



# **Bibliography of Medication Compliance**

**all topics**

**publications sorted by therapeutic areas**

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## Peer-reviewed papers

### Musculoskeletal Diseases

[De Klerk E, Van Der Heijde D, Landewe R, Van Der Tempel H, Urquhart J, Van Der Linden S.](#)

Patient compliance in rheumatoid arthritis, polymyalgia rheumatica, and gout.

J Rheumatol. 2003 Jan;30(1):44-54.

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Does adherence make a difference? Results from a community-based aquatic exercise program.

Nurs Res. 2002 Sep-Oct;51(5):285-91.

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Motivation as a crucial predictor of good compliance in adolescents with rheumatoid arthritis.

Int J Nurs Pract. 2002 Dec;8(6):336-41.

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Prevention of nonadherence to nonsteroidal anti-inflammatory medications for newly diagnosed patients with juvenile rheumatoid arthritis.

Health Psychol. 2002 Nov;21(6):620-3.

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Assessing and enhancing adherence to medical regimens for juvenile rheumatoid arthritis.

Pediatr Ann. 2002 Jun;31(6):373-9. Review.

[Hill J, Bird H, Johnson S.](#)

Effect of patient education on adherence to drug treatment for rheumatoid arthritis: a randomised controlled trial.

Ann Rheum Dis. 2001 Sep;60(9):869-75.

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A randomised, single-blind, crossover comparison of the acceptability of the calcium and vitamin D3 supplements Calcichew D3 Forte and Ad Cal D3 in elderly patients.

Curr Med Res Opin. 2001;16(4):245-51.

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Use of an electronic monitoring aid to investigate the medication pattern of analgesics and non-steroidal anti-inflammatory drugs prescribed for osteoarthritis.

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Determinants of compliance with medication in patients with rheumatoid arthritis: the importance of self-efficacy expectations.

Patient Educ Couns. 1999 Jan;36(1):57-64.

[de Klerk E, van der Heijde D, van der Tempel H, van der Linden S.](#)

Development of a questionnaire to investigate patient compliance with antirheumatic drug therapy. J Rheumatol. 1999 Dec;26(12):2635-41.

[Edworthy SM, Devins GM.](#)

Improving medication adherence through patient education distinguishing between appropriate and inappropriate utilization. Patient Education Study Group.

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[Viller F, Guillemin F, Briancon S, Moum T, Suurmeijer T, van den Heuvel W.](#)

Compliance to drug treatment of patients with rheumatoid arthritis: a 3 year longitudinal study.

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Compliance in rheumatoid arthritis and the role of formal patient education.

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[Compliance to therapy in daily practice--rheumatologic diseases]

Schweiz Rundsch Med Prax. 1993 Nov 30;82(48):1381-3. French.

[Saudan Y, Moret H.](#)

[Rheumatoid arthritis: what do patients do with our prescriptions?]

Schweiz Rundsch Med Prax. 1991 Feb 5;80(6):112-3. French.

[Lorish CD, Richards B, Brown S Jr.](#)

Perspective of the patient with rheumatoid arthritis on issues related to missed medication.

Arthritis Care Res. 1990 Jun;3(2):78-84.

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Adherence with treatment regimens among adult rheumatoid arthritis patients: current status and future directions.

Arthritis Care Res. 1989 Sep;2(3):S33-9. Review.

[Lorish CD, Richards B, Brown S.](#)

Missed medication doses in rheumatic arthritis patients: intentional and unintentional reasons.

Arthritis Care Res. 1989 Mar;2(1):3-9.

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Educational and behavioral strategies for improving medication compliance in juvenile rheumatoid arthritis.

Arch Phys Med Rehabil. 1988 Jun;69(6):439-41.

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Determinants of compliance in rheumatoid arthritic patients assessed in their home environment.

Br J Rheumatol. 1985 Nov;24(4):313-20.

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Role of self-esteem and autonomy in determining medication compliance among adolescents with juvenile rheumatoid arthritis.

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Medication problems of rheumatic patients assessed by domiciliary visits by pharmacists.

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Leu S. and Eng K. “**Determination of unclaimed prescriptions at an outpatient department, Songklanagarind Hospital.**” *Journal of Pharmacy Practice* (1999) **12**(6): 433-440.

Unclaimed prescriptions are an initial indication of noncompliance. Although the patients receive the best treatment, they may fail to take their medicines. As a result, the illness may not be relieved and this can lead to hospitalization or use of emergency services. This study was conducted to determine the characteristics and reasons for unclaimed prescriptions in a 680-bed and tertiary care center from July to October 1997. Patients' data were collected from medical records and from questionnaires that asked for the reasons prescriptions were not claimed. During the four-month period, 695 unclaimed prescriptions were identified, accounting for approximately 0.67% of all prescriptions filled. Results showed that patients least likely to claim a prescription included women, those who visited the hospital during official hours, those who had chronic disease, and those who went to see internal medicine physicians. Three most common diseases were those involving respiratory system (8.6%), musculoskeletal system (6.3%), and genitourinary system (6.0%). More than half (56.5%) were treated with the essential drugs. Neuromuscular agent was the most frequent drug class of unclaimed prescriptions, followed by respiratory agent, dermatological agent, and vitamins and minerals. Of the 695 patients, 152 patients responded to the questionnaires. Sixty-one patients indicated that they had received their medications later on and, therefore, were excluded from the analysis. Thus, 61 questionnaires were analyzed. The most important reason patients did not claim their prescriptions was cost (22.0%). The next most frequently mentioned reasons were forgetfulness (12.1%), business (11.0%), and lack of communication (8.8%). These patients need to be counseled about the importance of taking their medicines. In addition, health care providers should develop strategies to improve patient compliance with their medications.

Whitney C. W. and Dworkin S. F. “**Practical implications of noncompliance in randomized clinical trials for temporomandibular disorders.**” *Journal of Orofacial Pain.* (1997) **11**(2): 130-8.

Randomized clinical trials are recognized as providing the most rigorous evidence of treatment efficacy. For temporomandibular disorders, randomized clinical trials have been used to evaluate the efficacy of low-cost occlusal appliances or the adjunct use of cognitive behavioral interventions. However, noncompliance with treatment regimens and losses to follow up are common randomized clinical trial protocol violations that compromise the desired rigor of the trial. At times it is not clear to the investigator how to deal with these issues during the trial and at the data analysis phase. Often treatment efficacy is based on the compliant subjects, subjects who may no longer represent randomized groups or yield the desired "fair" estimate of treatment efficacy. This study focuses on management of compliance issues, the description and collection of data needed to obtain a more accurate assessment of treatment efficacy, and results particularly relevant to actual clinical practice and patient care decisions. These are applied to a

randomized clinical trial evaluating the efficacy of a cognitive-behavioral intervention for temporomandibular disorders.

Wolfe F. **“The epidemiology of drug treatment failure in rheumatoid arthritis.”** *Bailliere's clinical rheumatology* (1995) 9(4): 619-32.

The length of time that patients remain on anti-rheumatic therapy is an important measure of the effectiveness of that therapy since length of time on therapy is a composite measure that accounts for sustained, positive therapeutic benefit as well as negative therapeutic benefit (e.g. adverse reactions, unacceptable \*costs\* and loss of efficacy), and accounts for noise (\*non\*- \*compliance\*, psychological factors, misunderstanding, etc.). Effectiveness is a measure of how well a drug does work, while efficacy, the measure used in randomized controlled trials, means that a drug can work; however, efficacy may or may not translate to usefulness in the clinic. To understand drug effectiveness we reviewed studies of 5809 patients receiving various SMARDs. The average median time on drug ranged from 1.10 to 2.27 years, excluding methotrexate, with shortest survival times falling to sulfasalazine (1.10) and auranofin (1.16), intermediate times to hydroxychloroquine (1.59), penicillamine (1.42), IM gold (1.40), and the longest time to azathioprine (2.27). Overall, excluding methotrexate, the average median survival time was 1.41 for 3998 patients. Median time on drug was 3.3 times greater for all other drugs combined, averaging 4.61 years. Expressed in terms of '5-year survival,' an average of 55.7% of patients remained on methotrexate 5 years after it was started. Better results noted here for methotrexate stand in contradistinction to short-term randomized controlled trials which find most SMARDs to be equal in efficacy. Other factors that may influence drug survival time include age, age, education level, psychological status, presence of fibromyalgia, rank order of SMARD administration, disease severity or corticosteroid administration. Studies can provide more information if they also measure clinical variables as well as time on drug, providing area-under-the-curve measurements.

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Boll Chim Farm. 2000 May-Jun;139(3):146-8.

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How do terminally ill patients at home take their medication?  
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Spec Care Dentist. 1995 Nov-Dec;15(6):218-22.

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Patient compliance with prolonged low-dose oral etoposide for small cell lung cancer.  
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The effect of compliance with treatment on survival among patients with hematologic malignancies.

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Jones W. L., Dayal H. H., Grover P. L., Crowley M. J., Creech R. H., Engstrom P. F., et al. “**Research in cancer patient education and compliance.**” *Progress in clinical and biological research* (1983) **120**: 467-81.

A study design has been presented which has the advantage of combining the research questions of education program evaluation and \*patient\* \*compliance\*. While it would be possible to evaluate education programs in other ways (e.g., using a sample of all program participants rather than a sample of all patients for whom a regimen was recommended), such an alternative design would not assess the potentially significant proportion of \*noncompliance\* which might occur when the regimen recommendation is made. It is the specification of inception cohorts as the study population that allows the accrual of more complete compliance data for the regimen as well as evaluation data for the education program. Given the recognized need for data on the compliance of cancer patients, the added \*cost\* of specifying inception cohorts for education program evaluations seems small. The proposed research design has the potential to contribute to cancer control programs: 1. a careful evaluation of new education programs for patients; 2. modifications of education programs based on feedback from professionals and patients during the initial implementation; 3. needed data on cancer \*patient\* \*compliance\* with extended detection and treatment regimens; and 4. increased understanding of the process of \*patient\* \*compliance\*, including identification of key variables in the health belief model which account for compliance among cancer patients.

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Clin Cardiol. 2001 Feb;24(2):114-8.

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Background: Our purpose was to establish, by means of a survival analysis, the duration of therapeutic compliance and the probability of abandonment or prescription drugs in cardiovascular patients, as well as the prognostic factors that determine it. Patients and Method: Longitudinal observational study (1996-1998). By means of a consecutive sampling, 493 patients who initiated a cardiovascular treatment were selected. Through interviews, we obtained information on cardiovascular problems and treatment, concomitant diseases, consumption of other drugs and social and demographic variables. The consumption of prescribed drugs was established across 6 periodic observations. Results: During the observational period, 39.4% of drugs prescribed by the general practitioner (GP) were abandoned, as compared to 22.4% of those prescribed by specialists ( $p < 0.05$ ). The degree of abandonment was significantly higher among consumers of vasodilators and [left pointing guillemet]vasoprotective[right pointing guillemet] agents. Cardiac glycosides and angiotensin converting enzyme inhibitors were among the therapeutic subgroups in which a longer survival time was observed (average: 19.8 and 16.5 months, respectively). By a Cox regression analysis, we noticed that the risk of abandonment was higher in patients who took two or more doses of the drug per day (OR = 2.8; 95% IC, 21-37), in consumers of medicines with a daily cost lower than ptas. 100 (OR = 1.4; 95% CI, 1.0-1.8) and in subjects younger than 65 years (OR = 1.3; 95% CI, 1.0-1.8). Conclusions: A higher degree of abandonment of cardiovascular medication occurs when it is administered in primary health-care (i.e., drugs prescribed by the GP), mainly in relation to a greater

prescription of agents with a low therapeutic effectiveness. Abandonment is influenced by patients' social and demographic factors and also by the specific characteristics of the treatment.

Hansson L. **“Why don't you do as I tell you?’ Compliance and antihypertensive regimens.[comment].”** *International Journal of Clinical Practice.* (2002) **56**(3): 191-6.

Although hypertension is recognised as one of the major health hazards in the developed world, compliance with antihypertensive regimens is still undesirably low. This brings important costs, both to patients in increased morbidity and mortality, and to society in hospitalisations and lost productivity. This review surveys possible reasons for non-compliance with treatments generally and antihypertensive medications specifically. It also looks at how insights into reasons for non-compliance can help us design more effective treatments, and discusses current and emerging medications in the context of compliance. As one of the reasons for low compliance is thought to be the impact of a drug on the patient's lifestyle, recently developed agents such as angiotensin II-receptor blockers may be expected to have less effect on patients' daily lives than earlier treatments, which brings hope for increased compliance with these regimens. [References: 80]

Hussey L. C., Hardin S. and Blanchette C. **“Outpatient costs of medications for patients with chronic heart failure.”** *American Journal of Critical Care.* (2002) **11**(5): 474-8.

**BACKGROUND:** The outpatient costs of medications prescribed for chronic heart failure are high and are often borne by individual patients. Lack of financial resources may force noncompliance with use of medications. **OBJECTIVE:** To compare the outpatient costs of medications for patients with different New York Heart Association classifications of chronic heart failure. **METHODS:** The charts of 138 patients with chronic heart failure were reviewed retrospectively. Outpatient costs of medications were obtained from the Web sites of commercial pharmacies. Medications were classified by type according to the system of the American Heart Association. A mean cost for each classification of medication was used for analysis. **RESULTS:** The overall mean monthly cost of medications for chronic heart failure was \$438. Patients with class II and class III chronic heart failure had the highest costs: \$541 and \$514, respectively. Analysis of variance indicated that the differences in monthly costs of medications between the patients with the 4 stages of chronic heart failure were significant ( $F = 4.86, P = .003$ ). A post hoc Scheffe test revealed significant differences in costs between patients with class I and patients with class II heart failure ( $P = .02$ ) and between patients with class I and those with class III heart failure ( $P = .02$ ). **CONCLUSIONS:** The outpatient costs of medications for chronic heart failure are significant. Ability to pay for prescribed medications must be determined. Healthcare professionals must maintain an awareness of the costs of medications and patients' ability to pay.

Krumholz H. M., Amatruda J., Smith G. L., Mattera J. A., Roumanis S. A., Radford M. J., et al. **“Randomized trial of an education and support intervention to prevent readmission of patients with heart failure.”** *Journal of the American College of Cardiology.* (2002) **39**(1): 83-9.

**OBJECTIVES:** We determined the effect of a targeted education and support intervention on the rate of readmission or death and hospital costs in patients with heart failure (HF). **BACKGROUND:**

Disease management programs for patients with HF including medical components may reduce readmissions by 40% or more, but the value of an intervention focused on education and support is not known. **METHODS:** We conducted a prospective, randomized trial of a formal education and support intervention on one-year readmission or mortality and costs of care for patients hospitalized with HF. **RESULTS:** Among the 88 patients (44 intervention and 44 control) in the study, 25 patients (56.8%) in the intervention group and 36 patients (81.8%) in the control group had at least one readmission or died during one-year follow-up (relative risk = 0.69, 95% confidence interval [CI]: 0.52, 0.92;  $p = 0.01$ ). The intervention was associated with a 39% decrease in the total number of readmissions (intervention group: 49 readmissions; control group: 80 readmissions,  $p = 0.06$ ). After adjusting for clinical and demographic characteristics, the intervention group had a significantly lower risk of readmission compared with the control group (hazard ratio = 0.56, 95% CI: 0.32, 0.96;  $p = 0.03$ ) and hospital readmission costs of \$7,515 less per patient. **CONCLUSIONS:** A formal education and support intervention substantially reduced adverse clinical outcomes and costs for patients with HF.

Ambrosioni E. **“Pharmacoeconomic challenges in disease management of hypertension.”** *Journal of hypertension. Supplement : official journal of the International Society of Hypertension (2001)* **19 Suppl 3:** S33-40.

Hypertension is a major global economic burden. Blood pressure management remains one of the most *cost*-effective methods of cardiovascular risk factor reduction. However, current hypertension management strategies remain sub-optimal and blood pressure remains poorly controlled in a high proportion of patients. Conventional economic studies in well controlled clinical trial settings have not adequately assessed factors such as *non*-*compliance*\*, switching and discontinuation of treatment which have an important impact on the *costs*\* of antihypertensive therapy in actual clinical practice. Furthermore, most conventional, randomized clinical studies may not fully reveal long-term benefits (e.g reductions in end-organ damage) which may be associated with newer therapeutic strategies. First-line use of rational, low-dose combination therapy can offer important advantages in terms of improved efficacy, tolerability and compliance, with reduced end-organ damage compared with conventional monotherapy. For newer hypertension management strategies, comprehensive pharmacoeconomic studies are needed which consider all of these important factors. Early economic analyses which failed to consider some of these newer issues should not hinder the more widespread use of novel strategies, including first-line low-dose combination therapy.

Hagihara A., Murakami M., Chishaki A., Nabeshima F. and Nobutomo K. **“Rate of health insurance reimbursement and adherence to anti-hypertensive treatment among Japanese patients.”** *Health Policy. (2001)* **58(3):** 231-42.

