

Quantification and Classification of Errors Associated with Hand-Repackaging of Medications in Long-Term Care Facilities in Germany

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ABSTRACT

Objective: The aim of this study was to quantify and classify errors associated with the repackaging of residents' medications in long-term care facilities in Germany.

Methods: This was a prospective 8-week study conducted in 3 long-term care facilities. Pill organizers, each of which contained all repackaged solid oral dosage forms of long-term medications for a particular resident for an entire day, were inspected and checked against residents' medication sheets by the investigator-pharmacist. On agreement between the pharmacist and the registered nurse responsible for residents' medications, all errors were rectified before medications were administered. The primary study measure was the overall rate of incorrectly repackaged medications relative to all repackaged medications. Secondary measures were the proportion of all pill organizers with medication errors and the proportion of residents who would have been affected by these errors. Errors were categorized by type as follows: wrong time of administration, wrong dose, wrong medication, omission of a medication, extra dose, incorrect halving of tablets, and damaged medication.

Results: One hundred ninety-six residents were included in the study, representing 8798 daily pill organizers and 48,512 inspected medications. Residents received a mean of 5.4 solid oral dosage forms of long-term medications per day. Six hundred forty-five errors were detected, for an error rate of 1.3%; the errors involved 7.3% of daily pill organizers and 53.0% of residents. The largest proportion of errors involved incorrect halving of tablets (49.1%), followed by omission of a medication (22.0%), extra dose (9.8%), wrong time of administration (8.4%), damaged medication (6.4%), wrong dose (4.2%), and wrong medication (0.2%). These results may underestimate true rates of repackaging errors across long-term care facilities in Germany, as the conditions in the 3 facilities in this study were near-optimal in terms of the environment, process, and quality of repackaging.

Conclusions: Among 48,512 medications inspected over 8 weeks in 3 German long-term care facilities, the rate of repackaging errors was 1.3%, involving 7.3% of daily pill organizers and the medications of 53.0% of residents. The largest proportion of errors involved incorrect halving of tablets. (*Am J Geriatr Pharmacother.* 2008;6:212–219)
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Key words: multidose repackaging, long-term care, medication errors, administration of drugs, quality of care.

INTRODUCTION

The repackaging of medications, which involves transfer of a previously dispensed medication to another container, is an important aspect of quality of care. Repackaging is often used to apportion individual patients' medications from standard packs into pill organizers containing a daily or weekly supply. Because repackaging occurs between the pharmacist's dispensing of a medication and the patient's taking it, correct repackaging is a prerequisite for patient adherence to medications.

Repackaging is common in environments in which patients are unable to manage their own medications, such as hospitals, long-term care facilities, and outpatient nursing care settings. The individuals responsible for repackaging medications are designated by national and institutional regulations; in most cases, the responsibility falls to nursing staff or pharmacists/pharmacy staff. In German long-term care facilities, nursing staff generally prepare the daily pill organizers using residents' medication supplies, almost all of which are provided in blister packs that require removal of individual tablets or pills.

Studies of the quality of drug repackaging have been conducted primarily in the hospital setting. For example, Fontan et al¹ compared a computerized unit-dose drug repackaging system with a ward stock-distribution system on a French pediatric hospital ward. Use of the computerized repackaging system was associated with fewer prescription and administration errors compared with use of the ward stock-distribution system (22.5% vs 29.3%, respectively; $P < 0.001$). In a comparison of a ward stock system in a UK hospital, the traditional system in a German hospital, and a unit-dose system in another German hospital, Taxis et al² found that the unit-dose system was associated with numerically lower error rates (8.0%, 5.1%, and 2.4%, respectively). Although these hospital-based studies revealed deficiencies in the administration of medications, their results cannot be extrapolated directly to long-term care facilities. In addition to differences in the age structure of hospitals and long-term care facilities, there are differences in length of stay and patient morbidity. These differences, in turn, affect the care process, the frequency with which medications are taken, numbers of prescriptions, and the potential for drug interactions.

