



An Overview of Pharmaceutical Noncompliance: Scope and Impact in the U.S. and the World

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HCPC Background

- Not-for-profit trade association
- Established in 1990
- Members include manufacturers of pharmaceutical films, foils, paperboard, and blister packaging machinery
- Members also include contract packaging firms, repackaging firms, and consultants
- Individual HCPC members are primarily packaging engineers and designers
- www.unitdose.org



HCPC Background

- The HCPC mission:
 - Promote the many benefits of unit dose blister and strip packaging
 - Compliance-prompting designs are a primary benefit of unit dose formats
 - Other benefits – e.g., anti-counterfeiting, barcodes, non-reclosability – to be detailed throughout this Symposium
 - What is unit dose packaging?
 - Each dose unit is housed in a separate cavity
 - Each dosage unit is protected from the time the drug is manufactured until the time it is ingested

HCPC 2003 Compliance Pkg/Year



HCPC 2003 Compliance Pkg/Year – First Runner Up



HCPC 2003 Compliance Pkg/Year – Second Runner Up



Generics Too!





Note

- None of the data cited in this report were influenced in any way by the HCPC.
 - The HCPC did not fund, suggest, participate in research or otherwise contribute to the any of the quoted material in this presentation.
 - Virtually all materials cited in this presentation are readily available.



Pharmaceutical Noncompliance

- Forms of noncompliance:
 - Failing to fill a new Rx
 - Failing to refill an Rx as directed
 - Skipping a dose
 - Taking too much
 - Taking the wrong medication
 - Prematurely discontinuing medication
 - Taking dose at the wrong time
 - Taking a medication prescribed to someone else
 - Taking a dose with prohibited foods, etc.
 - Storing medications improperly
 - Improperly using medication administration devices (e.g., inhalers)



Pharmaceutical Noncompliance

- Factors that influence compliance*
 - **Length of time** – “patients required to take medications for longer periods of time were less compliant.”
 - Results in more days without taking any medication, more drug holidays, and more extra doses.

*“An Integrative Review of Patient Medication Compliance from 1990-1998,” Wood & Gray, *The Online Journal of Knowledge Synthesis for Nursing*, Vol. 7, Document Number 1, January 14, 2000



Pharmaceutical Noncompliance

- Factors that influence compliance

(Wood & Gray, continued)

- **Number of doses** – “Compliance decreased with the number of doses.”
- **Confidence in provider** – “Compliance rates were lowest when the physician displayed doubts about the treatment or a treatment was prescribed by a physician in training.”
- **Regimen complexity** – “With increased complexity compliance rates diminished.”



Pharmaceutical Noncompliance

- Factors that influence compliance (Wood & Gray, continued)
 - **Knowledge** – “Increased knowledge about medications was found to have both a positive effect and no effect on medication compliance.”
 - **Psychological factors** – “Belief in the efficacy of a medication and acceptance of one’s illness consistently had a positive effect on compliance.”



Pharmaceutical Noncompliance

- Who is most compliant/non-compliant?*
- “In conclusion, in our study [of 1,054 patients at nine different VA Medical Centers], older patients with more health problems appear to be more compliant with drug therapy than younger patients with fewer disorders.”
- “In addition, compliance was not associated with differences in total health care cost, quality of life measures, or risk of hospitalization.”

* “Relationship between Drug Therapy Noncompliance and Patient Characteristics, Health-Related Quality of Life, and Health Care Costs,” Billups, et. al., *Pharmacotherapy*, 20(8): 941-949, 2000



Pharmaceutical Noncompliance

- Physician, pharmacist and patient attitudes

2002 Survey of 1,043 physicians, pharmacists, and patients*		
	Drs. & Pharmacists	Patients
Who is responsible for Rx being taken correctly?	90% say patient has "little role" in taking Rx as directed	81.3% say they have responsibility for taking Rx as directed
Is there a problem with taking Rx correctly?	50+% say there is a problem	87% say there is no problem
•174 physicians, 287 pharmacists, 577 patients * <i>Journal of the American Pharmaceutical Assoc.</i> , 43(3) 394-402, 2003		



Pharmaceutical Noncompliance

- Scope of the problem/US

- Up to 28% of all emergency department visits were related to misuse of drugs
 - 70% of these were preventable
 - Up to 24% of these ER visits resulted in hospital admissions