**BACKGROUND:** Although several studies have reported the effects of free medical care on compliance in patients with hypertension, no study has reported the effects of an economic incentive, such as subsidized medical costs, on compliance with medication protocol, in patients with hypertension. The unique characteristics of the Japanese health insurance system provide for a 10% decrease in the subsidy for medication immediately on retirement (approximately 60 years of age) for insured patients, and a 100% subsidy for insured patients who are 70 years of age or older. We examined the association between level of health insurance coverage and follow-up rate of medical treatment among Japanese patients with

hypertension. **METHODS:** The subjects, from throughout Japan, were patients with hypertension (n=1236). The study was conducted in 1991. The odds of completing a 1-year treatment in relation to the rate of health insurance reimbursement were calculated using multiple logistic regression analysis. **RESULTS:** We found the following. (1) Compared with the base group, the odds of completing a 1-year treatment increased to 2.62 or 2.51 in the group whose reimbursement rate was 100%. (2) Compared with the base group, the odds of completing a 1-year treatment was no larger than 1 in the group whose reimbursement rate had been 100% for more than 6 years ('76-'). (3) Compared with the base level, the odds of completing a 1-year treatment increased to 1-1.81 in the group whose liability decreased to 80%. **CONCLUSION:** Although the results imply that even a small economic incentive might be effective in securing a patient's compliance with anti-hypertensive medical treatment, the effect appear limited in both duration and magnitude.

Paramore L. C., Halpern M. T., Lapuerta P., Hurley J. S., Frost F. J., Fairchild D. G., et al. **“Impact of poorly controlled hypertension on healthcare resource utilization and cost.”** *American Journal of Managed Care.* (2001) 7(4): 389-98.

**OBJECTIVE:** To examine the relation between blood pressure (BP) control and utilization and cost of healthcare resources. **STUDY DESIGN:** A retrospective database study of managed care patients in New Mexico from January 1, 1996, to December 31, 1997. **PATIENTS AND METHODS:** We stratified 1000 hypertensive patients into categories based on average and maximum BP. Antihypertensive medication use and cost, number of physician visits, and interval between hypertension-related physician visits were determined. **RESULTS:** Medication costs increased progressively across all BP categories from lowest to highest, and higher average systolic BP (SBP) was significantly correlated with increased cost ( $P < .001$ ). There were significant correlations between higher maximum BP and greater number of hypertension-related physician visits ( $P < .001$ ). Mean number of visits for BP groups was 5.5 for patients with a maximum diastolic BP (DBP)  $< 85$  mm Hg and 10.0 for those with a maximum DBP  $\geq 100$  mm Hg ( $P < .001$ ). Patients with a maximum SBP  $\geq 180$  mm Hg averaged 9.7 visits, whereas those with a maximum SBP  $< 120$  mm Hg averaged 4.1 visits ( $P < .001$ ). Both SBP and DBP were significantly correlated with time to next visit ( $P < .001$ ). Mean visit intervals ranged from 44 days for patients with an SBP  $< 85$  mm Hg to 25 days for those with an SBP  $\geq 180$  mm Hg ( $P < .001$ ). A similar association was found between DBP and visit interval. **CONCLUSIONS:** Poor control of hypertension is associated with higher drug costs and more physician visits. Aggressive treatment might help reduce managed care costs and resource utilization.

Urquhart J. **“Some economic consequences of noncompliance.”** *Current hypertension reports* (2001) 3: 473-480.

Valenti W. M. **“Treatment adherence improves outcomes and manages costs.”** *AIDS Reader.* (2001) 11(2): 77-80.

Our experience with other chronic diseases, such as hypertension, diabetes, and asthma, has shown that adherence to treatment over time is about 50%. In HIV treatment, a significantly higher rate of

adherence (i.e., 95% or greater) is required to achieve good outcomes. HAART is effective and cost-effective. Even with the high cost of antiretroviral drugs, the decrease in hospital utilization in addition to improved quality of life with HAART more than offsets the increased cost of drugs. This cost shifting from hospital utilization has been shown to result in a decrease of total monthly costs of care in many settings. In addition to decreased mortality and cost savings from decreased hospital utilization associated with HAART, the appropriate use of expensive antiretroviral drugs and the resultant reduction in antiretroviral resistance can save lives and money over the long term. However, we know that the performance of drugs in clinical trials is not always borne out in today's real world of ambulatory HIV care, underscoring the need for treatment adherence strategies in the HAART era. Our understanding of what improves adherence to antiretroviral treatment is still incomplete. However, there are a number of approaches that address the patient, the provider/multidisciplinary team, and the treatment regimen itself. The dedicated TAC, while not the only solution, has been shown to be an effective team member and a solution worth considering in managed care settings. When added to the costs of today's care, this team member should still prove cost-effective in the final analysis. [References: 10]

Bunzel B. and Laederach-Hofmann K. “[**Noncompliance in organ transplantation: a review**].” *Wiener Klinische Wochenschrift*. (2000) **112**(10): 423-40.

The effectiveness of medical treatment depends not only on the appropriateness of the treatment modality but also on the patient's compliance with the intended regimen. The consequences of failing to comply can be damaging and devastating for the individual patient and his/her family. Noncompliance also leads to waste in two areas: first, a reduction of the potential benefits of therapy, and second, the additional cost of treating the avoidable consequent morbidity. A dramatic example of the consequences of noncompliance with the treatment regimen concerns patients who have had organ transplants: life-long immunosuppression is a pre-requisite for good graft function, and noncompliance is often associated with the occurrence of late acute rejection episodes, graft loss, and death. Here it might be assumed that these patients constitute a highly motivated group, and that compliance would be high. Unfortunately, this is not the case: overall noncompliance rates vary from 20 to 50%. There is no systematic and comprehensive review of the literature on noncompliance and its consequences in organ transplant patients to date. This overview includes literature on heart, liver and kidney transplants in adult and paediatric transplant patients and addresses the following issues: preoperative behaviour patterns as predictors of postoperative compliance problems, compliance behaviour after transplantation, noncompliance and its relationship to organ loss and death, retransplantation outcome after graft loss due to noncompliance, reasons for postoperative noncompliance, and ways to promote compliance. [References: 93]

Fonseca T. and Clara J. G. “[**Polypharmacy and non-compliance in the hypertensive elderly patient**].” *Revista Portuguesa de Cardiologia*. (2000) **19**(9): 855-72.

**BACKGROUND:** Elderly patients are major consumers of prescription and nonprescription medications and the proper use of these agents can lead to more cost-effective strategies in reaching optimal health. The use of medications for the treatment of multiple co-morbid conditions in a single patient increases the risks of polypharmacy and non-compliance and raises the burden on the health care system and society. **OBJECTIVES:** To analyse the extent and nature of total and anti hypertensive, polypharmacy the most prevalent groups of drugs, the compliance rate and the costs related to polypharmacy in the hypertensive



elderly. **METHODS:** A descriptive cross-sectional study was made of sixty-nine patients 65 years of age or older on follow-up for arterial hypertension at a central hospital in Lisbon. The study protocol consisted of a questionnaire performed by the physician. We calculated the monthly amount of individual prescription expense, after cost reduction from social insurance. **RESULTS:** The patients used an average of 4.4 prescribed medications with a corresponding average of 6.4 pills per day. Drug use was greater in women than men. Hypertensive therapy involved a mean of 2 drugs. Antiplatelet drugs, coronary vasodilators, benzodiazepines, glucose regulators and hypolipidemic agents were the other major groups of drugs. Non-compliance was identified in only 14% of the patients. The average of individual prescription expenses was 5,076 Portuguese escudos (PTE) per month, of which 2,226 PTE was the average cost of antihypertensive agents. **CONCLUSIONS:** With this study we were able to show the extent of poly-pharmacotherapy in a population of hypertensive elderly patients. We found a high rate of compliance, although the costs were frequently high.

Laederach-Hofmann K. and Bunzel B. **“Noncompliance in organ transplant recipients: a literature review.”** *General Hospital Psychiatry.* (2000) **22**(6): 412-24.

The consequences of failing to comply to doctor's instructions can be damaging and devastating for the individual patient and their family. Noncompliance also leads to waste, as it reduces the potential benefits of therapy, and to the extra cost of treating avoidable consequent morbidity. Life-long immunosuppression is a prerequisite for good graft function, and noncompliance is often associated with late acute rejection episodes, graft loss, and death. It might be assumed that transplant patients constitute a highly motivated group, and that compliance would be high. Unfortunately, this is not the case: overall noncompliance rates vary from 20 to 50%. This overview includes literature on heart, liver, and kidney transplants in adult and pediatric transplant patients. Compliance behavior after transplantation, noncompliance and its relationship to organ loss and death, retransplantation outcome after graft loss due to noncompliance, and reasons for postoperative noncompliance will be addressed. [References: 81]

Persson M., Mjorndal T., Carlberg B., Bohlin J. and Lindholm L. H. **“Evaluation of a computer-based decision support system for treatment of hypertension with drugs: Retrospective, nonintervention testing of cost and guideline adherence.”** *Journal of Internal Medicine* (2000) **247**(1): 87-93.

**Objective.** To evaluate a computerized decision support system (DSS) for drug treatment of hypertension, regarding quality, safety, and cost compared to actual antihypertensive drug treatment. **Design.** The medical profiles of 338 hypertensive patients treated with drugs against hypertension were processed by the DSS. The drug treatment proposed by the system was then compared to actual treatment given by their physician. **Setting.** Four health centres in the county of Vasterbotten, in Sweden. **Subjects.** A list of hypertensive patients was extracted from the computerized medical records of each health centre and every fifth patient's medical profile was assessed by the system. **Interventions.** None. **Main outcome measures.** Drug used, drug used in relation to certain major diseases such as diabetes mellitus, asthma, ischaemic heart disease (IHD), and previous myocardial infarction. **Adherence to hypertension guidelines, safety, and cost.** **Results.** The DSS suggested significantly more thiazides and significantly fewer calcium antagonists than the physicians had prescribed, with a total cost reduction of 33-40%, depending on doses chosen. The DSS drug profile was more adherent to guidelines in patients with major complicating diseases, suggesting an improvement in treatment quality for these patients by the DSS. **Conclusion.** The DSS which

fully implements current guidelines may improve the quality of antihypertensive treatment, concurrently leading to a considerable reduction in drug costs.

Zyczynski T. M. and Coyne K. S. "**Hypertension and current issues in compliance and patient outcomes.**" *Current Hypertension Reports.* (2000) 2(6): 510-4.

Economic and human costs associated with untreated or inadequately controlled hypertension and its complications continue to be an issue in the United States despite the availability of numerous antihypertensive agents. Knowledge of hypertension, product profiles, tolerability concerns, convenience of dosing, health-related quality of life effects, and cost of therapy are some of the factors that may influence the compliance of patients to their medication regimens. Recent reports on patient noncompliance have focused on patient-provider relationships, psychosocial barriers, home blood pressure monitoring, and electronic monitoring systems to improve blood pressure control. The use of health-related quality of life assessment in antihypertensive studies and in routine clinical practice provides another opportunity to optimize a patient's regimen for short- and long-term hypertension control in a cost-effective manner. [References: 29]

Anonymous. "**Heart Association Fights Nation's Hidden Health Threat.**" *AORN Journal* (1999) 70(3): 491.

Aziz A. M. and Ibrahim M. I. "**Medication noncompliance--a thriving problem**" *Medical Journal of Malaysia.* (1999) 54(2): 192-9.

A study was conducted among out-patients attending the Melaka Tengah Health Clinic to determine their compliance status towards antihypertensive, antidiabetic and antiasthmatic drugs. A total of 585 patients were enrolled in this study. Assessment of compliance was carried out using pill-counting and house-to-house interviews 14 days from the date of medication dispensed at the counter. The noncompliance rate among the 464 successfully interviewed patients was 56%. The mean noncompliance percentage was 78.0 +/- 43.1% (range: -10.0-314.3%). Among the four variables of compliance studied, race was not seen as a determinant of compliance. The older age group and those taking two or more drugs were statistically significant to be a noncomplier. Females were highly likely not to comply with drug therapy. Patients who conform to their refill dates were not really drug compliers. Forgetting to take their drugs and inability to read instructions on drug labels were the main reasons given. Underdosing was more common than overdosing, with an estimated cost of RM20,261.00 of unused medications per year.

Fulmer T. T., Feldman P. H., Kim T. S., Carty B., Beers M., Molina M., et al. "**An intervention study to enhance medication compliance in community-dwelling elderly individuals.**" *Journal of Gerontological Nursing.* (1999) 25(8): 6-14.

OBJECTIVE: To determine whether daily videotelephone or regular telephone reminders would increase the proportion of prescribed cardiac medications taken in a sample of elderly individuals who have

congestive heart failure (CHF). **METHODS:** The authors recruited community-dwelling individuals age 65 and older who had the primary or secondary diagnosis of CHF into a randomized controlled trial of reminder calls designed to enhance medication compliance. There were three arms: a control group that received usual care; a group that received regular daily telephone call reminders; and a group that received daily videotelephone call reminders. Compliance was defined as the percent of therapeutic coverage as recorded by Medication Event Monitoring System (MEMS) caps. Subjects were recruited from 2 sources: a large urban home health care agency and a large urban ambulatory clinic of a major teaching hospital. Baseline and post-intervention MOS 36-Item Short-Form Health Survey (SF-36) scores and Minnesota Living with Heart Failure (MLHF) scores were obtained. **RESULTS:** There was a significant time effect during the course of the study from baseline to post-intervention ( $F[2,34] = 4.08, p < .05$ ). Over time the elderly individuals who were called, either by telephone or videotelephone, showed enhanced medication compliance relative to the control group. There was a trend, but no significant difference between the two intervention groups. Both SF-36 and MLHF scores improved from baseline to post-intervention for all groups. There was no significant change in the SF-36 scores for the sample, but there was a significant change for the MLHF scores ( $p < .001$ ). The control group had a significant fall off in the medication compliance rate during the course of the study, dropping from 81% to 57%. **CONCLUSIONS:** Telephone interventions are effective in enhancing medication compliance and may prove more cost effective than clinic visits or preparation of pre-poured pill boxes in the home. Technologic advances which enable clinicians to monitor and enhance patient medication compliance may reduce costly and distressing hospitalization for elderly individuals with CHF.

Joshi P. P., Mohanan C. J., Sengupta S. P. and Salkar R. G. **“Factors precipitating congestive heart failure--role of patient non-compliance.”** *Journal of the Association of Physicians of India* (1999) **47**(3): 294-5.

**OBJECTIVE:** This study was aimed to identify systematically the precipitating factors causing decompensation of heart failure and subsequent hospitalisation. We specially assessed the role of patient \*non\*-compliance\* with therapy as an important precipitating factor for heart failure, since it has not been systematically studied previously in an Indian setting where rheumatic heart disease is common. **METHODS:** In this cross-sectional analytical study, 125 cases of congestive heart failure hospitalized in Government Medical College, Nagpur, were studied. All the patients were thoroughly evaluated and investigated to identify the precipitating factors for heart failure. A patient was categorized as being non-compliant with therapy if he/she was consuming less than 80% prescribed drugs (assessed by pill count) or was non-compliant with dietary advice (assessed by an interviewer-administered questionnaire). **RESULTS:** Rheumatic heart disease was the commonest underlying heart disease (52.8%) followed by ischemic and/or hypertensive heart disease (27.2%). The most common precipitating factor was patient \*non\*-compliance\* with diet or drug therapy (49.6%) followed by arrhythmias (16.8%), uncontrolled hypertension (14.4%), infective endocarditis (13.6%), anemia (14.4%) and infections (11.2%). **CONCLUSION:** The results emphasize the importance of patient \*non\*-compliance\* with prescribed therapy as a leading precipitating factor for congestive heart failure in an Indian setting, which can be prevented by appropriate \*cost\*-effective strategies aimed to improve \*patient\* \*compliance\*.

Scheen A. J. **“Therapeutic non-compliance: a major problem in the prevention of cardiovascular**

diseases].” *Revue Medicale de Liege*. (1999) **54**(12): 914-20.

The prevention of cardiovascular diseases relies upon the correction of risk factors and, more particularly, the optimal management of various metabolic abnormalities such as obesity, dyslipidaemias, diabetes mellitus and arterial hypertension. Such an approach first requires the adherence to life-style habits (healthy diet, physical activity and no smoking) and, in case of failure, the use of lipid-lowering drugs, antidiabetic agents and/or antihypertensive medications. Sometimes, a monotherapy may be sufficient but, in most cases, a drug combination is mandatory because of the need to reach tight therapeutic targets and of the presence of a poly pathology, especially within the frame of the metabolic syndrome. Unfortunately, all surveys indicate that therapeutic compliance to non-pharmacological advice and even to drug prescriptions is far from being excellent. Such a non-compliance limits the efficacy of the prevention strategies and contributes to markedly increase the cost of metabolic diseases and associated complications.

Stason W. B. “**Compliance, quality of life, and cost effectiveness.**” *Current Hypertension Reports*. (1999) **1**(6): 471-4.

Stephenson J. “**Noncompliance May Cause Half of Antihypertensive Drug "Failures".(Medical News & Perspectives).**” *JAMA, The Journal of the American Medical Association* (1999) **282**(4): 313.

Urquhart J. “**Pharmacoeconomic consequences of variable patient compliance with prescribed drug regimens.**” *PharmacoEconomics* (1999) **15**(3): 217-228.