To date, few studies have been conducted in the long-term care facility environment, and a search of the literature identified only 1 study that explicitly addressed the repackaging of medications and the associ-

ated problems and remedies. In the study by Bader et al,³ a group of government pharmacy inspectors randomly investigated the repackaging of medications in 127 long-term care facilities in Germany in the course of conducting their other duties. The investigation was not, however, designed as a representative study. Analysis of 381 data sets revealed deficiencies in the repackaging of medications, with 120 errors involving the medications of 84 residents. Missing drugs accounted for 41% of the errors, wrong drugs for 29%, wrong dose for 15%, wrong time for 11%, and other errors for 4%. Two thirds of all errors occurred in 20% of the facilities under investigation.

The aim of the present study was to investigate the quality of hand-repackaging of solid oral dosage forms of residents' medications in long-term care facilities in Germany. Repackaging errors were both quantified and classified, with the hope of supporting assessments of the scale of the problem and the development of remedial strategies.

METHODS

Study Design

This was an 8-week prospective study conducted in 3 long-term care facilities in Germany. It was designed to be equivalent to an internal quality audit. Because the study constituted a quality assurance measure under the German Social Security Code, written consent of the residents was not required. Analyses were conducted in a completely anonymous manner and solely for the purposes of the study. In addition to data on residents' medications, all adjustments to prescribed drugs (change in dose, discontinuation, new prescription) were recorded. The admission and departure of residents was recorded, as were temporary hospital stays and deaths.

The study was approved by the University of Cologne Ethics Committee, which stipulated that any detected or suspected errors were to be reported to, checked, and corrected as necessary by the staff on duty to avoid knowingly administering incorrect medications to residents.

The Distribution, Repackaging, and Administration Process

After a medication is prescribed by a physician, the prescription is documented by hand on the resident's medication sheet. Medications are dispensed and delivered by a contract pharmacy, and pharmacy staff at each facility repackaged the medications into daily pill organizers based on residents' medication sheets. At 2 of

the facilities, residents' weekly medication supply is repackaged into 7 daily pill organizers once a week; in the other facility, weekly medication supplies are repackaged into 2 or 3 daily pill organizers 3 times a week. Each pill organizer contains 4 compartments for medication doses taken in the morning, at noon, in the evening, and at night. Repackaging is conducted in the morning (in a separate room in 2 of the facilities). When halving of tablets is necessary, a common manual tablet splitter is used.

The packed pill organizers are kept in a room to which only the registered nurses have access. The nurses are responsible for residents' medications, carrying them to residents in the organizers, giving residents the appropriate medication for each time of day, and making sure the medication is taken. If a prescription is changed after a resident's pill organizers have been packed, the nurse checks remaining pill organizers for that resident and removes the discontinued medication and/or adds the new one.

Inspection of the Repackaged Medications

Only solid oral dosage forms of long-term medications were inspected during the 8-week study. Liquids, semisolids, and as-needed medications were excluded for reasons of stability, shelf life, and hygiene. In the afternoons of days on which medications had been repackaged, an investigator-pharmacist (I.K.) checked the accuracy of the prepacked solid oral dosage forms of residents' medications against the medication sheets. The inspection was performed with reference to the 2006 edition of the *Gelbe Liste IDENTA* (Yellow List),⁴ which contains the names and photographs of all drugs. When an error was detected, the investigator-pharmacist contacted the registered nurse, whose confirmation was required.

As an indirect test of intrarater and interrater reliability, the pharmacist spent 2 weeks before the study inspecting daily pill organizers at 2 of the long-term care facilities. Her error reporting was compared with that of the registered nurses legally responsible for checking all pill organizers. The overall error rate was 1.1% (61 errors among 5422 medications dispensed); no false negatives (errors noted by the investigator that were not errors) were detected. Error rates at the 2 facilities were 1.3% (30 errors among 2380 medications dispensed), which would have affected 32 residents receiving a mean of 5.3 solid oral medications each, and 1.0% (31 errors among 3042 medications dispensed), potentially affecting 38 residents receiving a mean of 5.7 solid oral medications each.