* “Drug-Related Visits to the Emergency Department: How Big is the Problem?” Patel & Peter, *Pharmacotherapy* 22(7): 915-923, 2002



Pharmaceutical Noncompliance

- Patel & Peter (continued)
 - Drug classes often implicated in ER treatment:
 - Nonsteroidal anti-inflammatory drugs
 - Anti-convulsants
 - Anti-diabetic drugs
 - Antibiotics
 - Respiratory drugs
 - Hormones
 - Central nervous system drugs
 - Cardiovascular drugs



Pharmaceutical Noncompliance

- Patel & Peter (continued)
- Common drug-related problems resulting in ER visits were:
 - Adverse drug reactions
 - Inappropriate prescribing
 - Noncompliance
 - 28.3%



Pharmaceutical Noncompliance

- Scope of the problem/US*:
 - “medication nonadherence rates typically range from 30% to 60%.”
 - “one half of the patients for whom appropriate medication is prescribed fail to receive the full benefits because of inadequate adherence to treatment.”

* “Medication Nonadherence: Finding Solutions to a Costly Medical Problem,” Gottlieb, *Drug Benefit Trends* 12(6): 57-62, 2000



Pharmaceutical Noncompliance

- Scope of the problem/US

(Gottlieb, continued)

- “One study showed that 77% of patients demonstrated degrees of compliance with their medication regimen when the treatment was designed to cure a disease...
- And only 63% of patients complied when treatment was aimed at prevention.”



Pharmaceutical Noncompliance

- Scope of the problem/US

(Gottlieb, continued)

- “Studies show that 20% to 80% of patients make errors in taking medication and that 20% to 60% stop taking medications before being instructed to do so.”
- “The Minnesota Colon Cancer Control Study found...the best compliers were approximately 70 years old, the worst compliers were patients younger than 55 years and those older than 80 years.”



Pharmaceutical Noncompliance

- Scope of the problem/US
 - *Hospital Pharmacist Report*, September, 1999:
 - “[Surveyed pharmacists] said that during a typical week, on average, 9% of the Rxs they fill never get picked up by the patient.”



Pharmaceutical Noncompliance

- **Scope of the problem/US**

National Council on Patient Information and Education, August, 1995

Treatment	Compliance Rate
Penicillin prophylaxis for rheumatic fever	33
Anxiolytics in neurotics	54
Antipsychotics in schizophrenics	42
Tuberculosis medications	55
Various medications for diabetes or congestive heart failure	42
Various medications used in homes for the aged	69



Pharmaceutical Noncompliance

- NCPIE, 1995 (Continued)*

Treatment		Compliance Rate
Antihypertensives	One year	94
	Two years	65
	Three years	34

* "Prescription Medicine Compliance: A Review of the Baseline of Knowledge," NCPIE, 1995



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- **Scope of the problem/global:**
 - *Adherence to Long-Term Therapies: Evidence for Action, World Health Organization, 2003*
 - “Poor adherence to treatment of chronic disease is a worldwide problem of striking magnitude.”
 - “Adherence to long-term therapy for chronic illnesses in developed countries averages 50%. In developing countries, the rates are even lower. It is undeniable that many patients experience difficulty in following treatment recommendations.”



Pharmaceutical Noncompliance

- WHO findings (Continued):
 - “The consequences of poor adherence to long-term therapies are poor health outcomes and increased health care costs.”
 - “Poor adherence to long-term therapies severely compromises the effectiveness of treatment, making this a critical issue in population health from both the perspective of quality of life and of health economics.”



Pharmaceutical Noncompliance

- WHO Findings (continued):
 - “Interventions aimed at improving adherence would provide a significant positive return on investment through primary prevention (of risk factors) and secondary prevention of adverse health outcomes.”



Pharmaceutical Noncompliance

- **WHO Findings/Asthma:**

- “When patients were aware that they were being monitored [for proper use of inhaled corticosteroids], 60% of them were fully adherent, 20% were partially adherent (taking just 70% of the prescribed dose) and 20% were totally nonadherent.”
- “When patients were unaware of the monitoring, 6 out of 11 took between 30% and 51% of the prescribed doses.”



Pharmaceutical Noncompliance

- WHO Findings/Depression:
 - “In a study of patients with psychiatric disorders...43% of patients had discontinued their medications within 6 months.”
 - “A very large sample of HMO patients [revealed that] 6-8 weeks after starting treatment [for depression]...32-42% had not filled their prescriptions.”