Variable compliance with prescribed drug regimens is a leading source of variability in drug response. Specifics differ by drug and disease. The role of variable compliance was clearly defined in 2 trials of lipid-lowering agents, cholestyramine and gemfibrozil, in which exceptionally careful measurements of compliance were made, which has not been done in later trials. Economic consequences of variable compliance are estimated by converting dose-dependent changes in absolute risk of incident coronary disease into the uniconhort format, which designates how many patients must be treated to prevent, in a given time, a defined 'coronary event'. Two strong influences on the costs of treatment are (i) the shape of the relation between drug intake and risk reduction; and (ii) the strength of the linkage between intake and prescription refills. The intake-effect relation for cholestyramine is linear, making compliance-neutral the cost to prevent 1 coronary event, provided that refills match intake. If refills exceed intake, treatment costs rise. The intake-effect relation for gemfibrozil is more typically nonlinear, so poorer compliers purchase and take the drug in amounts that have little benefit, increasing the cost to prevent 1 coronary event. If refills run at a higher rate than intake, costs increase still further. A key question for future study is: do policies that encourage timely refills increase compliance enough to offset their potential to waste money in the purchasing of an untaken drug?.

Anonymous. “**Are you wasting money on efforts to cut noncompliance?**” *Capitation rates & data*

(1998) 3(9): 104-7.

Anonymous. **“Study shows poor persistence with lipid-lowering therapy, even when cost not a factor.”** *American Journal of Health-System Pharmacy*. (1998) 55(15): 1556, 1558.

Basskin L. **“Evaluating the Cost Effectiveness of Interventions to Reduce Noncompliance.”** *Formulary* (1998) 33: 359-360.

<Abstract> The methodology for evaluating the \*cost\* effectiveness of different interventions to reduce \*patient\* \*noncompliance\* with drug therapy and a pharmacoeconomic model for determining the \*costs\*, benefits, and net benefits of interventions to reduce \*noncompliance\* are discussed; the pharmacoeconomic model was applied to a hypothetical example involving patients with congestive heart failure who experienced an acute adverse outcome due to \*noncompliance\* with drug therapy.

Basskin L. **“How to Determine the Extent and Costs of Noncompliance with Drug Therapy.”** *Formulary* (1998) 33: 139-141.

<Abstract> An approach to assessing the pharmacoeconomics of \*patient\* \*noncompliance\* with drug therapy and the impact of interventions is presented, and the evaluation of consequences of \*noncompliance\* in congestive heart failure is used as a working example.

<Abstract2> 1

Dosing R., Weisser B., Mengden T. and Vetter H. **“Changes in antihypertensive therapy - The role of adverse effects and compliance.”** *Blood Pressure* (1998) 7(5-6): 313-315.

In a German multicentre study (1603 patients, 320 private practices), adverse effects and patient compliance during antihypertensive therapy were investigated using standardized questionnaires for both patient and physician. Patients with a change in antihypertensive therapy during the last six months were included in this study. The single most important reason for the change in therapy was inadequate blood pressure control (48.4%), followed by adverse effects (30.1%), patient dissatisfaction (20.0%), noncompliance (16.8%) and cost (4.9%). The most frequent adverse effects noted by the doctors were cough (51.9%), oedema (36.9%), flush (36.6) and dizziness (27.8%). In comparing the answers of the physicians and patients, it becomes obvious that compliance may be overestimated by the doctors (good: 41.7%; medium: 57.3%; bad: 1.0%), since only 32.3% of the patients stated that they never missed a dose, 54.8% were occasionally non-compliant and 12.9% admitted missing a dose frequently. The predominant reasons for non-compliance (assessed by the patients) were forgetfulness (40.4%), followed by adverse effects (9.6%) and irregular lifestyle (6.5%). Thus, lack of effectiveness and adverse effects/patient dissatisfaction/non-compliance contributed roughly equally to the decision to change therapy. In addition, forgetfulness was shown to be an important contributor to suboptimal compliance. Lastly, physicians may still underestimate the extent of non-compliance.

Dusing R., Weisser B., Mengden T. and Vetter H. **“Changes in antihypertensive therapy--the role of adverse effects and compliance.”** *Blood Pressure*. (1998) 7(5-6): 313-5.

In a German multicentre study (1603 patients, 320 private practices), adverse effects and patient compliance during antihypertensive therapy were investigated using standardized questionnaires for both patient and physician. Patients with a change in antihypertensive therapy during the last six months were included in this study. The single most important reason for the change in therapy was inadequate blood pressure control (48.4%), followed by adverse effects (30.1%), patient dissatisfaction (20.0%), non-compliance (16.8%) and cost (4.9%). The most frequent adverse effects noted by the doctors were cough (51.9%), oedema (36.9%), flush (36.6) and dizziness (27.8%). In comparing the answers of the physicians and patients, it becomes obvious that compliance may be overestimated by the doctors (good: 41.7%; medium: 57.3%; bad: 1.0%), since only 32.3% of the patients stated that they never missed a dose, 54.8% were occasionally non-compliant and 12.9% admitted missing a dose frequently. The predominant reasons for non-compliance (assessed by the patients) were forgetfulness (40.4%), followed by adverse effects (9.6%) and irregular lifestyle (6.5%). Thus, lack of effectiveness and adverse effects/patient dissatisfaction/non-compliance contributed roughly equally to the decision to change therapy. In addition, forgetfulness was shown to be an important contributor to suboptimal compliance. Lastly, physicians may still underestimate the extent of non-compliance.

Rodgers P. T. and Ruffin D. M. **“Medication nonadherence: Part II--A pilot study in patients with congestive heart failure.”** *Managed Care Interface*. (1998) 11(9): 67-9, 75.

Nonadherence is a significant medical problem in the United States, leading to excessive morbidity, mortality, and medical costs. In the conclusion to this two-part article, the authors describe a pilot study involving 311 patients taking an angiotensin-converting enzyme inhibitor that evaluates the principal factors for nonadherence to pharmaceutical therapy in patients with congestive heart failure.

Rodgers P. T. and Ruffin D. M. **“Medication nonadherence--Part I: The health and humanistic consequences.”** *Managed Care Interface*. (1998) 11(8): 58-60.

Nonadherence is a significant medical problem in the United States, leading to excessive morbidity, mortality, and medical costs. In this first installment of a two-part article, the authors review the literature and discuss the effects of the problem, with particular reference to patients with congestive heart failure. [References: 19]

Rudd P. **“Compliance with antihypertensive therapy: raising the bar of expectations.”** *American Journal of Managed Care*. (1998) 4(7): 957-66.

Recent advances in the effectiveness of antihypertensive therapies and the measurement of medication-taking behavior have raised the bar of expectations, both for patients and prescribing clinicians. This article reviews the principal findings and makes recommendations to improve pill taking among patients with hypertension. It summarizes several studies related to hypertension epidemiology, component behaviors

contributing to suboptimal compliance with prescribed antihypertensive medications, the direct and indirect costs of nonadherent behaviors, and measures of pill-taking behavior. Based on this analysis, current levels of hypertension detection, treatment, and control remain suboptimal. Heuristics for adjusting antihypertensive regimens may be misleading and too simplistic. More than half of those patients failing to achieve goal blood pressure display suboptimal compliance rather than an inadequate regimen. In conclusion, there is a need for enhanced sophistication about medication-taking behavior, especially for hypertension, so that more patients with this condition can fully benefit from effective treatments. [References: 66]

Anonymous. **“Pharmacist-led hypertension disease management program cuts utilization and costs.”** *Healthcare Demand & Disease Management*. (1997) **3**(12): 191-2.

Making sure your hypertensive patients are compliant with drug medications requires eyes and ears beyond the doctor's office. Pharmacists in one group practice in Beverly Hills are demonstrating that they can play a key role in keeping patients on track with drug regimens, and save a lot of money in the process.

Rizzo J. A. and Simons W. R. **“Variations in compliance among hypertensive patients by drug class: implications for health care costs.”** *Clinical Therapeutics*. (1997) **19**(6): 1446-57; discussion 1424-5.

Health care decision-makers require more information on differences in compliance rates associated with alternative classes of antihypertensive drugs and the implications of these differences for health care utilization and costs. We examined medical claims data from the Pennsylvania Medicaid Management Information System to investigate compliance rates for four major antihypertensive drug classes (angiotensin-converting enzyme [ACE] inhibitors, beta-blockers, calcium antagonists, and diuretics) and the health care costs associated with noncompliance. Multivariate analysis was used to relate antihypertensive drug class with compliance and variations in compliance with health care costs. The highest estimated rates of compliance were associated with ACE inhibitors and calcium antagonists, and these rates were significantly greater than with beta-blockers and diuretics. Moreover, poor compliance was associated with higher health care costs. Efforts to increase compliance with antihypertensive drug therapy are needed to improve patient outcomes and reduce health care costs.

Bailey J. E., Lee M. D., Somes G. W. and Graham R. L. **“Risk factors for antihypertensive medication refill failure by patients under Medicaid managed care.”** *Clinical Therapeutics*. (1996) **18**(6): 1252-62.

Antihypertensive medication noncompliance is common and leads to substantial morbidity for patients and increased health care costs for managed-care organizations. A retrospective cohort study using pharmacy prescription profiles to estimate noncompliance was conducted to determine important risk factors for patient noncompliance with antihypertensive therapy for Medicaid enrollees participating in a managed-care plan. The pharmacy and claims data for 1395 patients with uncomplicated hypertension who were enrollees of Tennessee's Medicaid managed-care program were analyzed to determine the frequency of the enrollees' failure to obtain timely antihypertensive medication refills (hereafter referred to as refill failure) and to identify the predictors of refill failure. Overall, refill failure occurred in 33% of 7413 refill

opportunities studied, whereas refill failure occurred in 32% of the cases in which medication was dosed once daily and in 35% of the cases in which medication was dosed more than once daily. For patients taking alpha-blockers, there was a significantly lower rate of refill failure (11.0%) than for patients taking angiotensin-converting enzyme inhibitors, direct vasodilators, and thiazide diuretics. Patients taking calcium channel blockers, had a significantly lower rate of refill failure (38.5%) than for patients taking thiazide diuretics (45.5%). Younger age, medication class, multiple-daily dosing regimen, and fewer provider visits were all found to be significant independent predictors of refill failure, whereas gender and regimen complexity were not significant predictors in this population. Health care systems planning pharmacy-based interventions to improve patient compliance with antihypertensive medication for patients in a Medicaid managed-care program can expect to encounter high levels of refill failure and may want to target enrollee subgroups by age, medication class, or dosing regimen for intensive intervention efforts.

Flack J. M., Novikov S. V. and Ferrario C. M. **“Benefits of adherence to anti-hypertensive drug therapy.”** *European Heart Journal.* (1996) **17**(Suppl A): 16-20.

Long-term adherence or compliance with anti-hypertensive drug therapy is poor. It has been estimated that within the first year of treatment 16-50% of hypertensives discontinue their anti-hypertensive medications. Even among those who remain on therapy long term, missed medication doses are common. Epidemiological studies have shown that drug-treated hypertensives have higher blood pressures than age-, gender- and body mass index-matched normotensives. In addition, drug-treated hypertensive men and women who achieve blood pressure normalization are less likely to die over a 9.5-year period than those whose blood pressure remains elevated while taking anti-hypertensive drugs. Thus, one reason for less than optimal reduction of blood pressure-related cardiovascular-renal risk in drug-treated hypertensives is inadequate blood pressure lowering. Quantifiable excess risk has been documented even in the short term (< 1 year) after interruption or discontinuation of anti-hypertensive medications as total healthcare costs are higher, mostly because of higher hospitalization rates. Data from the Treatment of Mild Hypertension Study (TOMHS) are relevant to long-term adherence to various anti-hypertensive drug monotherapies. At 48 months, 82.5% and 77.8% of participants remained on amlodipine and acebutolol, respectively (both  $P < 0.01$  compared with placebo). However, only 67.5%, 66.1% and 68.1%, respectively, of chlorthalidone, doxazosin and enalapril participants remained on these drugs as monotherapy at 48 months. Differential adherence to long-term anti-hypertensive drug therapy could translate into a greater risk of blood pressure-related complications and higher overall healthcare expenditures. Strategies to minimize the deleterious impact of therapeutic non-adherence with anti-hypertensive medications as well as the clinical and cost implications of the TOMHS data will be discussed.

Navarro R. P. **“The issue of noncompliance.”** *Medical interface* (1996) **9**(8): 70, 72.

Stergachis A. and Sullivan S. D. **“Epidemiology and Pharmacoeconomics of Medication Related Issues.”** *ASHP Annual Meeting* (1996) **53**(June): P-I84.

<Abstract> Pharmaceuticals are a large expenditure item for most managed care organizations. When used appropriately, drugs are of great value in reducing suffering from symptoms and disease and



have been shown to be \*cost\*-saving in terms of overall medical care expenditures. A recent study estimates that prescription drug misuse \*costs\* the economy more than \$76 billion annually. Among the most important drug-related problems is \*patient\* \*noncompliance\* with medication regimens. One estimate suggests that approximately \$7.8 billion in direct hospitalization \*costs\* annually are associated with \*noncompliance\*. This presentation will provide an overview of various estimates of the prevalence and economic impact of medication-related problems. Targets and opportunities for improved management of medication usage will be discussed. Learning objectives: 1. Introduce the methods of epidemiology and health economics as applied to determining the scope of medication-related problems. 2. Provide estimates of the prevalence and \*cost\* of medication-related problems in the U.S. 3. Describe how pharmaceutical care interventions may improve patient outcomes. Self-assessment questions: 1. Prescription drug misuse is comparable in \*cost\* to cardiovascular disease, diabetes and obesity in its adverse impact on the U.S. consumer. 2. The \*cost\* associated with \*noncompliance\* can be divided into direct medical \*costs\* and indirect \*costs\*. 3. Effective pharmaceutical care has the potential for reducing the total \*cost\* of medical care. Answers: 1. T; 2. T; 3. T.

Urquhart J. “**Patient non-compliance with drug regimens: measurement, clinical correlates, economic impact.**” *European heart journal* (1996) **17**(Suppl. A): 8-15.

Bittar N. “**Maintaining long-term control of blood pressure: the role of improved compliance.**” *Clinical cardiology* (1995) **18**(6 Suppl 3): Iii 12-6.

Mild-to-moderate essential hypertension is a major risk factor for stroke and cardiovascular mortality and morbidity. Morbidity can be reduced significantly by lowering high blood pressure, and with the effective antihypertensive drugs now available, it is ever more important to identify and treat the estimated 50 to 60 million hypertensive persons in the United States. Yet a high percentage of persons being treated stop taking their medication and refuse to comply with their therapeutic regimen. Many problems relate to maintaining long-term therapy in the hypertensive population. They include the \*cost\* of medication, a lack of written instructions, unclear instructions, noninvolvement of the patient in designing the treatment plan, lack of patient education about the disease, side effects, and inconvenient dosing schedules. Numerous studies have found that compliance increases as drug-dosage frequency decreases, as with the use of once-daily or sustained-release drug preparations. Other contributors to compliance include prescription-refill reminders, appointment reminders, simple written instructions about drug use, and patient education about the need for treatment and the consequences of \*noncompliance\*. Many classes of antihypertensive drugs are available, and more are in development. With such an extensive armamentarium available, all patients, regardless of coexisting medical conditions, should be able to be given effective, individualized antihypertensive therapy.

Burke L. E. and Dunbar-Jacob J. “**Adherence to medication, diet, and activity recommendations: from assessment to maintenance.**” *Journal of Cardiovascular Nursing*. (1995) **9**(2): 62-79.

Inadequate adherence to treatment regimens has been a concern of health care providers for more than two decades. However, it continues to have a significant impact on morbidity and health care cost.

Poor adherence crosses ethnic and age groups, socioeconomic strata, acute and chronic diseases, and treatment regimens. Depending on the population, the prescribed regimen, and the definition or measure of adherence used, rates vary from 10% to 85%. The consequences of absent or partial adherence are observed in the research arena and all types of clinical settings. Educational and behavioral strategies may prevent or remediate adherence problems. [References: 97]

Fishman T. **“The 90-Second Intervention: a patient compliance mediated technique to improve and control hypertension.”** *Public Health Reports.* (1995) **110**(2): 173-8.

Hypertension, a leading risk factor for cardiovascular and renal diseases, occurs in up to 50 million Americans. Despite mounting evidence of the effectiveness of prevention and treatment, physicians are still unable to get their patients to adopt and adhere to treatment protocols. This project presents an innovative approach to compliance which is based on general systems theory and its applications in family therapy. The "90-Second Intervention" ("90 SI") incorporates the use of family and friends; it utilizes the therapeutic relationship or alliance of the physician-patient; and it embraces the well-established fact that social support plays a key role in promoting health, decreasing susceptibility to disease, and facilitating recovery from illness. The physician asks the patients to identify who in their life loves or cares for them and would help them adhere to the treatment protocol. To implement the "90 SI," the physician instructs the patient to telephone, in his or her presence, the identified helper(s) who then agree to support the patients' medical regimen. Specifically, the "90 SI" seeks to create a context to support the patients in a regimen of low to moderate intensity exercise, which is proven to be a powerful, cost-effective, and safe treatment. Patients who are identified with new onset or uncontrolled hypertension at three clinics in urban Philadelphia are the target population.

Schulz R. M., Lingle E. W., Chubon S. J. and Coster-Schulz M. A. **“Drug use behavior under the constraints of a Medicaid prescription cap.”** *Clinical Therapeutics* (1995) **17**(2): 330-340.