Error Classification and Analysis

This investigation involved only errors in repackaging; incorrect documentation of prescriptions in residents' files was excluded. The substitution of an equivalent generic for a brand-name medication was not considered an error. Each error in repackaging was documented by type and frequency. The types of error were classified as follows⁵⁻⁷: wrong time of administration (eg, medication was taken in the morning instead of at night); wrong dosage (eg, a resident received 75 mg of an active ingredient instead of the prescribed 50 mg); wrong medication (the resident received a medication not listed on the medication sheet); omission of a medication (a medication that should have been administered according to the medication sheet was not included among the repackaged medications); extra dose (eg, the resident received a double dose of a medication that he or she should have received only once); incorrect halving of tablets (a tablet was inaccurately split 75:25 rather than in halves); and damaged medication (eg, part of a tablet was broken off). Each error was assigned to a single error category. All error types were equally weighted; for example, the omission of a medication was not rated as more serious than the incorrect halving of tablets.

An initial error could lead to subsequent errors if a weekly or half-weekly supply of medication was packed in daily pill organizers for several days at a time. For instance, if an antihypertensive drug to be taken in the morning was placed in the compartment for medications to be taken at noon in the pill organizers for Monday through Thursday, this would count as an initial error and 3 subsequent errors. Subsequent errors, hence, occurred only until the next repackaging of medication.

The primary study measure was the rate of incorrectly repackaged solid oral dosage forms relative to all repackaged solid oral dosage forms. Secondary measures included the proportion of pill organizers with errors and the proportion of residents who would have received the wrong medication. It was calculated using Pearson-Clopper values that inspection of at least 8000 daily pill organizers would be necessary to attain a 95% CI of <1% for the primary outcome measure.

RESULTS

Over the 8-week study, 8798 pill organizers were inspected for 196 residents of the 3 long-term care facilities. An additional 11 residents were not included, 10 who were responsible for their own medication and 1 who was receiving no solid oral dosage forms of long-

term medications. There were 16 admissions, 7 departures, and 27 hospital stays during the study period; 7 residents died. One hundred ninety medication adjustments occurred during the study, including 61 new prescriptions. The 8798 pill organizers inspected contained a total of 48,512 medications. Ninety-six residents received ≤ 5 long-term medications per day and 100 received >5 . Residents were administered a mean of 5.4 solid oral dosage forms of long-term medications per day: 39 (19.9%) received 1 to 3 such medications, 114 (58.2%) received 4 to 7, and 43 (21.9%) received between 8 and 12. **Table I** summarizes the baseline demographic and clinical characteristics of the 196 residents included in the study. **Table II** summarizes their medications and the times of administration of these medications.

Inspection of the 48,512 medications identified 645 errors, corresponding to an error rate of 1.3%; the rate of daily pill organizers with errors was 7.3%, potentially affecting 53.0% of residents. It was calculated that 48.2% of errors occurred in the first 4 weeks of the study and 51.8% in the second 4 weeks. Overall, 1 error occurred in every 13.6 pill organizers. **Figure 1** illustrates the distribution of errors by type. Incorrect halving of tablets was the most frequently occurring error type (49.1%), followed by omission of a medication (22.0%). Administration of the wrong medication was the least frequently occurring type of error (0.2%).

Halving of tablets was performed in the case of 13,399 (27.6%) of the 48,512 medications inspected; 2.4% of these tablets were split incorrectly. Among these 13,399 tablets, 588 (4.4% of all halved tablets) were split that should not have been split because of their galenic preparation (eg, a formulation that has been coated to provide controlled release or to be resistant to gastric acid); of these, 159 (27.0%) were split incorrectly.

Two hundred seventy-eight of all errors (43.1%) were errors that occurred subsequent to an initial error. The most frequently occurring subsequent error was incorrect halving of tablets (51.4%), followed by omission of a medication (23.4%) (**Figure 2**).

