129]. Therefore, the results of such varied appraisals cannot be compared without carefully verifying the kind of events studied.

Relying on these different ways of expressing adverse drug events, it can be considered that drugs are involved in more than half of iatrogenic disease cases and in about half of adverse events in multidose drug distribution systems [75,83,130,131]. In traditional systems, many more patients are affected by adverse drug events than when they are treated in a unit-dose drug distribution system [75–92]. However, the data in question are aggregate data, including overall causes of adverse drug events, even when they did not occur in hospitals. The corresponding graph, presented in Figure 3, seriously suggests that unit-dose drug distribution systems decrease the rates of adverse drug events and their part in nosocomial iatrogenic disease, notably by reducing errors and negligence [86,130]. However, there is not sufficient information available to determine with certainty the safety levels of the different organization methods of the hospital drug use process. So the research needed, as expressed in the introduction, retains its urgency in the matter of prevalence of adverse drug events and of its correlation with the drug use process.

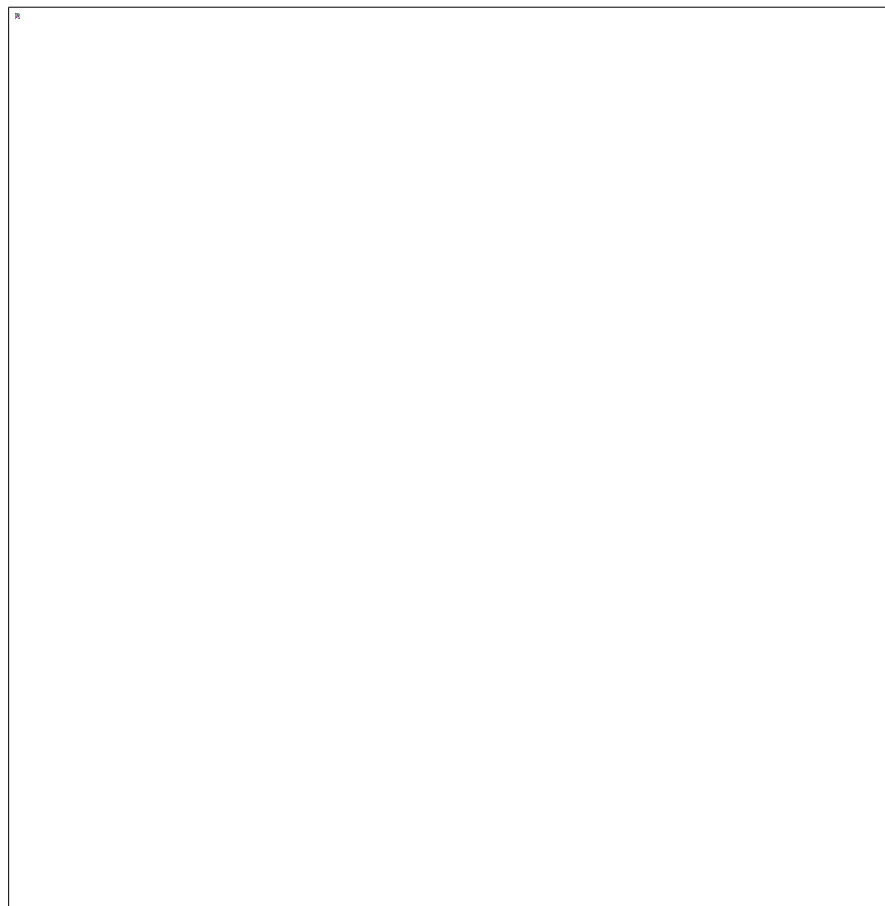


Figure 3. Effects of the hospital drug use process on the incidence of adverse drug events.

Some studies have assessed the consequences of clinical pharmacy interventions in terms of preventing the clinical risks or adverse drug events and they confirm the effective improvement of the patient's therapeutic safety [79,117,132–135]. The pharmaceutical interventions are even more efficient since they are integrated into a unit-dose drug distribution system. The effectiveness in preventing prescription or transcription errors is due to the fact that pharmaceutical interventions occur before any administration of drugs. This evidence is strengthened by a study about delays and opportunities for pharmacists' interventions. In a computerized unit-dose drug distribution system, almost two-thirds of the problems are settled before any medication administration [135]. This notion responds in part to the

concept of DISCON, that is to say “drug DIStribution CONTrOl information”, as advocated by Brodie and Barker. The basic principle of the unit-dose drug distribution system is precisely grounded in permanent pharmaceutical control at each stage of the drug use process [136].

For a long time, the effects of medication errors on nosocomial pathology were considered to be minor because it is very difficult to reveal a correlation between medication errors and adverse drug events, as their clinical consequence. Recent approaches to iatrogenesis risk factors in hospital, in particular nosocomial adverse drug events, have provided new perspectives on this question [88–90,137]. Medication errors leading to potential adverse drug events have the capacity to cause injury, but sometimes fail to do so, either by chance or because they are intercepted [137]. Bates succeeded in establishing a correlation between medication errors and adverse drug events, but only in a computerized unit-dose drug distribution system, proving that there occurs, on average, one nosocomial adverse drug event for every 100 medication errors [90].

When they are preventable, adverse drug events have to be considered as the product of hospital activity and, more precisely, as the clinical consequences of errors and negligence. They can, therefore, be classified as nosocomial because they arise from medication errors made by the health professionals working in the drug use process. Quite obviously, and no matter what the studied criterion might be, unit-dose drug distribution systems constantly reduce the incidence of adverse drug events, as strengthened by the diagram presented in Figure 3. We really owe the decrease in medication errors to individualization of the drug use process. From this point of view, medication errors are the most sensitive quality indicator of the hospital drug use process [8,32,42,137–143]. The knowledge of this risk is one of the main justifications for improving organization of the drug use process.

CONCLUSION

In comparison with traditional drug distribution systems, unit-dose drug distribution systems really improve the quality of care. Whatever the assessment method used, unit-dose dispensing significantly reduces medication errors. The relationship between medication errors and nosocomial adverse drug events is only proved in unit-dose drug distribution systems because it is perhaps easier to reveal it in this context. Strong assumptions exist that the implementation of a unit-dose drug distribution system results in decreasing the prevalence of nosocomial adverse drug events, as attested by the reductions in adverse drug reaction rates [79,144,145], length of patient stay [145–149] or mortality [150-151]. However, the appropriate comparative studies still remain to be undertaken that are necessary to clarify the impact of such an organizational change of the drug use process on the current prevalence of nosocomial drug related disease.

We reviewed the criteria, confirming that unit-dose drug distribution systems bring a real and appreciable safety to hospitalized patients. In this manner, we hope to meet Delaney’s demand. For those who, like him, are afraid of the necessary investment, it still remains necessary to correlate these indicators of quality and efficiency with the economic analysis of the costs associated with the drug use process, in particular by updating the results obtained by Hynniman and Schnell in the 1970s [59,152].

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