Limiting the number of prescriptions reimbursed per month is a cost-containment measure used by state Medicaid programs. The purpose of this study was to identify and examine the strategies used by patients who exceed the limits of the cap. Nineteen patients identified by community pharmacists as meeting this criterion were interviewed in their homes by a member of the project team. The sample consisted predominantly of women. Seven of the 19 individuals reported that they had altered the way they took their medication, primarily by reducing the frequency of dosing, to make the medication last longer. Eight individuals reported that, at some time during the past year, they did not obtain a prescribed medication because of the prescription cap. These medications were prescribed for a variety of conditions, including diabetes, asthma, and congestive heart failure. Patients made the purchase/nonpurchase decision based primarily on importance of the condition for which the medication was prescribed. What was deemed important, however, could change over time as a result of changing symptoms. Patients obtained some help from friends, family, and health care professionals in coping with the constraints of the prescription cap. However, the cap forced a significant group of patients into noncompliance, and thus placed them at risk for poor health outcomes.

Shaw E., Anderson J. G., Maloney M., Jay S. J. and Fagan D. **“Factors associated with noncompliance of patients taking antihypertensive medications.”** *Hospital Pharmacy*. (1995) **30**(3): 201-3, 206-7.

Poor adherence to drug therapy decreases the effectiveness of antihypertensive treatment. Patients must take more than 80% of their antihypertensive drugs to maintain adequate blood pressure control. To understand the incidence of noncompliance and contributing factors, a pilot study was conducted in which a questionnaire was devised and administered to a random sample of 243 hypertensive patients of the adult ambulatory care clinic at Methodist Hospital of Indiana. Ninety-eight patients completed the telephone survey. Demographic data were obtained through chart reviews. The results indicated that 30-46% of the patients were noncompliant with their antihypertensive drug regimens. Factors found to be associated with noncompliance were; employment ( $P = .0077$ ), use of home remedies ( $P = .0043$ ), age ( $P = .0165$ ), experience of side effects ( $P = .0051$ ), level of concern with missed doses ( $P = .0043$ ), and cost ( $P = .014$ ). The incidence of noncompliance in this pilot sample is lower than the estimated 50% noncompliance rate of published data. More research is needed to understand the determinants of noncompliance in order to design interventions to improve compliance.

Lee A. and Oldenburg B. **“A survey of patients with cardiac disease: Risk factors for admissions.”** *Australian Journal of Hospital Pharmacy* (1993) **23**(2): 104-108.

Objective: To determine the prevalence of drug-related admissions in patients who had a history of heart disease and to identify risk factors associated with hospital admission. Design: A survey in which data were collected from patients' medical records and structured interviews. Setting, participants: The study was conducted at a university-affiliated teaching hospital in Sydney, New South Wales. One hundred and twelve patients with known cardiac history were recruited over a 14-week period. Main outcome measures: Measures of medication-taking behaviour and factors associated with health provider consultations. Results: The prevalence of drug-related admissions was 34%; these consisted of drug noncompliance (10%), inadequate drug effect in compliant patients (11%) and adverse drug reactions (13%). The number of medications taken at admission increased the risk of drug-related admission. Patients taking five or more medications were 2.5 times more likely to be admitted to hospital with drug-related problems than those patients taking less than five medications (95% CI: 1.1-5.7). Angiotensin converting enzyme inhibitors, beta-blockers, diuretics and sorbide nitrate was frequently associated with drug-related admissions. Conclusion: The results of this study suggest that drug-related admissions are an important problem in cardiac patients. Strategies and educational programs to promote rational drug use may lower the rate of hospital admissions and associated costs.

Richardson M. A., Simons-Morton B. and Annegers J. F. **“Effect of perceived barriers on compliance with antihypertensive medication.”** *Health Education Quarterly*. (1993) **20**(4): 489-503.

Noncompliance with antihypertensive medication remains an obstacle to the management of hypertension, and despite research efforts over the past decade, the predictors of noncompliance remain unclear. According to values expectancy theory, individuals rationally choose noncompliance when the barriers or costs of treatment outweigh the expected benefits. Noncompliance, therefore, is likely to occur when net costs of treatment are high. Using a cross-sectional study design among subjects ( $n = 197$ ) attending a specialized clinic for hypertension, we measured "net barriers" (costs), self-reported compliance, and possible determinants of noncompliance, including socio-demographics, the medical regimen, and locus

of control. The effect of each quartile of the net barriers score (none, low, moderate, and high) on compliance, controlling for potential effect modifiers, was assessed using logistic regression modeling. Noncompliance (47%) was associated with younger age, higher salt use, longer duration of treatment, and higher levels of net barriers, but duration of treatment modified the effect of net barriers. Among subjects in short-term treatment, noncompliance increased with severity of net barriers suggesting a dose-response effect. In contrast, patients in long-term treatment showed no dose-response effect but a consistent association between noncompliance and levels of net barriers. Subjects at greater risk for noncompliance, however, were those who reported high net barriers, regardless of duration of treatment. Net barriers accounted for 50% of the noncompliance and appeared most important for patients who were younger or in the early stages of treatment. Implications for health care providers are discussed.

Sherbourne C. D., Hays R. D., Ordway L., DiMatteo M. R. and Kravitz R. L. “**Antecedents of adherence to medical recommendations: results from the Medical Outcomes Study.**” *Journal of behavioral medicine* (1992) **15**(5): 447-68.

A longitudinal study of patients with chronic medical diseases (hypertension, diabetes, heart disease) was conducted to identify antecedents of adherence to medical recommendations. Data are from 1198 patients in three health-care provision systems in Los Angeles, Chicago, and Boston. \*Nonadherence\* at the beginning of the study was the strongest predictor of \*nonadherence\* 2 years later. Other significant predictors varied by type of adherence outcome. Patients who were younger and who relied upon avoidant coping strategies tended to be less likely to follow their doctor's specific recommendations. Patients who were distressed about their health, used avoidant coping strategies, or who reported worse physical and role functioning were less likely to adhere in general. Patient satisfaction with two features of care (interpersonal quality and financial aspects) was positively related to adherence in some models, but satisfaction with the technical quality of care was negatively associated with adherence to specific recommendations among heart disease patients. Social support contributed to specific adherence among diabetic patients. Implications of the study for medical care providers are discussed.

Wiseman I. C. and Miller R. “**Quantifying non-compliance in patients receiving digoxin--a pharmacokinetic approach.**” *South African medical journal. Suid-Afrikaanse tydskrif vir geneeskunde* (1991) **79**(3): 155-7.

\*Non\*-*\*compliance\** has a major influence on the successful outcome of a therapeutic regimen. It also unnecessarily increases the *\*costs\** of health care. In a study involving 137 outpatients receiving digoxin 55 patients (40%) were found to be non-compliant. Patients who experienced communication problems and who lacked a meaningful relationship with their doctor showed a marked deterioration in compliance. An applied pharmacokinetic approach was used to predict the serum digoxin concentration for each patient. The creatinine clearance was determined and the degree of severity of heart failure was assessed. Total body clearance was then calculated. The predicted concentration was also calculated and compared with the measured digoxin concentration enabling an objective assessment of compliance. Twenty-four of the non-compliant patients who had subtherapeutic levels of digoxin (less than 0.8 ng/ml) had signs of cardiac failure. Eighteen of these patients were receiving additional medication (1.7 +/- 0.5 items) for the treatment of cardiac failure.

Anonymous. “**Noncompliance Costs Staggering--NIH Study Indicates RPhs Can Help.**” *American Druggist* (1990) **201**(Feb): 14.

<Abstract> The economic impact of \*patient\* \*noncompliance\* with drug therapy and the pharmacist's role in promoting compliance are discussed. In a study involving approximately 100 hypertensive patients and pharmacists who received a 10 h intensive course in counseling, patients who received counseling improved their compliance, as measured by unannounced pill counts, far more than did those in the control group.

Neal W. W. “**Reducing costs and improving compliance.**” *American Journal of Cardiology*. (1989) **63**(4): 17B-20B.

The cost-effectiveness of antihypertensive therapy is defined as the costs of treatment less the savings from the prevention of stroke and myocardial infarction, relative to the therapeutic effectiveness of treatment. Since antihypertensive therapy actually increases the dollar cost of medical care, the use of more expensive agents needs to be justified in terms of better blood pressure control, improved quality of life, and reduced cardiovascular morbidity and mortality. Data from the clinical trials have not shown the more expensive agents such as angiotensin-converting enzyme inhibitors and calcium channel blockers to be superior to the less expensive agents such as diuretic drugs in reducing blood pressure or cardiovascular morbidity and mortality. Poor compliance may reduce both the effectiveness and cost-effectiveness of treatment. Physicians must play an active role in prompting compliance by assuring the patient's ability to incorporate the prescribed dosage regimen into daily routine, by actively monitoring compliance, by modifying the regimen appropriately to remove the cause of noncompliance, and by switching medication if it is ineffective or if adverse effects occur. [References: 9]

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Morningstar B. A., Sketris I. S., Kephart G. C. and Sclar D. A. “**Variation in pharmacy prescription refill adherence measures by type of oral antihyperglycaemic drug therapy in seniors in Nova Scotia, Canada.**” *Journal of Clinical Pharmacy & Therapeutics* (2002) **27**(3): 213-220.

Objective: To examine the association between pharmacy prescription refill adherence by type of oral antihyperglycaemic medications used in seniors in Nova Scotia, Canada. Research design and methods: Pharmacy and health care utilization data from April 1993 to March 1996 for Nova Scotia Seniors' Pharmacare beneficiaries treated with 1st and 2nd generation sulphonylureas and biguanides was analysed. Refill adherence was quantified by two proportions: number of days beneficiaries had a medication surplus compared with the total period of observation and gaps in treatment compared with the total period of observation. Analysis examined association of type of oral antihyperglycaemic agent and dosing on refill adherence, after adjustment for age, gender and hospital use. Results: A total of 3358 beneficiaries met the study criteria. The mean refill adherence rate [continuous multiple-interval measure of medication availability (CMA)] was 86 +/- 0.4% SE and continuous measure of medication gaps (CMG) was 16 +/- 0.4% SE. Use of biguanides was associated with lower odds of having a medication surplus. The use of 2nd generation sulphonylureas and biguanides, and use of agents with a dosage frequency of more than one dose per day was associated with medication gaps. Conclusions: Many beneficiaries taking anti-hyperglycaemic agents adhered well to prescribed therapy. The proportion of days not covered by medications averaged 16%. Beneficiaries taking medications once a day were more likely to have good refill adherence. Further work is needed to compare prescription refill adherence rates with other adherence measures and clinical outcomes. These methods are useful for establishing baseline adherence, monitoring the success of programmes designed to improve adherence, and determining cost-effectiveness of drug regimens.

## **Eye and Skin Diseases**

Taylor S. A., Galbraith S. M. and Mills R. P. “**Causes of non-compliance with drug regimens in glaucoma patients: A qualitative study.**” *Journal of Ocular Pharmacology & Therapeutics* (2002) **18**(5): 401-409.

The purpose of this study was to gain insights into why patients are not compliant with their glaucoma medications. Patients were recruited from lists provided by two ophthalmologists. Each patient had seen a minimum of two ophthalmologists for their glaucoma, and was taking at least two topical medications for glaucoma. Qualitative methodology was utilized, including two focus groups and eleven in-depth interviews in patients' homes. The results showed that forgetfulness was the number one reported reason for noncompliance. Patients did not claim to be non-compliant specifically because of side effects, but they did complain about them. Communication between physicians and patients is a key factor in compliance for glaucoma patients. Specifically, patients would like their physicians to teach them how to instill their eye drops, tell them about new/alternate medications and procedures as they become available, and offer new ways to make their regimen easier. Patients often do not tell their physician if they experience a side effect unless it is intolerable to them, yet they do realize the seriousness of glaucoma, and the consequences of not following their doctor's orders. Finally, while cost was not a reported deterrence to compliance, some patients would prefer less expensive alternatives. [References: 19]

Leu S. and Eng K. “**Determination of unclaimed prescriptions at an outpatient department, Songklanagarind Hospital.**” *Journal of Pharmacy Practice* (1999) **12**(6): 433-440.

Unclaimed prescriptions are an initial indication of noncompliance. Although the patients receive the best treatment, they may fail to take their medicines. As a result, the illness may not be relieved and this can lead to hospitalization or use of emergency services. This study was conducted to determine the characteristics and reasons for unclaimed prescriptions in a 680-bed and tertiary care center from July to October 1997. Patients' data were collected from medical records and from questionnaires that asked for the reasons prescriptions were not claimed. During the four-month period, 695 unclaimed prescriptions were identified, accounting for approximately 0.67% of all prescriptions filled. Results showed that patients least likely to claim a prescription included women, those who visited the hospital during official hours, those who had chronic disease, and those who went to see internal medicine physicians. Three most common diseases were those involving respiratory system (8.6%), musculoskeletal system (6.3%), and genitourinary system (6.0%). More than half (56.5%) were treated with the essential drugs. Neuromuscular agent was the most frequent drug class of unclaimed prescriptions, followed by respiratory agent, dermatological agent, and vitamins and minerals. Of the 695 patients, 152 patients responded to the questionnaires. Sixty-one patients indicated that they had received their medications later on and, therefore, were excluded from the analysis. Thus, 61 questionnaires were analyzed. The most important reason patients did not claim their prescriptions was cost (22.0%). The next most frequently mentioned reasons were forgetfulness (12.1%), business (11.0%), and lack of communication (8.8%). These patients need to be counseled about the importance of taking their medicines. In addition, health care providers should develop strategies to improve patient compliance with their medications.

## **Infections**

Kardas P. **“Patient compliance with antibiotic treatment for respiratory tract infections.”** *Journal of Antimicrobial Chemotherapy.* (2002) **49**(6): 897-903.

Despite doctors' expectations, non-compliance is common in short-term antibiotic therapy of respiratory tract infections (RTIs). This phenomenon has profound practical implications. It leads to ineffective management, the deterioration of patients' health, hospital admissions, additional costs and the emergence of antibiotic-resistant microorganisms. This article reviews methods of measuring compliance with antibiotics in the outpatient-based management of RTIs and research results. Causes of non-compliance are also discussed. Factors influencing compliance are analysed, as well as practical strategies for addressing non-compliance with antibiotic therapies for RTIs. The influence of the frequency of doses on compliance is particularly stressed, as it has been observed that once daily dosing has almost a 100% compliance rate. As a number of once-daily antibiotic preparations are available now, the possibility of using once-daily schedules for improving compliance in RTI cases is stressed. [References: 46]

O'Boyle S. J., Power J. J., Ibrahim M. Y. and Watson J. P. **“Factors affecting patient compliance with anti-tuberculosis chemotherapy using the directly observed treatment, short-course strategy (DOTS).”** *International Journal of Tuberculosis & Lung Disease.* (2002) **6**(4): 307-12.

SETTING: Kota Kinabalu and surrounding communities in Sabah, Malaysia. OBJECTIVES: To establish factors affecting compliance of patients with anti-tuberculosis chemotherapy, their knowledge of the disease, and views on improving the DOTS strategy. DESIGN: Interviews with compliant patients attending clinics for DOTS treatment and with non-compliant patients in their homes, in August and September 2000. RESULTS: A total of 63 compliant and 23 non-compliant patients were interviewed. For non-compliant patients, reaching the treatment centre entailed greater cost ( $P < 0.005$ ) and travel time ( $P < 0.005$ ) compared to compliant patients. Cost of transport was the reason most frequently given for non-attendance. Non-compliant patients were more likely to have completed secondary education ( $P < 0.05$ ), and to be working ( $P < 0.01$ ). More non-compliant patients had family members who had had the disease ( $P < 0.01$ ). There was no difference between the groups for overall tuberculosis knowledge scores; however, non-compliant patients were more likely to think that treatment could be stopped once they were symptom free ( $P < 0.01$ ). Most patients (73%) felt that the DOTS system could be improved by provision of more information about tuberculosis. CONCLUSION: Compliance with DOTS in the Kota Kinabalu area is affected by travel expenses, time spent travelling to treatment centres, and having family members who have had the disease. Patients would like more information on tuberculosis.

Anonymous. **“S.F. provider follows tuberculosis model in developing medication compliance program.(Brief Article).”** *Mental Health Weekly* (2001) **11**(40): 1.

Spiritus E. **“Antibiotic usage for respiratory tract infections in an era of rising resistance and increased cost pressure.”** *American journal of managed care* (2000) **6**(23 Suppl): S1216-21.

Pharmacoeconomic study models have a number of inherent problems that significantly limit their

use within the medical community. They are frequently retrospective and thus have only limited relevance in a field in which resistance patterns are highly volatile. Moreover, the study models do little to consider the numerous economic perspectives involved, such as the patients themselves as well as society at large. Prescribing patterns profoundly affect overall healthcare \*costs\*. As much as \$8.4 billion is spent on community-acquired pneumonia each year; 8% of that \*cost\* is for antibiotic therapies. Moreover, studies show that inappropriate prescribing for upper respiratory tract infections is the norm not the exception, with significant \*cost\* and health consequences. Also adding to \*costs\* is \*patient\* \*noncompliance\*, which could possibly be reduced with once-daily dosing regimens and widespread patient education about appropriate use of antibiotics.