Across the 3 long-term care facilities, 1 to 3 errors occurred in the medications of 24.0% of residents, 4 to 6 errors in the medications of 13.0%, 7 to 9 errors in the medications of 6.0%, and >9 errors in the medications of 10.0%. No errors occurred in the medications of 47.0% of the residents (**Figure 3**).

Among residents receiving 1 to 3 medications daily, 41 of 3673 (1.1%) medications (2.4% of pill organizers) involved errors, for a mean of 1.1 errors per resident over the study period. In residents receiving 4 to 7 medi-

Table I. Baseline characteristics of long-term care facility residents (N = 196).

Characteristic	No. (%) of Residents
Sex	
Male	148 (75.5)
Female	48 (24.5)
Medical conditions	
Hypertension	100 (51.0)
Dementia	78 (39.8)
Heart failure	64 (32.7)
Diabetes mellitus	61 (31.1)
Coronary heart disease	41 (20.9)
Depression/neurosis	34 (17.3)
Osteoporosis	30 (15.3)
Hyperlipidemia	24 (12.2)
Parkinson's disease	22 (11.2)
Epilepsy	14 (7.1)

cations daily, 368 of 27,227 (1.4%) medications (7.3% of pill organizers) involved errors, for a mean of 3.2 errors per resident. In the group receiving 8 to 12 medications daily, 236 of 17,612 (1.3%) medications (11.8% of pill organizers) involved errors, for a mean of 5.5 errors per resident.

DISCUSSION

This study examined the quality of hand-repackaging of solid oral dosage forms of residents' medications in 3 long-term care facilities in Germany over 8 weeks. Altogether, the error rate among all medications inspected was 1.3%, involving 7.3% of daily pill organizers and 53.0% of residents. As noted earlier, all errors agreed upon by the investigator-pharmacist and supervising registered nurse were corrected before administration of medications, in compliance with ethical review board requirements.

Based on an examination of the distribution of error types, it is possible to reach preliminary conclusions about the causes of errors and suggest possible remedial measures. The most frequently occurring error type involved incorrect halving of tablets. Although only 2.4% of halved tablets were incorrectly split, the consequences can be significant. The large proportion of solid oral dosage forms that required halving (27.6%) in these 3 facilities can be explained by the strong eco-

Table II. Residents' medications and times of administration (N = 196).

Type of Medication	No. of Residents	Time of Administration, by No. of Residents			
		Morning	Noon	Evening	Night
Antidiabetic					
Biguanide	11	9	4	5	0
Glitinide	2	2	1	2	1
Insulin	31	NA	NA	NA	NA
Sulfonylurea	22	21	0	2	0
Cardiovascular					
Angiotensin-converting enzyme Inhibitor	80	75	4	20	0
Angiotensin-II receptor blocker	13	13	0	0	0
β -Blocker	67	67	2	31	0
Calcium channel blocker	27	27	5	14	0
Digitoxin	15	15	0	0	0
Digoxin	12	12	0	0	0
Diuretic	172	163	38	10	0
Psychotropic					
Benzodiazepine	15	10	7	9	6
Donepezil	7	3	3	1	0
Galantamine	2	1	1	0	0
Haloperidol	2	2	0	1	1
Melperon	16	3	5	7	7
Memantine	7	7	0	1	0
Piracetam	3	3	3	0	0
Risperidone	15	12	2	12	2
Trimipramine	2	2	0	2	0

NA = not applicable.

conomic incentives built into the German health care system. Individual physicians are assigned an annual budget for prescriptions based on their patients' morbidities and the average budget for comparable physicians; those who exceed their budget are held accountable for the surplus if they cannot show that their patients had greater morbidity than those of comparable physicians. Furthermore, double-strength tablets cost less than tablets of the same medication that are half the strength (eg, a standard pack of 25- μ g tablets of L-thyroxine cost €11.60 in Germany in 2006, whereas a package of the same number of 50- μ g tablets cost €12.77⁸). Because patients make copayments by the medication package, they would save ~50% on copayments by getting a package of double-strength tablets, which would last twice as long as a package of tablets that are half the strength.