Pharmaceutical Noncompliance

○ **WHO Findings/Hypertension:**

- “Despite the availability of effective treatment, over half the patients being treated for hypertension drop out of care entirely within a year of diagnosis, and of those who remain under medical supervision, only about 50% take at least 80% of their prescribed medications.”
- “Because of poor adherence to anti-hypertensive treatment, approximately 75% of patients with a diagnosis of hypertension do not achieve optimum blood-pressure control.”



Pharmaceutical Noncompliance

- Estimating the Costs of Noncompliance
 - How big is big?
 - How big is too big?
 - When is enough enough?



Pharmaceutical Noncompliance

- Direct costs of noncompliance
 - Excessive hospital expenditures
 - Excessive nursing home expenditures
 - Excessive treatment costs of ambulatory care
- Indirect costs of noncompliance
 - Reductions in worker productivity
 - More sick days, less efficient work
 - Premature death



Pharmaceutical Noncompliance

- “Noncompliance with Medications: An Economic Tragedy with Important Implications for Health Care Reforms,” Task Force for Compliance (November 1993, Revised 1994)
- The Task Force for Compliance was an ad hoc group of “20 major pharmaceutical companies whose mission is to assess, organize and disseminate information needed to improve patient adherence with prescribed treatment, having the overall objectives of improving patient health and reducing health care costs.”



Pharmaceutical Noncompliance

○ Task Force for Compliance:

- Economic impact on retail pharmacies and pharmaceutical manufacturers:

- If 20% of all written Rx's were never filled or refilled:

- "At a \$20 average prescription charge, the gross revenues lost to pharmacy would be \$8 billion."
- "Assuming \$4 dispensing fee, pharmacy loss equals \$1.6 billion (***with no associated costs of goods sold***)." (emphasis added)
- Shering Report (1990): "Annual shortfall at the pharmacy counter [is] about \$2.8 billion."
- "All of the [pharmacy] losses...are also felt by pharmaceutical companies."



Pharmaceutical Noncompliance

- **Task Force for Compliance:**

<i>Annual Costs of Noncompliance</i>	<i>\$ Billion</i>
Lost revenue unfilled Rxs (new & refill)	8
Unnecessary hospital admissions	25
Nursing home admissions	5
Lost productivity	50+
Premature death	?
Health costs in ambulatory patients	?
Total	\$100+



Pharmaceutical Noncompliance

- 1995, Canada: “A conservative estimate of the economic costs of noncompliance in Canada is at least \$7 to \$9 billion per year.” *

* *Review of the Scientific Literature of the Prevalence, Consequences, and Health Costs of Noncompliance & Inappropriate Use of Prescription Medication in Canada*, Robert B. Coombs, et. al., 1995



Pharmaceutical Noncompliance

- 1999, USA: “Two large landmark trials of the use of cholesterol-lowering drugs to prevent coronary heart disease included concerted and disciplined efforts to collect compliance data. These trials provide a useful framework to illustrate the pharmacoeconomic consequences of compliance rates.” *

* *Drug and Therapy Perspectives*, 14(10): 14-16, 1999

Pharmaceutical Noncompliance

Level of Compliance	Dose Taken	Drug Cost*	Total Cost of Care*
Cholestyramine			
Full	6 packets/day	\$180	\$180
Partial	2.7 packets/day	\$174	\$387
Poor	1.5 packets/day	\$162	\$651
Gemfibrozil			
Full	100% of prescribed	\$148	\$148
Partial	84% of prescribed	\$216	\$258
Poor	50% of prescribed	\$260	\$519
*Lowest end parameters of range			
<i>Drug & Therapy Perspectives 14(10) 14-16, 1999</i>			



Pharmaceutical Noncompliance

- Johnson & Bootman, 1995*
 - Cost of “ambulatory drug-related problems” equals \$76.6 billion/year
 - Untreated indication
 - Improper drug selection
 - Subtherapeutic dosage
 - Failure to receive drugs
 - Overdosage
 - Adverse drug reactions
 - Drug interactions
 - Drug use without indication

* *Archives of Internal Medicine*, Vol. 155: 1949-56, 1995



Pharmaceutical Noncompliance

- “In other papers and news reports, Johnson and Bootman estimated that 40% of the costs – and 120,000 deaths – were preventable through increased efforts of pharmacists to assure proper medication use.” *Pharmacy Today*, 7(3), 2001