Lee M., Kemp J. A., Canning A., Egan C., Tataronis G. and Farraye F. A. “**A Randomized Controlled Trial of an Enhanced Patient Compliance Program for Helicobacter pylori Therapy.**” *Archives of Internal Medicine* (1999) **159**(19): 2312.

Objectives: To determine whether an enhanced compliance program (ECP) improves patient compliance with bismuth subsalicylate, metronidazole, and tetracycline hydrochloride (BMT) triple therapy for the treatment of Helicobacter pylori infection and to identify factors that affect compliance with therapy. Design: A randomized controlled trial conducted in 4 staff-model health centers of a health maintenance organization in Massachusetts. Patients and Methods: A total of 125 patients 18 years of age or older with peptic ulcer disease or dyspepsia whose clinicians prescribed BMT triple therapy for 14 days were randomized to a control group or to the ECP group. The ECP group received medication counseling (written and oral) from a pharmacist, along with a medication calendar and a minipillbox, as well as a follow-up telephone call after initiation of therapy. Compliance was assessed by a pill count, and factors affecting adherence to the regimen were identified by patients' reports. Results: There was no statistically significant difference between the 2 groups in the number of patients taking more than 60% of the medications (89% of the control group vs 95% of the ECP group; P (is greater than) .30). However, there was a statistically significant difference in the number of patients taking more than 90% of the medications (67% of the control group vs 89% of the ECP group; P (is less than) .01). An intention-to-treat analysis confirmed these results. The most frequently reported adverse effect was gastrointestinal intolerance. Other factors reported to affect compliance included the frequency of dosing and the number of pills. Conclusions: These findings suggest that although adverse effects were common, most patients were able to complete 60% or more of the 2-week regimen. An ECP further improved the percentage of medications taken. Arch Intern Med. 1999;159:2312-2316

Namias N., Harvill S., Ball S., McKenney M. G., Salomone J. P. and Civetta J. M. “**Cost and morbidity associated with antibiotic prophylaxis in the ICU.[comment].**” *Journal of the American College of Surgeons*. (1999) **188**(3): 225-30.

BACKGROUND: Although the high cost and inappropriate use of antibiotics have been documented before, we are not aware of any data on nonsurgical site infectious morbidity associated with prolonged courses of prophylactic antibiotics (PA). STUDY DESIGN: Data regarding antibiotic orders were collected using a custom designed microbiology database in the Surgical Intensive Care Unit of a teaching hospital from October 1, 1995 through April 30, 1997. The database was retrospectively reviewed. The cost of PA in excess of 1 day was calculated. Frequency of bacteremia and line infections

were compared in patients receiving 1 day or less of PA versus more than 4 days of PA. RESULTS: Sixty-one percent of PA orders were continued for more than 1 day. Cost of PA beyond 1 day totaled \$44,893. Bacteremia and line infection were more frequent in the patients receiving more than 4 days of PA. CONCLUSIONS: There was poor compliance with the protocol of stopping PA at 24 hours. The cost of noncompliance was \$44,893. There were more bacteremias and line infections in patients with duration of PA of more than 4 days.

Snyder D. C. and Chin D. P. “**Cost-effectiveness analysis of directly observed therapy for patients with tuberculosis at low risk for treatment default.**” *American Journal of Respiratory & Critical Care Medicine.* (1999) **160**(2): 582-6.

To determine the incremental cost of directly observed therapy (DOT) for patients with tuberculosis at low risk for treatment default, we applied a model of DOT effectiveness to 1,377 low-risk patients in California during 1995. The default rate for this cohort, which consisted of those with no recent history of substance abuse, homelessness, or incarceration, was 1.7%. The model predicted that DOT and self-administered therapy (SAT) cured 93.1 and 90.8% of these patients, respectively. DOT would initially cost \$1.83 million more than SAT, but avert \$569,191 in treatment cost for relapse cases and their contacts, for a net incremental cost of \$1.27 million (\$919 per patient treated), or \$40,620 per additional case cured. The cost-effectiveness of DOT was sensitive to the default rate and relapse rate after completing SAT. DOT would generate cost savings only when the default and relapse rates were more than 32.2 and 9.2%, respectively. Given the low default rate and resulting high incremental cost of DOT, provision of DOT to low-risk patients in California should be evaluated in the context of resource availability, competing program priorities, and program success in completing self-administered therapy with a low relapse rate.

Weis S. E., Foresman B., Matty K. J., Brown A., Blais F. X., Burgess G., et al. “**Treatment costs of directly observed therapy and traditional therapy for Mycobacterium tuberculosis: a comparative analysis.**” *International Journal of Tuberculosis & Lung Disease.* (1999) **3**(11): 976-84.

OBJECTIVE: Treatment of tuberculosis is a time-consuming and expensive process, often complicated by patient non-adherence. Directly observed therapy (DOT), an out-patient management strategy designed to ensure adherence, is not widely used because it is perceived to be too expensive. This study compared costs of tuberculosis treatment in DOT to the same factors in traditional therapy. DESIGN: A retrospective economic evaluation of 659 tuberculosis cases was reported to a major metropolitan county public health department between 1980 and 1994. Out-patient costs, in-patient costs and the cost impact of relapse and acquired resistance were estimated in 1995 dollars. RESULTS: Treatment costs were lower with DOT: \$15,670 per case for in-patient care and \$700 per case for out-patient care ( $P < 0.001$ ). These cost differences resulted from shorter therapy duration (334 vs 550 days), fewer patient hospitalizations (58 vs 75%) and shorter hospital stays (26 vs 55 days per hospitalized patient). Relapse or acquired resistance occurred in 10.9% of patients and accounted for 35.7% of cost with traditional therapy, as compared to 1.2% of patients and 6.0% of cost with observed therapy. CONCLUSIONS: Directly observed therapy is less costly than traditional therapy.

Davidson B. L. “**A Controlled Comparison of Directly Observed Therapy vs Self-administered Therapy for Active Tuberculosis in the Urban United States()**.” *Chest* (1998) **114**(5): 1239(1).

Gourevitch M. N., Alcabes P., Wasserman W. C. and Arno P. S. “**Cost-effectiveness of directly observed chemoprophylaxis of tuberculosis among drug users at high risk for tuberculosis.**” *International Journal of Tuberculosis and Lung Disease* (1998) **2**(7): 531-540.

SETTING: A methadone treatment program with on-site medical care in the Bronx, New York. OBJECTIVE: To define whether costs associated with directly observed preventive therapy (DOPT) of tuberculosis are justified by cases and costs of tuberculosis prevented among persons at high risk for active disease. DESIGN: Detailed data were collected on drug users in treatment regarding human immunodeficiency virus (HIV) and tuberculosis infection and disease, and costs of screening, chemoprophylaxis, direct observation and treatment of active disease. The cost-effectiveness of providing DOPT to this population was modeled. RESULTS: We assessed the impact of providing DOPT to 151 eligible persons. Assuming 65% isoniazid effectiveness, and incorporating costs of screening, observed chemoprophylaxis and clinical monitoring, a net savings in tuberculosis-related hospital costs of \$285 284 (\$563 per person screened) was associated with DOPT (\$10274 per case prevented). Direct observation of chemoprophylaxis proved cost-effective if associated with even a 10% increment in overall isoniazid effectiveness compared with self-administered chemoprophylaxis. DOPT costs per tuberculosis case averted remained below the in-patient costs of a single case of drug-sensitive disease across a range of parameter values. CONCLUSIONS: Providing DOPT is a highly cost-effective intervention for drug users in treatment. Commitment of additional resources required for DOPT should be given priority in this and other populations at high risk for tuberculosis.

Handsfield H. H. and Stamm W. E. “**Treating chlamydial infection: compliance versus cost.[comment].**” *Sexually Transmitted Diseases*. (1998) **25**(1): 12-3.

Palmer C. S., Miller B., Halpern M. T. and Geiter L. J. “**A model of the cost-effectiveness of directly observed therapy for treatment of tuberculosis.**” *Journal of Public Health Management & Practice*. (1998) **4**(3): 1-13.

A hypothetical cohort of 25,000 TB patients and their contacts were followed for a 10-year period; rates of treatment default, infectiousness following partial treatment, relapse, hospitalization, and development of drug-resistant TB were included. The average cost per case cured was \$16,846 with 15% of patients starting DOT, \$17,323 with 100% starting DOT, and \$20,106 with none starting DOT. The incremental cost per additional case cured was \$24,064 when all patients, started treatment on DOT, indicating that outpatient DOT provides a cost-effective method of improving health outcomes for TB patients and their contacts while controlling direct costs.

Zwarenstein M., Schoeman J. H., Vundule C., Lombard C. J. and Tatley M. “**Randomised controlled**

**trial of self-supervised and directly observed treatment of tuberculosis.”** *The Lancet* (1998): 1340(1).

Self-supervised drug therapy may be as effective, and less expensive, than directly observed therapy (DOT) for tuberculosis. DOT requires patients to take their antibiotic medication in the presence of a health care worker to ensure compliance with drug treatment. Researchers in South Africa compared DOT with self-supervised drug treatment in the care of 216 adults with tuberculosis. Sixty percent of self-supervised patients completed their treatment, compared to 54% of patients in DOT. The \*cost\* of treating patients without directly observing their care is lower than DOT.

Boyles S. **“DOT more cost effective than self-administered therapy. (directly observed therapy).”** *AIDS Weekly Plus* (1997): p25(2).

Burman W. J., Cohn D. L., Rietmeijer C. A., Judson F. N., Sbarbaro J. A. and Reves R. R. **“Noncompliance with directly observed therapy for tuberculosis: epidemiology and effect on the outcome of treatment.”** *Chest* (1997) v111(n5): p1168(6).

Giuffrida A. and Torgerson D. J. **“Should we pay the patient? Review of financial incentives to enhance patient compliance.”** *British Medical Journal* (1997) v315(n7110): p703(5).

Cash payments to patients seem to work as \*cost\* -effective incentives to improve compliance with their treatment. Non-compliance in cases such as those of patients with infectious disease can be both dangerous to community health and ultimately much more expensive than an incentive payment. Non-compliance can lead to drug resistant strains of bacteria or infection of others as well as higher treatment \*costs\* later in the progression of the disease, for example, in treating tuberculosis. In all situations, non-compliance wastes limited medical resources.

Klaus B. D. and Grodesky M. J. **“Assessing and Enhancing Compliance with Antiretroviral Therapy.”** *Nurse Practitioner* (1997) 22: 211-212.

<Abstract> The importance of \*patient\* \*compliance\* during therapy with antiretroviral agents in the treatment of human immunodeficiency virus (HIV) infection is discussed, and the \*costs\* and various forms of \*noncompliance\*, different ways to assess compliance, and various means to assist patients with medication compliance that take into account cognitive, behavioral, and social factors are considered.

Pablos-Mendez A., Knirsch C. A., Barr R. G., Lerner B. H. and Frieden T. R. **“Nonadherence in tuberculosis treatment: Predictors and consequences in New York City.”** *American Journal of Medicine* (1997) 102(2): 164-170.

BACKGROUND: Poor adherence to antituberculosis treatment is the most important obstacle to



tuberculosis control. **PURPOSE:** To identify and analyze predictors and consequences of nonadherence to antituberculosis treatment. **PATIENTS AND METHODS:** Retrospective study of a citywide cohort of 184 patients with tuberculosis in New York City, newly diagnosed by culture in April 1991 before the strengthening of its control program and followed up through 1994. Follow-up information was collected through the New York City tuberculosis registry. Nonadherence was defined as treatment default for at least 2 months. **RESULTS:** Eighty-eight of the 184 (48%) patients were nonadherent. Greater nonadherence was noted among blacks (unadjusted relative risk [RR] 3.0, 95% confidence interval [CI] 1.1 to 8.6, compared with whites), injection drug users (RR 1.5, 95% CI 1.1 to 2.0), homeless (RR 1.4, 95% CI 1.0 to 1.8), alcoholics (RR 1.4, 95% CI 1.0 to 1.9), and HIV-infected patients (RR 1.4, 95% CI 1.1 to 1.9); also, census-derived estimates of household income were lower among nonadherent patients ( $P = 0.018$ ). In multivariate analysis, only injection drug use and homelessness predicted nonadherence, yet 46 (39%) of 117 patients who were neither homeless nor drug users were nonadherent. Nonadherent patients took longer to convert to negative culture (254 versus 64 days,  $P < 0.001$ ), were more likely to acquire drug resistance (RR 5.6, 95% CI 0.7 to 44.2), required longer treatment regimens (560 versus 324 days,  $P < 0.0001$ ), and were less likely to complete treatment (RR 0.5, 95% CI 0.4 to 0.7). There was no association between treatment adherence and all-cause mortality. **CONCLUSIONS:** In the absence of public health intervention, half the patients defaulted treatment for 2 months or longer. Although common among the homeless and injection drug users, the problem occurred frequently and unpredictably in other patients. Nonadherence may contribute to the spread of tuberculosis and the emergence of drug resistance, and may increase the cost of treatment. These data lend support to directly observed therapy in tuberculosis.

Sewing K. F. “**Modern antibiotic therapy of respiratory tract infections: Cost reduction by optimized disease management and patient compliance [3]. [German].**” *Antiinfective Drugs & Chemotherapy* (1997) **15**(2-3): 120.

Wandstrat T. L. and Kaplan B. “**Pharmacoeconomic impact of factors affecting compliance with antibiotic regimens in the treatment of acute otitis media.**” *Pediatric Infectious Disease Journal* (1997) **16**(2 SUPPL.): S27-S29.

**Background.** The total cost of treating otitis media in the United States alone is estimated at >3.5 billion dollars annually. Therefore treatment approaches that reduce the cost of managing otitis media can have a large impact on overall health care costs. **Methods.** In this study cost effectiveness factors of various antimicrobial agents, such as adverse events and overall patient acceptance, were examined. **Results.** Decreased patient acceptance and higher incidence of adverse events had a negative impact on the cost of treatment. Amoxicillin/clavulanate, cefprozil, erythromycin/sulfisoxazole and trimethoprim/sulfamethoxazole were found to be associated with decreased patient acceptance compared with cefixime. Cefixime also had the lowest number of adverse events of any of the drugs used. Amoxicillin had the lowest total cost for a single course of treatment, exclusive of costs of recurrence, which were examined in a previous study. **Conclusion.** This study concluded that in cases in which several antibiotics may be clinically effective, comparative tolerability and patient acceptance data should be considered for selection of appropriate therapy. High compliance and lower morbidity can result in lower costs and better quality of life.

Morse D. I. “**Directly observed therapy for tuberculosis: spend now or pay later.(Editorial).**” *British Medical Journal* (1996) **312**(7033): 719(2).

Woodward W. C. “**Should directly observed therapy be considered for treatment of HIV?(Letter to the Editor).**” *JAMA, The Journal of the American Medical Association* (1996) **276**(24): 1956(1).

MacDonald T. M. “**The economic evaluation of antibiotic therapy: Relevance to urinary tract infection.**” *Journal of Antimicrobial Chemotherapy* (1994) **33**(SUPPL. A): 137-145.

Economic analyses of health care interventions can be performed with various levels of sophistication but all aid in decision-making processes which determine funding priorities. Pharmacoeconomics is the application of health economic techniques to the evaluation of drug therapy. In this article the pharmacoeconomic principles underlying the rational choice of an antibiotic for the treatment of urinary tract infections are discussed. Examples of pharmacoeconomic, adverse reaction and noncompliance studies are quoted to illustrate these principles. Efficacy and freedom from adverse effects are the principal determinants of favourable cost-effectiveness ratios, rather than antibiotic costs alone. Doctors should bear this in mind when choosing drugs to treat urinary tract infection.

Helitzer-Allen D. L., McFarland D. A., Wirima J. J. and Macheso A. P. “**Malaria chemoprophylaxis compliance in pregnant women: A cost-effectiveness analysis of alternative interventions.**” *Social Science & Medicine* (1993) **36**(4): 403-407.

Compliance to malaria chemoprophylaxis among pregnant women in Malawi has historically been low. Three separate interventions, based upon an ethnographic study of malaria beliefs among pregnant women in Malawi, were introduced to increase compliance to the malaria chemoprophylaxis program provided by the Ministry of Health. Each intervention consisted of a health education message and an antimalarial drug. A cost-effectiveness analysis of the interventions was conducted to compare the interventions as alternative strategies to increase compliance among pregnant women.

Prince B. S., Goetz C. M., Rihn T. L. and Olsky M. “**Drug-related emergency department visits and hospital admissions.**” *American Journal of Hospital Pharmacy*. (1992) **49**(7): 1696-700.

The incidence and causes of drug-related hospital admissions and visits to an emergency department were evaluated. A retrospective chart review was conducted to identify drug-related visits and admissions for all patients who visited the emergency department of a 517-bed tertiary-care institution during a four-month period. Drug-related illnesses were classified as adverse drug reaction (ADR), overdose or abuse, noncompliance, drug interaction, or toxicity. Patient data included demographic characteristics, medication history, serum drug concentrations, length of hospital stay, and hospital admission charges. Of 10,184 patients who visited the emergency department, 293 (2.9%) had drug-related illnesses; 71 (24%) of these

patients were admitted. The drug classes most commonly involved were drugs of abuse (23.2%), anticonvulsants (17.1%), antibiotics (12.6%), respiratory drugs (8.9%), and pain medications (8.9%). The most common category of drug-related illness was overdose or abuse (35%) followed by noncompliance (28%), ADR (28%), toxicity (8%), and drug interaction (1%). The average length of stay for patients who were admitted was 5.8 days, and the average cost of admission was \$8888. Drug-related illnesses accounted for 2.9% of hospital admissions and visits for patients in the emergency department. The most commonly identified drug-related illnesses were overdose or abuse, noncompliance, and ADRs; the drug classes most commonly implicated were drugs of abuse, anticonvulsants, and antibiotics.