A single error in halving will yield 2 errors, since one part of the broken tablet will be too large and the other too small. Moreover, attempts to halve nonscored tablets can result in dosing inaccuracies. Even if tablets are scored, it is easy to miss an instruction to halve them. It is likely that rates of incorrect halving in this study were lower than might be expected, given that the procedure was performed by pharmacy staff under well-controlled conditions. Also, the visual determination of incorrect halving was fairly conservative, as only tablets that were split 75:25 were considered incorrectly halved.

One solution to the problems associated with incorrect halving of medications during repackaging would be for physicians to prescribe lower-dose tablets, although this would have to be remedied at the level of national health policy. At the level of the individual institution, if halving is to be continued, staff should be instructed that

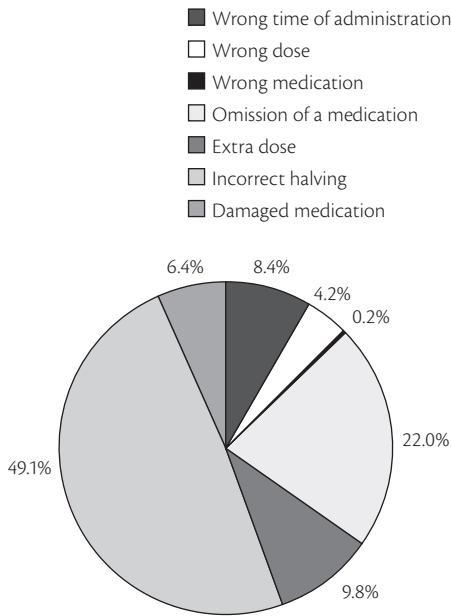


Figure 1. Distribution of errors by type. (Percentages may not total 100 due to rounding.)

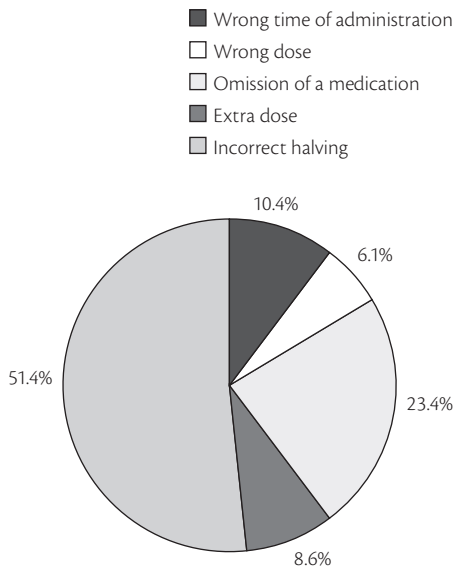


Figure 2. Distribution of subsequent errors by type. (Percentages may not total 100 due to rounding.)

certain medications are not to be halved. Moreover, staff should be alerted to the potential for adverse effects associated with overdosage or underdosage resulting from incorrect halving. Physician education may be appropri-

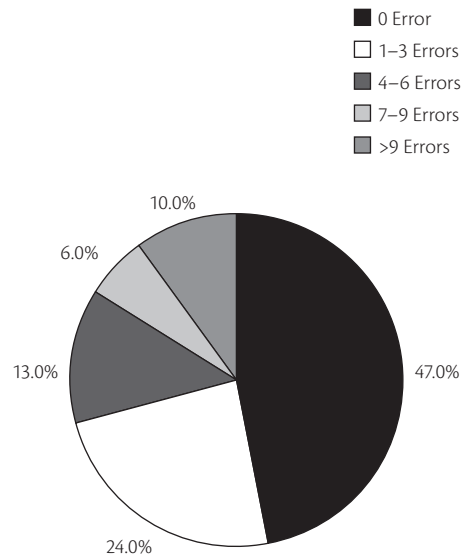


Figure 3. Number of errors per resident.

ate, as physicians may not be aware of the error potential in their prescribing behavior. Finally, German state sickness funds might be allowed to negotiate rebates with pharmaceutical companies for often-prescribed drugs that need to be halved, giving physicians an incentive to prescribe the correct strength.