Pharmaceutical Noncompliance

- Ernst & Grizzle, 2000 update of Johnson & Bootman*
 - Overall cost of drug-related morbidity and mortality exceeded **\$177.4 billion**
 - Using Johnson & Bootman model, hospital admissions equal nearly 70% of the total cost
 - **\$121.5 billion** of total costs in 2000
 - Long-term-care admissions account for 18%
 - **\$32.8 billion** of total costs in 2000

* *Journal of the American Pharmaceutical Association* 41(2): 192-199, 2001



Pharmaceutical Noncompliance

- Ernst & Grizzle (continued)

- Average cost of hospitalization due to drug-related problems in 2000:
 - \$12,646
- Average cost of long-term-care stay due to drug-related problems in 2000:
 - \$9,489 (three months at \$3,135/resident/month)
- Average cost for a physician visit caused by drug-related problems in 2000:
 - \$376



Pharmaceutical Noncompliance

- Ernst & Drizzle conclusion:
 - “Drug-related morbidity and mortality continue to pose a serious medical and economic problem for society. More attention should be directed toward developing solutions that reduce preventable morbidity, mortality, and the costs associated with [drug-related problems].”



Pharmaceutical Noncompliance

- Overall conclusion:
 - “Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the [world] population than any improvement in medical treatment.”
 - RB Haynes, as quoted in *Adherence to Long-Term Therapies: Evidence for Action*, World Health Organization, 2003



Packaging & Compliance

- U.S. Compliance with Oral Contraceptives (birth control pills)
 - 92 percent*
- U.S. Compliance with organ rejection drugs
 - 82 percent*

* NCPIE



Compliance & Packaging

- Modulus, Inc. Hormone Replacement Therapy*
 - Two groups of 50 women
 - Each given two prescriptions
 - Estrogen & Progesterone
 - Control group = amber vials, one for each Rx
 - Research group = compliance prompting blister card housing both medications
 - Results:
 - Control group compliance = 30%
 - Research group compliance = 82%

* MATURITAS, September 1984, the International Journal for the Study of the Climacteric



Compliance & Packaging

- Unit Dose Packaging and Elderly Patient Compliance*
 - 84 elderly patients
 - Research group = 45 using compliance-prompting blister packs
 - Control group = 39 using amber vials
 - Compliance rates at discharge
 - 86.7%/Research v. 66.7%/Control
 - Compliance rates at 10 days
 - 68.8%/Research v. 41.0%/Control
 - Compliance rates at one month
 - 64.4%/Research v. 38.5%/Control
 - Compliance rates at three months
 - 48.9%/Research v. 23.1%/Control

* Unit-of-Use – Contemporary Issues Open Conference, Baltimore, Maryland, December 13-15, 1992



Compliance & Packaging

- A Project to Increase Medication Compliance and Reduce Costs in Domiciliares*
 - Bulk medications put up in compliance-prompting formats for assisted living facilities in Alabama
 - Conclusions:
 - “Results indicated significant improvements in average compliance”
 - “Overall average compliance improved from 85 percent to 95 percent”

* U.S. Department of Health and Human Services Grant Award 90-AM-0433, Jefferson County Office of Senior Citizens Activities, Birmingham, Alabama, February, 1992



Compliance & Packaging

- “Effect of Value-Added Utilities in Promoting Prescription Refill Compliance Among Patients with Hypertension” *
 - 128 hypertensive patients monitored for one year
 - Interventions & compliance rates:
 - Control (no intervention) = 0.64
 - Reminder card = 0.71
 - Compliance-prompting package = 0.75
 - Packaging & reminder = 0.87

* Current Therapeutic Research, Vol. 53, No. 3, March, 1993



Compliance & Packaging

- “Use of Blister Packaging to Improve Patient Medication Compliance in the Treatment of Depression” *
 - 150 patients, 43 different sites throughout Canada, monitored for 12 weeks
 - Control group = amber vials
 - Research group = compliance-prompting blisters
 - Results:
 - Baseline Beck Depression Index (BID) = 27.5 for both groups
 - Mean BID for control group at 24 weeks = 13.1
 - Mean BID for research group at 24 weeks = 11.0
 - “Patients randomized to the blister pack arm preferred the blister packaging scheme over traditional bottle formats”