Sanson-Fisher R., Bowman J. and Armstrong S. “**Factors affecting nonadherence with antibiotics.**” *Diagnostic microbiology and infectious disease* (1992) **15**(4 Suppl): 103s-109s.

\*Nonadherence\* with antibiotic therapy has profound implications both for patient health and the health care system that bears the financial \*costs\* incurred. Significant levels of \*nonadherence\* with antibiotic prescriptions have been demonstrated. Of the many proposed variables involved, those that are potentially modifiable relate to aspects of the doctor-patient interaction and drug regimen. Despite the potential for intervention with these variables, there have been very few methodologically sound studies examining their effect on adherence with either medications generally or antibiotics specifically. Only two studies were located that had tested the effectiveness of reduced complexity of antibiotic dosage schedules. The results suggest that the less complex the schedule, the greater is the adherence. Both practitioners and patients must be encouraged to use and accept simpler dosage schedules, preferably once-daily schedules wherever possible. The paucity of well-controlled studies to date highlights the need for further research evaluating intervention strategies that utilize variations in dosage schedule and elements of the doctor-patient interaction to improve adherence with antibiotic medications.

Nixon S. A. “**Vulvovaginitis: the role of patient compliance in treatment success.**” *American Journal of Obstetrics & Gynecology*. (1991) **165**(4 Pt 2): 1207-9.

Vulvovaginitis caused by *Candida* organisms accounts for a large number of annual office visits to physicians, often for recurrent infection. Despite the availability of many effective antifungal preparations, treatment failures continue to occur because of poor compliance with therapy. Several factors may foster noncompliance. Those involving the patient include denial of illness, misconceptions regarding the nature of the infection or its treatment, a misunderstanding of symptomatic relief versus microbiologic cure, dislike of the dosage form, nonsupport of the sexual consort, or intolerance of side effects. The cost of treatment, inconvenient dosage form, and prolonged duration of therapy may also contribute to noncompliance. This article offers suggestions for optimizing compliance and successful treatment. Two perceived means to this end are improved patient education and the use of short-term therapy in convenient dosage form.

### **Gastrointestinal Diseases**

Levy R. L. and Feld A. D. “**Increasing patient adherence to gastroenterology treatment and prevention regimens.**” *American journal of gastroenterology* (1999) **94**(7): 1733-42.

Many gastroenterology treatments would be minimally effective if patients did not adhere to prescribed therapeutic regimens. However, considerable evidence exists that patients often do not adhere. Factors associated with \*nonadherence\* include the physician's or other health care provider's behavior, the prescribed regimen, and the illness. These factors affect patient adherence such that: 1) patients do not have the skills or knowledge necessary to complete an assignment; 2) patients do not believe that they will be helped by the prevention or intervention activity, or they do not accept the activity because they do not believe that its value will outweigh its \*costs\*; and 3) patients' environments are not supportive of, or interfere with, adherence. Strategies that can increase adherence include attention to the physician/patient relationship, direct skill training, setting up a reward structure, and reminders, among others. Specific methods that gastroenterology health care providers can utilize to enhance adherence in their practice are presented.

## **Mental Health**

Corrigan P. W. “**Adherence to anti-psychotic medications and Health Behavior theories.**” *Journal of Mental Health* (2002) **11**(3): 243-254.

Although most persons with serious mental illness benefit from anti-psychotic medications, many choose not to adhere to prescribed medication regimens. In this paper, we use health behavior (HB) theories to explain the phenomenon of noncompliance and pose corresponding interventions that might ameliorate the problem. Two factors from HB theories - value expectancies (perceptions of the cost and benefits of a disorder and its treatment) and social support (interactions with health care providers and family support) - were juxtaposed with the cognitive and social disabilities that result from psychosis and its treatment in the public mental health system. The combination of HB factors and disabilities was a useful heuristic for explaining noncompliance, as well as the positive impact of putative interventions that might improve adherence. Implications of this model for a HB paradigm that explains adherence to treatments in general are proffered.

Li J., McCombs Jeffrey S. and Stimmel Glen L. “**Cost of treating bipolar disorder in the California Medicaid (Medi-Cal) program.**” *Journal of affective disorders* (2002) **71**(1-3): 131-9.

**BACKGROUND:** Bipolar disorder affects approximately 1% of the population at an annual \*cost\* of \$45 billion in the US. Estimates of \*non\*-*\*compliance\** with mood stabilizer therapy range as high as 64%. The objective of this study was to document the use patterns with mood stabilizers achieved by patients with bipolar disorder and to estimate the direct health care \*costs\* associated with sub-optimal drug therapy. **METHODS:** Paid claims for 3,349 California Medicaid patients with bipolar disorder were used to document the use patterns for mood stabilizers achieved by patients with bipolar disorder. The impact of the patient's drug use patterns on likelihood of antipsychotic or antidepressant use within 1 year and health care \*costs\* incurred during the first posttreatment year were also estimated. **RESULTS:** Only 42.4% of patients used a mood stabilizer during the first posttreatment year; over 60% of treated patients switch or augment their initial therapy within 1 year, and only 5.5% of patients used a mood stabilizer consistently for 1 year. Direct health care \*costs\* were significantly higher among those patients who delayed or did not use mood-stabilizing agents during the first year. **LIMITATIONS:** Medi-Cal covers poor and disabled patients and is not representative of the general population. Paid claims data do not include clinical markers for severity of illness or treatment response. **CONCLUSIONS:** Suboptimal use patterns for mood stabilizing medications were frequent and costly. Strategies to improve compliance with mood stabilizer regimens, along with new treatment options, are needed to improve treatment outcomes.

Love R. C. “**Strategies for increasing treatment compliance: The role of long-acting antipsychotics.**” *American Journal of Health-System Pharmacy* (2002) **59**(SUPPL. 8): S10-S15.

Increased patient compliance with antipsychotic medications is associated with increased efficacy and reduced rates of rehospitalization. It can improve treatment outcomes for patients and reduce costs for society. An understanding of the reasons for noncompliance is essential in formulating strategies to provide better health and economic outcomes. Time-tested strategies such as addressing adverse effects, educating patients, and forming patient-provider alliances with those receiving medications can have a dramatic impact on compliance. Depot antipsychotics have been the mainstay of treatment for patients with schizophrenia

who are known to be noncompliant. These agents are especially effective when combined with social support. Atypical antipsychotics, with their improved efficacy and tolerability, appear to increase compliance and reduce rehospitalization compared with conventional oral and depot agents. A new long-acting formulation of an atypical antipsychotic agent combines the advantages of depot drugs and atypical agents. However, such a drug also poses challenges in the changing setting of community mental health. These challenges present pharmacists with an opportunity to assume new roles in the management of patients requiring antipsychotic therapy.

Misdrahi D., Llorca P. M., Lancon C. and Bayle F. J. **“Compliance in schizophrenia: Predictive factors, therapeutical considerations and research implications. [French].”** *Encephale* (2002) **28**(3 I): 266-272.

Compliance has been defined as the extent to which a person's behavior coincides with the medical advice given. Medication compliance is one of the foremost problems affecting neuroleptic efficacy in psychiatric patients. Since chlorpromazine introduction in 1952, antipsychotics are the principal element of schizophrenia treatment. Actually progress links to the use of new antipsychotics are conditioned by quality of compliance. The problem of nonadherence to medication could concern 50 % of prescription. The reported incidence of non-compliance with antipsychotic medication ranges from 11 to 80 %. In a two thirds of case rehospitalization is the result of complete or partial noncompliance. After one year of first hospitalisation, 40 % of relapse results from non adherence to medication. Medication adherence problems increase hospitalisation, morbidity and mortality. Social consequences, professional problems and family troubles linked to hospitalisations lead to low quality of life for patients and high cost for society. There are three main methods of measuring compliance. These include patient and clinical self-report, pill counts, and biological measures. Self-report methods are generally the most cost-effective and time-efficient way of obtaining an indication of compliance. In psychiatric research, the most commonly used self-report measure of compliance is the Drug Attitude Inventory (DAI) originally devised by Hogan et al. On the basis of criticism concerning DAI reliability, a new questionnaire of medication compliance was proposed: the [left pointing guillemet] Medication Adherence Rating scale [right pointing guillemet] (MARS). The main goal of compliance evaluation is to quantify this phenomenon with accuracy and to find predictive factors of medication non-adherence. Three types of factors influencing compliance are identified: factors due to medications, factors linked to patients and factors depending on the therapeutic relation with the clinician. Tolerance is considered as the principal reason explaining a bad compliance. Neurologic, endocrine and anti-cholinergic side-effects are the first fact of treatment stop. Medication prescription complexity is although important to take under consideration. Some psychotic's symptoms, comorbid addictive behavior, poor insight are mentioned in the case of noncompliance. Some effective actions to improve compliance are described. Information and communication with the patient, simplification of therapeutic plan, consultation planning and account of side effect are simple and effective actions. Social support is very important for improvement of compliance. The communication attitude of the clinician, therapeutic relation and prescription use are main points of compliance. Compared to a conventional care, psychoeducational programmes of compliance show their superiority. More research on compliance evaluation is needed. Information and tools must be proposed to practitioners.

Perkins D. O. **“Predictors of noncompliance in patients with schizophrenia.”** *Journal of Clinical*

*Psychiatry*. (2002) **63**(12): 1121-8.

**BACKGROUND:** Around 50% of patients with schizophrenia do not fully comply with treatment, and noncompliance is linked to relapse, rehospitalization, poor outcome, and high economic costs. The health belief model views noncompliance as a decision made by the patient, arrived at after weighing the perceived risks and benefits of treatment. **DATA SOURCES:** A MEDLINE search for the years 1980-2002 using combinations of the keywords schizophrenia, compliance, adherence, antipsychotics, tolerability, and side effects was used to identify articles investigating the factors influencing compliance in schizophrenia. **RESULTS:** Many factors influence compliance, including those that affect patients' beliefs about their illness and the benefits of treatment (e.g., insight into illness, belief that medication can ameliorate symptoms), perceived costs of treatment (e.g., medication side effects), and barriers to treatment (e.g., ease of access to treatment, degree of family or social support). Medication side effects that are distressing to patients and linked to noncompliance include extrapyramidal side effects, neuroleptic dysphoria, akathisia, sexual dysfunction, and weight gain. Compliance can be improved by cognitive-behavioral therapies, such as compliance therapy, and other psychosocial interventions associated with improved social functioning and a lower risk of rehospitalization. Treatment adherence may also be improved by use of atypical antipsychotics with few perceived side effects. **CONCLUSION:** By considering the factors leading to noncompliance and adopting a comprehensive strategy for improving compliance, encompassing psychosocial intervention and optimum choice of medication, the management of schizophrenia could be greatly improved. [References: 62]

Pomerantz J. M. "**Patient Noncompliance with Medication: Antidepressants.**" *Drug Benefit Trends* (2002) **14**(4): 22-23.

<Abstract> This article discusses the reasons for \*noncompliance\* with antidepressants, namely, the low efficacy of the drugs and the side effects associated with the drugs.

Crown W. H., Treglia M., Meneades L. and White A. "**Long-term costs of treatment for depression: impact of drug selection and guideline adherence.**" *Value in Health*. (2001) **4**(4): 295-307.

**OBJECTIVES:** This paper examines three processes: SSRI antidepressant choice, adherence to treatment guidelines, and long-term health care expenditures associated with antidepressant treatment for patients with a diagnosis of depression. **METHODS:** Patient records were abstracted from a medical claims database covering employer-provided health care plans. Treatment episodes required a 6-month antidepressant-free prior period; initial treatment with sertraline, paroxetine or fluoxetine; and data on direct medical costs over the 24 months following the initial prescription. The multivariate model of drug selection, patient adherence to antidepressant use guidelines, and cost was subjected to specification testing to rule out the possibility that nonrandom initial antidepressant selection might lead to sample selection bias. Further tests indicated that the results were free of bias due to a possible correlation between antidepressant selection and use of the medication, or because of the endogeneity of use patterns in the process driving cost. However, there was evidence of unobserved variables correlated with both achieving guideline adherent use and expenditures, which might have led to sample selection bias. **RESULTS:** Subjects who met the study criteria included 796 initiating therapy with sertraline, 352 with paroxetine, and 882 with fluoxetine. Fluoxetine patients were significantly more likely than sertraline or paroxetine patients to achieve a use pattern that was consistent with guidelines for treating depressive disorder ( $p < .05$ ). There were no

statistically significant differences between the three treatment cohorts in total direct health care expenditures over the 2-year period ( $p < .05$ ), and depression-related expenditures, other mental health expenditures, and non-mental health care expenditures did not show significant differences across the treatments ( $p < .05$ ). Natural logged values of antidepressant drug expenditures were predicted to be highest for fluoxetine, followed by sertraline, then paroxetine ( $p < .01$ ). Predicted log values of mental health expenditures were lower for sertraline relative to fluoxetine. **CONCLUSIONS:** Fluoxetine patients had the highest likelihood of using antidepressant medication according to treatment guidelines that were developed to assure quality care. This benefit was achieved without incurring greater total health care expenditures.

Cruz M. and Cruz R. F. **“Compliance and costs in a case management model.”** *Community Mental Health Journal.* (2001) **37**(1): 69-77.

Case management (CM) team models are a well-established mode for delivery of mental health services to individuals with serious and persistent mental illnesses. Although numerous aspects of CM models have been investigated, a neglected component is compliance to outpatient appointments. This pilot, quality assurance study examined the relationship between compliance to psychiatric outpatient appointments and costs in an integrated service delivery system using CM for treating seriously and persistently mentally ill individuals. Two groups of participants were randomly selected based on a single compliance data point and examined using cross-sectional and longitudinal methods. Results revealed relatively high compliance rates that were significantly different between groups over time. However, no differences in costs for services over time, and no demographic variables predictive of noncompliance (i.e., age, miles from residence to site, ethnicity, diagnostic group, level of functioning) were identified. Implications for CM in public mental health integrated service delivery systems, and quality assurance studies are discussed.

Svarstad B. L., Shireman T. I. and Sweeney J. K. **“Using drug claims data to assess the relationship of medication adherence with hospitalization and costs.”** *Psychiatric Services* (2001) **52**(6): 805-811.

**Objective:** This naturalistic study used claims data to examine the relationship of medication nonadherence to hospital use and costs among severely mentally ill clients in Wisconsin. **Methods:** Data for 619 clients were obtained from Medicaid drug and hospital claims, county records, and case managers as part of a larger study in eight county-based mental health systems. Study participants were eligible for Medicaid, had a severe and persistent mental illness, were 18 years or older, and were receiving neuroleptics, lithium, or antidepressants. Drug claims were analyzed for a 12-month period to determine how regularly clients obtained their medications. Regression analyses were used to assess the effects of irregular medication use on any hospitalization for psychiatric problems, the number of days hospitalized, and hospital costs. The analyses controlled for several risk factors. **Results:** Among clients with schizophrenia or schizoaffective disorder, 31 percent used medications irregularly. The rates were 33 percent among those with bipolar disorder and 41 percent among those with other severe mental illnesses. In the total sample, irregular users had significantly higher rates of hospitalization than regular users (42 percent versus 20 percent), more hospital days (16 days versus four days), and higher hospital costs (\$3,992 versus \$1,048). Irregular medication use was one of the strongest predictors of hospital use and costs even after the analyses controlled for diagnosis, demographic characteristics, baseline functioning, and



previous hospitalizations. Conclusions: The availability of drug claims data and the ability to use them in predictive analyses make them a potentially useful data source in studies of medication adherence among persons with severe mental illness.

Chen R. S., Nadkarni P. M., Levin F. L., Miller P. L., Erdos J. and Rosenheck R. A. **“Using a computer database to monitor compliance with pharmacotherapeutic guidelines for schizophrenia.”**

*Psychiatric Services* (2000) **51**(6): 791-794.

Objective: The study examined whether prescription data from a computerized database could be used to measure conformance with treatment recommendations of the Schizophrenia Patient Outcomes Research Team (PORT). Methods: Records of an academically affiliated Veterans Affairs medical center were reviewed to identify patients who were hospitalized for schizophrenia and later seen for at least two outpatient visits in the six months after discharge (N = 353). Results: Conformance with only three of the 18 PORT pharmacotherapeutic recommendations could be measured with the available data. In regard to the recommendation to use antipsychotics other than clozapine as first-line treatments in acute episodes, 77 percent of the sample filled a prescription for an antipsychotic during the acute episode. Of these, only 6 percent received an antipsychotic regimen that included clozapine. In regard to the PORT recommendation on dosage during acute symptom episodes, 42 percent of the patients on conventional antipsychotics received dosages below the recommended range, 5 percent were above the range, and 53 percent were within it. In contrast, of the 53 patients who received clozapine or risperidone, 87 percent received prescriptions within the recommended dosage range. As for the recommendation to offer a trial of clozapine to patients who do not respond to adequate trials of two different classes of conventional drugs, 10 percent of patients who were switched from conventional regimens to clozapine were receiving dosages of conventional medications below the recommended range. Conclusions: Patient prescription data can provide preliminary measures to cost-effectively assess conformance with treatment. However, the approach has several limitations, and complementary analyses would enhance its usefulness.