At 22.0%, the omission of a medication was the second most frequently occurring repackaging error. Lapses in concentration while working can easily lead to overlooking a medication. Measures could be implemented to keep track of medications already repackaged (eg, by staff ticking off each medication on a form after repackaging), although this might increase the amount of time spent on repackaging. Wrong time of administration constituted 8.4% of all errors. This type of error is easily made when a drug removed from a blister pack by hand falls into the wrong compartment of the pill organizer. Removal from blister packs can also cause tablets to break apart, resulting in damaged medication, which was the cause of 6.4% of all errors.

Because orodispersible tablets are formulated to dissolve in the mouth, exposure to even a small amount of humidity can affect their stability. If, in the course of repackaging, a week's supply of such tablets is removed from blister packs at one time, this might lead to increasing instability and ensuing loss of effectiveness of the medication.

As mentioned previously, almost all medications used in long-term care facilities in Germany must be re-

moved from the blister packs in which they are provided. Given the rigorous quality assurance requirements of the European Medicines Agency and the German Federal Drug Administration, damaged branded or generic medications cannot be shipped, and errors of this type clearly occur at the level of the individual institution. One remedy to this problem would be for manufacturers to provide medications in bulk packaging rather than blister packs. At the level of individual facilities, removal from blister packs could be performed at a table before transferring the tablets into residents' pill organizers.

Wrong doses were responsible for 4.2% of repackaging errors. This type of error can be caused by difficulty deciphering the handwriting in residents' files. However, only 1 error (0.2%) involving the wrong medication was detected in the course of the study. This finding may be explained by the fact that the 3 long-term care facilities store each resident's long-term medications in separate containers in the medication room. In addition, the contract pharmacies label each medication package with the resident's name, date of birth, and living quarters (specific facility and floor, ward, or apartment, as applicable).

In this study, more than half of errors involving the wrong time of administration and the wrong dose were subsequent errors. Fewer than half of errors involving omission of a medication, an extra dose, and incorrect halving of tablets were subsequent errors.

Rates of repackaging errors in this study may represent an underestimate of errors occurring in long-term care facilities in Germany, as medications were repackaged under near-optimal conditions. Medications were repackaged exclusively by pharmacy staff. Repackaging was always conducted in the morning and, in 2 of the 3 facilities, in a separate medication room. Working conditions were optimal in terms of lighting, freedom from disturbance, and lack of time pressure. The 3 long-term care facilities had been certified under a quality management system that integrates goals, strategies for goal attainment, regular assessments, and appropriate strategy adjustments, which may have positively affected the quality of repackaging of medications.

It should be noted that this study was limited by a lack of dual control in error detection; although errors were remedied in consultation with nursing staff. It cannot be completely ruled out that the staff performing the repackaging were aware that pill organizers were being inspected within the context of a study and may have been particularly meticulous in carrying out their work. The study results may therefore represent a

conservative estimate of error rates. Another limitation is that the study did not examine the potential impact of repackaging errors at the individual level. A study is currently under way that is using the methods of Taxis et al² to evaluate the severity of potential adverse effects.

There is a clear need for improvement in the repackaging of medications in terms of all error types investigated. One possible approach would be to increase internal control of repackaging within the framework of a quality management program. Automated packaging of weekly blister packs for individual residents might allow better use of registered nurses' and pharmacy staff's time.

CONCLUSIONS

The results of this 8-week study conducted in 3 German long-term care facilities point to a need for improvement in the repackaging of residents' long-term medications. Among 48,512 medications inspected, the rate of repackaging errors was 1.3%, involving 7.3% of daily pill organizers and potentially affecting 53.0% of residents. The largest proportion of errors involved incorrect halving of tablets.

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