* SmithKline Beecham, Inc. Oakville, Ontario, 1996



Compliance & Packaging

- Hospital Pharmacist Report Survey*
 - “Does your pharmacy offer any of the following compliance aids to patients?”
 - Number 1 answer, 49%
 - “Containers with weekly/monthly drug compartments”

* Hospital Pharmacist Report, September, 1999



Compliance & Packaging

- “Medication Nonadherence: Finding Solutions to a Costly Medical Problem” *
 - Conclusion:
 - “Drug manufacturers...can offer products that have simpler regimens, rather than multiple dose regimens, and they can discourage awkward packaging of medications **by favoring single-unit packaging.**”

* Drug Benefit Trends, 12(6): 57-62, June, 2000 (emphasis added)

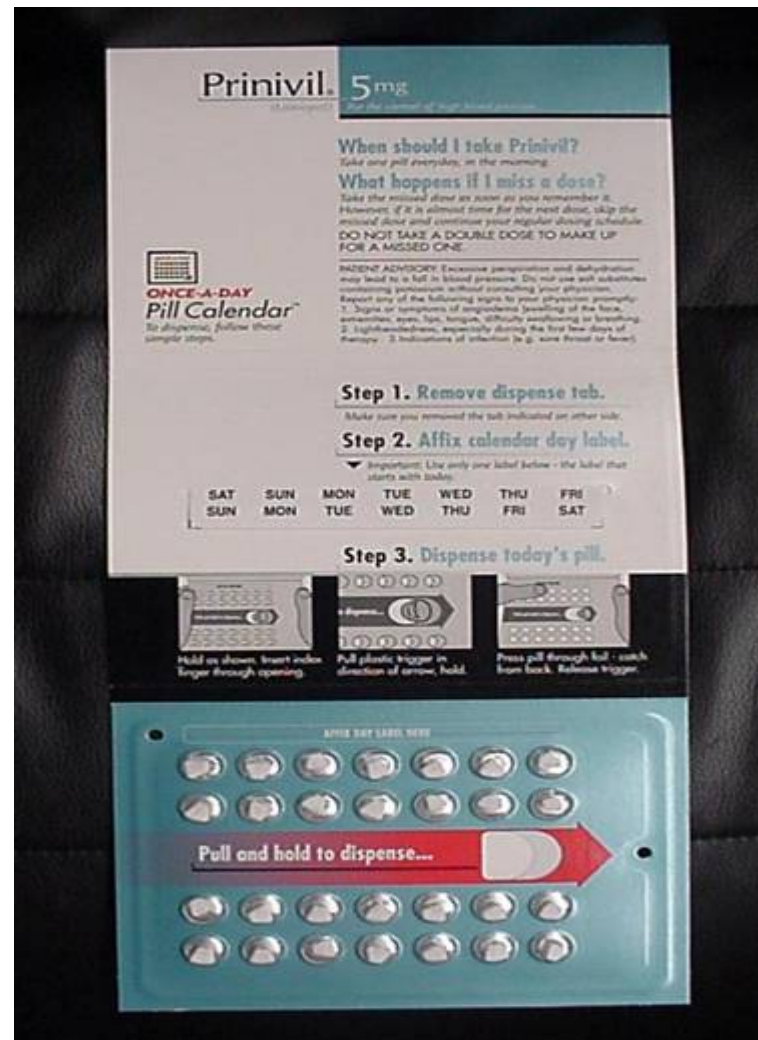


Packaging & Compliance

- “Impact of Innovative Packaging on Adherence and Treatment Outcome in Elderly Patients with Hypertension” *
 - On-going research, 99 patient enrolled (goal is 300)
 - Pharmacy data available for 88 patients
 - Control group (43 patients) = amber vials
 - Study group (45 patients) = compliance-prompting blister cards
 - Medical data available for 62 patients (1st/2nd/3rd visits)
 - Study group = 38/31/9
 - Control group = 28/23/9

* Ohio State University, Phil Schneider, Presented at HCPC 12th Annual National Symposium on Patient Compliance, May, 2004

Compliance & Packaging





Compliance & Packaging

- Ohio State University Study (Continued)
 - Preliminary results
 - Percent on-time refill
 - Control group = 37.3%
 - Study group = 55.2%
 - Change in blood pressure (1st-2nd visit)
 - DBP/Control = +0.9
 - DBP/Study = -5.7
 - SBP/Control = -0.2
 - SBP/Study = -5.3



Thank you

- Questions?