Ciechanowski P. S., Katon W. J. and Russo J. E. **“Depression and diabetes: impact of depressive symptoms on adherence, function, and costs.”** *Archives of internal medicine* (2000) **160**(21): 3278-85.

BACKGROUND: Depression is common among patients with chronic medical illness. We explored the impact of depressive symptoms in primary care patients with diabetes on diabetes self-care, adherence to medication regimens, functioning, and health care \*costs\*. METHODS: We administered a questionnaire to 367 patients with types 1 and 2 diabetes from 2 health maintenance organization primary care clinics to obtain data on demographics, depressive symptoms, diabetes knowledge, functioning, and diabetes self-care. On the basis of automated data, we measured medical comorbidity, health care \*costs\*, glycosylated hemoglobin (HbA(1c)) levels, and oral hypoglycemic prescription refills. Using depressive symptom severity tertiles (low, medium, or high), we performed regression analyses to determine the impact of depressive symptoms on adherence to diabetes self-care and oral hypoglycemic regimens, HbA(1c) levels, functional impairment, and health care \*costs\*. RESULTS: Compared with patients in the low-severity depression symptom tertile, those in the medium- and high-severity tertiles were significantly less adherent to dietary recommendations. Patients in the high-severity tertile were significantly distinct from those in the low-severity tertile by having a higher percentage of days in \*nonadherence\* to oral

hypoglycemic regimens (15% vs 7%); poorer physical and mental functioning; greater probability of having any emergency department, primary care, specialty care, medical inpatient, and mental health \*costs\*; and among users of health care within categories, higher primary (51% higher), ambulatory (75% higher), and total health care \*costs\* (86% higher). CONCLUSIONS: Depressive symptom severity is associated with poorer diet and medication regimen adherence, functional impairment, and higher health care \*costs\* in primary care diabetic patients. Further studies testing the effectiveness and \*cost\*-effectiveness of enhanced models of care of diabetic patients with depression are needed. Arch Intern Med. 2000;160:3278-3285.

Delgado P. L. “**Approaches to the enhancement of patient adherence to antidepressant medication treatment.**” *Journal of Clinical Psychiatry* (2000) **61**(SUPPL. 2): 6-9.

The number of safe and effective medication treatments for depression has increased significantly over the past 10 years. Relative to the older tricyclic antidepressants and monoamine oxidase inhibitors, the newer medications offer comparable efficacy with fewer side effects and a markedly reduced risk for serious adverse effects. In spite of these benefits, and in spite of the extensive and successful efforts that have been made to inform the general population about the diagnosis and treatment of depression, many patients do not comply with treatment recommendations. Although specific factors such as side effects lead to high rates of noncompliance with medication treatment, noncompliance is a multifactorial phenomenon. The reasons for noncompliance can include rational and intentional decisions based on beliefs about the illness, concerns over side effects, ineffectiveness of treatment, costs of the medication, decisions influenced by the symptoms of the disorder, and many other cultural and attitudinal factors. Some of the important concepts that should be addressed with depressed patients are reviewed. Strategies aimed at informing patients about depression and its treatment and providing a collaborative treatment environment have the potential to significantly improve treatment outcome and treatment adherence.

Jefferson J. “**Patient Compliance in Depression.**” *American Journal of Managed Care* (2000) **6**(Feb Suppl 2): S31-S38.

<Abstract> Compliance and \*noncompliance\* are discussed as significant factors that contribute to the overall success and \*cost\* effectiveness of treatment of depression. Treatment must be seen as a 2 fold process involving continuation and maintenance of therapy to avoid relapses, which become more and more frequent after each depressive episode. Ensuring that patients comply with their medication regimens is a major challenge for physicians and requires patient understanding and cooperation. This article is 1 in a series of 5 that together qualify for 2 hours U.S. CE credit by the ACPE.

<Abstract2> 14

Jones M. T. and Cockrum P. C. “**A critical review of published economic modelling studies in depression.**” *Pharmacoeconomics* (2000) **17**(6): 555-583.

Depression is a very costly chronic disease. An important cost driver is treatment failure caused by patient noncompliance due, in part, to the adverse effects of medications. Additionally, inadequate duration of therapy and inappropriate medication switching contribute to the high cost of treatment. With the epidemiological data for depression demonstrating a rise in both incidence and prevalence over the last 20

years, and the fact that many of the newer antidepressants will see patent expiry in the near future, previous antidepressant cost-effectiveness scenarios are likely to change. As economic models play an increasingly important role in therapeutic decision-making, clinicians are encouraged to understand the strategies and methods involved in modelling antidepressant therapy. The aim of this review of the literature and synthesis of the various techniques important to the modelling of antidepressant therapies is for the practitioner to gain an increased understanding of the modelling methods previously utilised and be in a position to better evaluate future health economic models for the treatment of depression.

Lindstrom E. and Binglefors K. **‘Patient compliance with drug therapy in schizophrenia: Economic and clinical issues.’** *Pharmacoeconomics* (2000) **18**(2): 105-124.

The effectiveness of drug treatment in clinical practice is considerably lower than the efficacy shown in controlled studies. The lower effectiveness in practice presumably leads to lower cost effectiveness of drug treatment in real-life situations compared with that demonstrated by studies based on results from controlled trials. Improved cost effectiveness in routine clinical practice would be a significant advantage in the treatment of schizophrenia, one of the most costly diseases in society. The aetiology of schizophrenia is unknown, and there is no cure. The main aims of therapy with antipsychotic medication include the effective relief of symptoms without the introduction of adverse effects or serious adverse events, improved quality of life, cost effectiveness and a positive long term outcome. The older classical antipsychotic drugs do not always meet these requirements because of their well-known limitations, such as a lack of response in a subgroup of individuals with schizophrenia and intolerable adverse effects. There has long been a need for new antipsychotics that can ameliorate more symptoms and have no or few adverse effects. Some of the recently introduced antipsychotics have been shown to be more effective in certain clinical situations and to have a more favourable adverse effect profile than the classical antipsychotics. A major factor contributing to the lower effectiveness of drug treatment is noncompliance, which may be very high in schizophrenia. There are several factors influencing compliance, including drug type and formulation, patient, disease status, physician, health care system, community care and family. There have been very few studies of compliance improvement strategies in schizophrenia or, indeed, in medicine in general. Current methods are relatively complex and there are differing opinions on their effectiveness. There are several ways to increase compliance in schizophrenia - the evidence is strongest for psychoeducative methods, changing to a new drug or using a depot formulation. However, considerably more research is needed in the field of compliance strategies.

Coley K. C., Carter C. S., DaPos S. V., Maxwell R., Wilson J. W. and Branch R. A. **‘Effectiveness of antipsychotic therapy in a naturalistic setting: a comparison between risperidone, perphenazine, and haloperidol.’** *Journal of Clinical Psychiatry*. (1999) **60**(12): 850-6.

**BACKGROUND:** Therapeutic ineffectiveness and noncompliance with antipsychotic agents are major contributors to rehospitalization in patients with psychotic disorders. It is unknown whether risperidone's favorable side effect profile compared with that of the conventional antipsychotics results in improved compliance and reduced hospitalizations in a naturalistic setting. The purpose of this study was to test the hypothesis that treatment with risperidone reduces readmission rates and associated costs when compared with treatment with perphenazine or haloperidol. **METHOD:** Inpatients prescribed either risperidone, perphenazine, or haloperidol between January 1, 1995, and December 31, 1995, as a single

oral antipsychotic at discharge were retrospectively identified. Data were collected for that index hospitalization and for a 1-year follow-up period. Primary outcome measures included re-admission rates, changes in antipsychotic therapy, anticholinergic drug use, and costs. **RESULTS:** There were 202 evaluable patients (81 treated with risperidone, 78 with perphenazine, and 43 with haloperidol). Baseline demographics were similar between groups except that more patients in the risperidone group had a primary diagnosis of psychotic disorder or had been hospitalized in the year prior to study. The percentage of patients readmitted during the 1-year follow-up period was similar among drug groups (41% risperidone, 26% perphenazine, and 35% haloperidol) when controlled for baseline differences in diagnosis and hospitalization history ( $p = .32$ ). Anticholinergic drug use was more common in the haloperidol group ( $p = .004$ ). Mean yearly cost (drug + hospitalization) in the risperidone group was \$20,317, nearly double that in the other treatment groups ( $p < .001$ ). **CONCLUSION:** The results from this naturalistic study indicate that the high cost of risperidone is not offset by a reduction in readmission rates when compared with conventional antipsychotics.

Durrenberger S., Rogers T., Walker R. and De Leon J. **“The high costs of care for four patients with mania who were not compliant with treatment.”** *Psychiatric Services* (1999) **50**(12): 1539-1540+1542.

Perkins D. O. **“Adherence to antipsychotic medications.”** *Journal of Clinical Psychiatry*. (1999) **60**(Suppl 21): 25-30.

Taking antipsychotic medication as prescribed is one of the best means patients have of managing psychotic symptoms and preventing relapse. Yet, for various reasons, patients may discontinue taking their medication or skip doses, either occasionally or frequently. Among patients treated with conventional neuroleptics, approximately 40% stop taking their antipsychotic medication within 1 year, and about 75% stop taking the medication within 2 years. Although adverse effects play a large role in a patient's decision to discontinue antipsychotic therapy, other factors also have an effect. Using the health belief model, clinicians can assess the relative impact of various factors on medication adherence. This model posits that adherence to treatment is determined by the patient's assessment of the perceived benefits of treatment and risks of illness versus the costs of treatment (including adverse effects such as weight gain). Other factors in the decision are barriers to adherence and cues to act (i.e., reminders to take medication). Patients who believe the risks of treatment outweigh the benefits are likely to discontinue their medication and are candidates for intervention to increase adherence. [References: 54]

Breen R. and Thornhill J. T. **“Noncompliance with medication for psychiatric disorders: Reasons and remedies.”** *CNS Drugs* (1998) **9**(6): 457-471.

Noncompliance remains one of the greatest challenges when prescribing psychotropic medication and can render any treatment regimen wasteful and ineffective. While rates reported in studies of noncompliance vary widely, non-compliance can clearly increase treatment costs and prolong the duration of hospitalisation. Furthermore, noncompliance has a human cost in terms of morbidity and mortality. The reasons for noncompliance can be divided into 3 categories: medication-, patient- and provider-specific

factors. Adverse effects are likely to be the most common reason for patients to not comply with prescribed medication regimens. Ineffectiveness, complexity of the regimen and cost are also important medication-related factors contributing to noncompliance. The use of newer effective medications that have fewer adverse effects, drug holidays and low-dose treatment strategies may ameliorate adverse effects. In addition, the aggressive treatment of adverse effects such as antipsychotic-induced extrapyramidal syndromes and akathisia and tricyclic antidepressant-induced anticholinergic effects can increase compliance. In some cases, the complexity of regimens and the cost of medications can be reduced. The symptoms of a psychiatric disorder, the presence of substance abuse, and culture and attitude are patient-specific factors that may interfere with compliance. Noncompliance related to patient attitudes can be remedied through improving the patient-provider relationship, using depot antipsychotics and possibly medicating patients by force of judicial orders. Treatment of dual diagnosis, greater understanding of a patient's culture and the involvement of families in treatment can all be used to foster increased compliance. Psychosocial rehabilitation can also help increase compliance. Noncompliance increases when practitioners' views of their patients' prognosis or the effectiveness of treatment differ from that of their patients. How physicians communicate and what information they present to their patients and families plays a significant role in determining compliance. Physicians who believe in the medications they are prescribing and actively involve their patients in treatment decisions are likely to increase compliance. Expressing an understanding, empathic and caring manner will further promote compliance. Compliance should increase when good and clear lines of communication exist and patients feel free to ask questions. Specialised treatment options that practitioners can use to increase compliance include education, cognitive behavioural interventions, behaviour modification techniques, and using direct rewards for compliance. Psychotherapy can also be used as a tool to improve the practitioner-patient relationship.

Kihlstrom L. C. “**Managed care and medication compliance: Implications for chronic depression.**” *Journal of Behavioral Health Services and Research* (1998) **25(4)**: 367-376.

An emerging trend within managed care, 'disease management' (DM), will affect consumers and providers of mental health services, clinicians, and mental health administrators. Central to DM programs is the idea that particular diseases, especially chronic illnesses (including depression), can be 'carved out' and managed. Pharmaceutical benefit management (PBM) firms may specialize in managing prescription benefits for employers and other managed care organizations by using DM programs. However, given what is known from the theoretical and empirical literature on adherence to medication for chronic illnesses such as depression, it is questionable whether the techniques that are used by PBMs will be effective in managing illnesses that require a multifaceted approach to care. Because the management of antidepressants may have an impact on members of vulnerable populations (e.g., the elderly), more research is required on the approaches used by PBMs and on the cost and quality of the services provided.

Marder S. R. “**Facilitating compliance with antipsychotic medication.**” *Journal of Clinical Psychiatry*. (1998) **59(Suppl 3)**: 21-5.

Noncompliance with medication is common among patients who have schizophrenia and is a leading cause of rehospitalization in this population. Both standard and subjective risk-factor assessments have been used to identify patients who are likely to refuse or discontinue treatment. Noncompliant patients who have schizophrenia commonly have been treated with potent D2 dopamine-receptor antagonists and therefore

may have experienced extrapyramidal side effects. The newer antipsychotics (i.e., serotonin-dopamine antagonists) are efficacious in reducing the symptoms of schizophrenia without associated dysphoria and motor side effects. Clozapine and other newer antipsychotics may improve certain aspects of cognition. The improved psychiatric state and cognitive function may facilitate "involved compliance" as a result of increased insight, awareness, and judgment. These cognitive faculties allow patients to appreciate their improved state and take steps to maintain it. The periodic visits for blood monitoring mandated for clozapine therapy also facilitate the formation of a therapeutic alliance that allows the clinician to monitor compliance. Facilitating involved compliance this way among patients who have schizophrenia may reduce the cost of this disorder to society. [References: 57]

Peterson C. "Cost-Effective Schizophrenia Care Gaining Slow, Steady Recognition." *Managed Healthcare* (1998) 8(May): 36-38.

<Abstract> The economic assessment of antipsychotic strategies for schizophrenia in the managed care setting is discussed, including quality of life and medical changes, the impact of \*patient\* \*noncompliance\* with drug protocols, proof of \*cost\*-effectiveness, antipsychotic agents, and the use of drug formularies.

Hirschfeld R. M., Keller M. B., Panico S., Arons B. S., Barlow D., Davidoff F., et al. "The National Depressive and Manic-Depressive Association consensus statement on the undertreatment of depression.[comment]." *Jama*. (1997) 277(4): 333-40.

OBJECTIVE: A consensus conference on the reasons for the undertreatment of depression was organized by the National Depressive and Manic Depressive Association (NDMDA) on January 17-18, 1996. The target audience included health policymakers, clinicians, patients and their families, and the public at large. Six key questions were addressed: (1) Is depression undertreated in the community and in the clinic? (2) What is the economic cost to society of depression? (3) What have been the efforts in the past to redress undertreatment and how successful have they been? (4) What are the reasons for the gap between our knowledge of the diagnosis and treatment of depression and actual treatment received in this country? (5) What can we do to narrow this gap? (6) What can we do immediately to narrow this gap?

PARTICIPANTS: Consensus panel members were drawn from psychiatry, psychology, family practice, internal medicine, managed care and public health, consumers, and the general public. The panelists listened to a set of presentations with background papers from experts on diagnosis, epidemiology, treatment, and cost of treatment. EVIDENCE: Experts summarized relevant data from the world scientific literature on the 6 questions posed for the conference. CONSENSUS PROCESS: Panel members discussed openly all material presented to them in executive session. Selected panelists prepared first drafts of the consensus statements for each question. All of these drafts were read by all panelists and were edited and reedited until consensus was achieved. CONCLUSIONS: There is overwhelming evidence that individuals with depression are being seriously undertreated. Safe, effective, and economical treatments are available. The cost to individuals and society of this undertreatment is substantial. Long suffering, suicide, occupational impairment, and impairment in interpersonal and family relationships exist. Efforts to redress this gap have included provider educational programs and public educational programs. Reasons for the continuing gap include patient, provider, and health care system factors. Patient-based reasons include failure to recognize the symptoms, underestimating the severity, limited access, reluctance to see a mental health care specialist

due to stigma, noncompliance with treatment, and lack of health insurance. Provider factors include poor professional school education about depression, limited training in interpersonal skills, stigma, inadequate time to evaluate and treat depression, failure to consider psychotherapeutic approaches, and prescription of inadequate doses of antidepressant medication for inadequate durations. Mental health care systems create barriers to receiving optimal treatment. Strategies to narrow the gap include enhancing the role of patients and families as participants in care and advocates; developing performance standards for behavioral health care systems, including incentives for positive identification, assessment, and treatment of depression; enhancing educational programs for providers and the public; enhancing collaboration among provider subtypes (eg, primary care providers and mental health professionals); and conducting research on development and testing of new treatments for depression. [References: 38]

Budd R. J., Hughes I. C. and Smith J. A. "**Health beliefs and compliance with antipsychotic medication.**" *British Journal of Clinical Psychology*. (1996) **35**(Pt 3): 393-7.

The utility of the Health Belief Model to explain compliance with depot neuroleptic medication is examined. Perceived severity, susceptibility and benefits were found to be related to compliance, although costs were not. In addition, insight, knowledge about schizophrenia and health locus of control were not found to be related to compliance.

Anonymous. "**Patient compliance with SSRIs and tricyclic antidepressants.**" *American Family Physician* (1995) **52**(5): 1563(2).

Bebbington P. E. "**The content and context of compliance.**" *International clinical psychopharmacology* (1995) **9 Suppl 5**: 41-50.

Compliance is adherence to a prescribed and appropriate treatment, not necessarily pharmacological. \*Non\*- \*compliance\* may occur in up to 50% of patients with schizophrenia who are prescribed neuroleptics. It may be commoner in young people, particularly if male or from certain ethnic minority groups, but demographic factors are relatively unimportant. Clinical features such as positive symptoms are associated with \*non\*- \*compliance\* but the strongest clinical relationship is with a "dual diagnosis", usually with an associated alcohol abuse. Patients' and relatives' beliefs about schizophrenia and about medication are of considerable importance in determining compliance, and can be understood in terms of the "health belief model". However, a full understanding of \*non\*- \*compliance\* must take into account the relationship between patients and doctors in the context of the sick role. Several techniques for increasing compliance have been described, but they contain common elements--the provision of information within the context of a warm and equitable therapeutic relationship, preferably maintained over some time, and the use of the relationship to encourage and prompt compliance and to establish more productive views of the illness and medication. The \*costs\* of poor compliance to sufferers and to society alike are considerable, and effective ways of improving it are a crucial part of good management.

Lakshman M., Fernando D. and Kazarian S. S. **“Patient education in the drug treatment of psychiatric disorders. Effect on compliance and outcome.”** *CNS Drugs* (1995) **3**(4): 291-304.

Both drug therapy and psychosocial interventions have been shown to be effective treatments for psychiatric disorders. However, noncompliance with treatment regimens is a serious problem, and results in significant economic and psychosocial costs to the individual and society. Noncompliance can be caused by a number of factors, but can be positively affected by clinician-patient interactions and the patients' knowledge of and readiness to undergo treatment. Patient preparedness in the form of education about treatment, in general, and medication, in particular, is likely to be associated with improved adherence to treatment, psychological well-being and quality of life.

Weiden P. J. and Olfson M. **“Cost of relapse in schizophrenia.”** *Schizophrenia Bulletin*. (1995) **21**(3): 419-29.

To estimate the national annual cost of rehospitalization for multiple-episode schizophrenia outpatients, and to determine the relative cost burden from loss of medication efficacy and from medication noncompliance, the yearly number of neuroleptic-responsive multiple-episode schizophrenia inpatients in the United States who are discharged back to outpatient treatment was estimated. The cohort at risk for future relapse and rehospitalization was determined. The research literature on the expected rates of relapse for schizophrenia patients on maintenance antipsychotic medication was reviewed; in particular, monthly relapse rates under the optimal medication conditions of compliant patients taking optimal doses of a depot neuroleptic (optimal neuroleptic dose) and under the less optimal conditions of patients stopping medication (medication noncompliant) was estimated. Using established noncompliance rates from the literature, it became possible to estimate a "real world" rehospitalization rate for this cohort, as well as the relative burden accruing from loss of medication efficacy and from medication noncompliance. Finally, cost estimates for index hospitalizations and rehospitalizations were derived from data on national expenditures for inpatient mental health care. The monthly relapse rates are estimated to be 3.5 percent per month for patients on maintenance neuroleptics and 11.0 percent per month for patients who have discontinued their medication. Postdischarge noncompliance rates in community settings are estimated to be 7.6 percent per month. These estimates were entered into a survival analysis model to determine the real world relapse rate of this cohort. An estimated 257,446 multiple-episode (> or = two hospitalizations) schizophrenia patients were discharged from short-stay (< or = 90 days) inpatient units in the United States during 1986. The estimated aggregate baseline inpatient cost for the index hospitalizations of this cohort was \$2.3 billion (1993 dollars). Within 2 years after discharge, the aggregate cost of readmission approached \$2 billion. Loss of neuroleptic efficacy accounted for roughly 60 percent of the rehospitalization costs and neuroleptic noncompliance for roughly 40 percent. The economic burden due to loss of efficacy is relatively higher during the first postdischarge year, whereas the burden from noncompliance is higher in the second year. Because loss of medication efficacy and medication noncompliance act synergistically on relapse, substantial inpatient cost savings can be realized by linking better pharmacologic treatments of schizophrenia with more effective strategies to manage medication noncompliance.

Henry J. A. and Hale A. S. **“Selective serotonin reuptake inhibitors. Unsuccessful treatment may be related to non-response or non-compliance.”** *BMJ (Clinical research ed.)* (1994) **309**(6961): 1083; discussion 1085.



Kissling W. **“Compliance, quality assurance and standards for relapse prevention in schizophrenia.”** *Acta Psychiatrica Scandinavica, Supplement (1994)* **89**(382): 16-24.

The treatment and, above all, the prophylaxis of schizophrenic psychoses has made great progress in the last 40 years due to the introduction of the neuroleptics and the use of psychosocial treatment strategies. Unfortunately, the potentialities inherent in neuroleptic relapse prevention are far from being fully utilized. As a consequence, the relapse rate for this severe mental illness is still 3 times higher than it ought to be. In view of the severe consequences of this disease for each individual patient and his family, but also in view of the immense costs incurred by each relapse, we must not rest content with this situation. By use of compliance improving measures and quality assurance it would probably be possible within a few years to increase the efficiency of neuroleptic relapse prevention so far as to reduce the high relapse rates of schizophrenic patients at least by half. It is time we began trying.

Botelho R. J. and Dudrak R., 2nd. **“Home assessment of adherence to long-term medication in the elderly.”** *Journal of Family Practice.* (1992) **35**(1): 61-5.

**BACKGROUND.** Drug nonadherence to long-term medication is a common and poorly understood problem in the elderly. A study was conducted to assess whether elderly patients would accept a research assistant conducting pill counts in their homes, and to examine how nonadherence was associated with patient variables. **METHODS.** A letter and a telephone follow-up call were used to identify eligible patients (aged 65 years and over, with two or more chronic diseases). **RESULTS.** A total of 98 eligible patients were identified. Fifty-nine agreed to participate in the study. Of the 59 participants, 54.7% were nonadherent to their medication regimen. Nonadherence was defined as an overall mean level of compliance of less than 80%. Drug regimen nonadherence was associated with the inability to read medication labels (P less than .01), but not with impaired visual acuity, the number of prescribed medications, the type of medication container lid, depression, cognitive impairment, perceived health status, or the cost of medications. Frequency of drug administration affected patient adherence to the medication regimen. Mean adherence of patients to prescriptions for drugs to be taken once or twice daily was 72%, whereas drugs to be taken three or four times daily had a mean adherence rate of 54% (P less than .01). **CONCLUSIONS.** Using the simple pill count method on home visits, rates of nonadherence to long-term medication were comparable to those found in studies using electronic pill-counting devices. Larger studies are needed to clarify how other variables, in addition to patient inability to read medication labels, are associated with noncompliance with medication regimens for chronic diseases in elderly patients.

Goodman A. **“Medication noncompliance and the psychodynamics of pharmacotherapy.”** *Integrative Psychiatry* (1992) **8**(3): 181-190.

Following a statement of the extent and costs of medication noncompliance in psychiatry factors that may influence noncompliance are enumerated. The present essay focuses on psychodynamic factors in noncompliance an issue that has been less fully acknowledged and addressed than other factors. The discussion begins with a description of emotionally significant meanings for the patient that are associated with having medication prescribed ingesting medication and experiencing drug-induced changes. Emotionally

significant meanings for the physician that are associated with prescribing medication are also noted. The discussion proceeds to consider how these psychodynamic factors may then be expressed through noncompliance with the medication regimen modification of response to a drug and influences on the doctor-patient relationship. The final section addresses how this information may be applied in clinical practice with consideration of the different objectives of two general types of psychiatric practice to which it is applicable: pharmacotherapy with or without components of supportive psychotherapy and psychoanalytic or insight-oriented psychotherapy in which medication plays an adjunctive role. In either case the clinician must be able effectively to address psychodynamic factors in medication noncompliance lest the therapeutic value of modern psychopharmacology be unnecessarily diminished.

Kissling W., Fleischhacker W. W., Helmchen H., Pietsch-Breitfeld B., Buchkremer G., Linden M., et al. **“Optimising prophylactic treatment of schizophrenia by means of treatment standards and compliance improvement.”** *Pharmacopsychiatry* (1992) **25**(2): 69-71.

1. The course of schizophrenia under routine treatment conditions is still very unsatisfactory. Present relapse rates are unnecessarily high. 2. As we cannot wait until the cause for schizophrenia has been discovered and/or new highly effective antipsychotics with no side-effects have been found, we must try to optimise neuroleptic relapse prevention with classical neuroleptics. The two most important strategies in this context are, firstly, to formulate and implement optimal treatment standards and, secondly, to take measures to improve compliance. Among those practical steps that are primarily required, the following seem to be especially important: a) Consensus on treatment standards concerning the most important practical aspects of neuroleptic relapse prevention (indication, duration, minimal effective dosage etc.). This issue could be followed up by the German psychiatric associations. b) More psychoeducative groups for schizophrenic patients and their relatives. These groups should also be held in private practices and be financed by health insurance. c) More intensive research on compliance and during phase IV. If with the help of these measures 80% instead of the current 40% of schizophrenic patients would adhere to a continuous neuroleptic relapse prevention, half of all schizophrenic relapses could be prevented. Considering the enormous costs and - above all- the human suffering caused by these avoidable relapses, an attempt at optimisation of neuroleptic relapse prevention appears to be well worth-while.

Tarrier N. **“Some aspects of family interventions in schizophrenia. I: Adherence to intervention programmes.”** *British Journal of Psychiatry* (1991) **159**: 475(6).

Although treatment failures are important to the further definition and development of successful treatment strategies, they are rarely reported in the literature. Treatment failures can be classified into four groups: patient refusal, treatment drop-outs, treatment nonresponders, and those who relapse into illness. Treatment adherence problems (i.e., treatment drop-outs and refusal to participate in treatment) in family management programs for the treatment of families of schizophrenic patients are discussed. Research has shown that family involvement in the treatment of schizophrenics significantly reduces relapse when used in combination with medication. Unfortunately, however, families often lack the enthusiasm to participate in family interventions. Many of those who do not refuse to participate outright drop out of treatment prematurely. By studying treatment failures, psychologists have used a \*cost\*-benefit analysis model to describe the decision-making that leads to treatment noncompliance. Factors such as the family's perceived susceptibility to the illness (or perceived likelihood of relapse, in this case), the perceived effectiveness of the

intervention, and the perceived \*costs\*, including psychological, physical, and economic \*costs\*, have been identified as central. These must all be interpreted in the context of characteristics of the client, characteristics of the treatment regimen, features of the disease, the relationship between the health care provider and the client (or family), and the clinical setting. The determinants of adherence in individual families needs to be assessed and methods to maximize adherence need to be designed. Given the success of treating schizophrenics when family intervention is included, the problem of the family's adherence to treatment cannot be ignored. (Consumer Summary produced by Reliance Medical Information, Inc.)

Greengard S. **‘Doctor's orders; why don't patients do what their physicians say?’** *American Medical News* (1990) **33**(6): 29.

## **Neurological Disorders**

Garnett W. R. “**Antiepileptic drug treatment: outcomes and adherence.**” *Pharmacotherapy*. (2000) **20**(8 Pt 2): 191S-199S.

The goal in treating patients with epilepsy is a cost-effective approach to the elimination of seizures or a reduction in their number and frequency while avoiding drug interactions and side effects, so as to achieve the best possible quality of life. Among the desirable outcomes are an enhanced understanding of epilepsy by patients, caregivers, and society, and a lessening of the psychosocial risks of this disease. Patients fail to achieve their goals and outcomes when they fail to adhere to the drug regimen or when a less-than-adequate drug regimen is prescribed. To help improve adherence, once- or twice-daily formulations should be used. New antiepileptic drugs (AEDs) increase the possibility of effective treatment for a patient who initially fails therapy. Working together, patients and clinicians can maximize the effectiveness of AED therapy and the potential for achieving desired goals and outcomes. [References: 68]

Van Berge Henegouwen M. T. H., Van Driel H. F. and Kasteleijn-Nolst Trenite D. G. A. “**A patient diary as a tool to improve medicine compliance.**” *Pharmacy World and Science* (1999) **21**(1): 21-24.

Compliance is a well recognised but still unresolved health problem; improvement of compliance to treatment would increase cost-effectiveness, one of the current methods used to measure treatment compliance in a clinical drug trial is through the use of a patient diary. In order to interpret data in these diaries it is important to also assess how compliant patients are in completing diaries. Patient compliance of standard diary completion was measured in 69 patients with perennial rhinitis, who were randomized into a double blind, placebo controlled trial with a new corticosteroid drug. During 3 months the patients were instructed to complete a diary twice a day for the following parameters: rhinitis signs and symptoms, dosage times, concomitant medication, use of rescue medication and comments. Diaries were reviewed by the physician at scheduled visits. Twenty patients (30%) completed their diaries for all items perfectly, while 62 patients (94%) completed more than 95% of all items. The compliance of diary completion in a well controlled trial is high. Overall completion of the diary was not influenced by age, gender, race, use of concomitant medication or treatment failure. Significant correlations were found for study duration and physician. This study suggests that completion of a daily diary is positively correlated with patient compliance in medication intake. Physicians could consider using diaries to try to improve compliance. More explicit investigations are needed.

Leppik I. E. “**How to get patients with epilepsy to take their medication. The problem of noncompliance.**” *Postgraduate Medicine*. (1990) **88**(1): 253-6.

Noncompliance in patients with epilepsy is a serious hindrance to successful treatment. It can result in increased healthcare costs and put both the patients and others around them at unnecessary risk. Noncompliance should be considered whenever a patient has (1) an unexpected increase in number or severity of seizures, (2) serum levels of anticonvulsant medications below the expected range, or (3) a change in medical reimbursement systems. Effective intervention strategies are based on assessment of life-style issues and possible barriers to compliance. Communication with the patient about medication regimens and the value of treatment is extremely important, and a real partnership between physician and patient is needed to set and achieve goals.

Leppik I. E. “**Compliance during treatment of epilepsy.**” *Epilepsia*. (1988) **29**(Suppl 2): S79-84.

Noncompliance is a major factor in suboptimal control of epileptic seizures. As many as one-third to one-half of persons with epilepsy may be noncompliant. Noncompliance negates the usefulness of the advances made in the diagnosis and treatment of epilepsy and is perhaps the single most important factor in increasing the costs of care for people with epilepsy. Although the issue of noncompliance is very complex, realization that it is a multidimensional problem and varies from patient to patient should help individualize its evaluation and approach. Noncompliance can be described by three dimensions: behavior, extent, and intentionality. The simplest methods for determining noncompliance are measurements of the antiepileptic drug concentration and patient interview. Calculation of a coefficient of variation for serial anticonvulsant drug levels may be more descriptive, however. Education and devices to simplify dosing are the primary strategies for improving compliance.

Dodrill C. B., Batzel L. W., Wilensky A. J. and Yerby M. S. “**The role of psychosocial and financial factors in medication noncompliance in epilepsy.**” *International Journal of Psychiatry in Medicine*. (1987) **17**(2): 143-54.

Noncompliance in the taking of medication for a chronic disorder was related to emotional adjustment, psychosocial adjustment, ability to assume responsibility in life generally, and financial factors. Of 282 adults with epilepsy, eighty were identified by physicians' ratings as definitely compliant and forty-two as noncompliant. Results showed: 1) there were no differences between compliers and noncompliers in emotional adjustment; 2) noncompliance is not related to the cost of medications or to whether or not they are free; 3) noncompliance is more likely when patients report general financial distress, regardless of actual financial status; 4) persons with regular responsibilities in life also tend to take their medication regularly; and, 5) when reported financial distress and ability to assume responsibilities are considered simultaneously, the likelihood of noncompliance is four times as great in some patient groups as in others.

## **Respiratory Diseases**

Bender B. G. “**Overcoming barriers to nonadherence in asthma treatment.**” *Journal of Allergy & Clinical Immunology*. (2002) **109**(6 Suppl): S554-9.

Inadequate patient adherence to prescribed treatment regimens is a major cause of poor clinical outcomes in the treatment of asthma. Among children with asthma, adherence rates are often below 50%. Multiple treatment-, clinician-, and patient-related barriers prevent the achievement of satisfactory levels of adherence. Treatment-related barriers include prolonged and complex regimens, adverse effects, cost, and delayed onset of action. Clinician-related barriers include difficulty in scheduling, treatment by one different care giver after another, perceived clinician disinterest, and time constraints. Patient-related barriers include mild or severe asthma, poor understanding of the need for treatment, insufficient confidence in the clinician or medication, the presence of psychological problems, and low motivation to change behavior. Although all of these factors must be addressed to maximize adherence, patient motivation may be the most critical. This task falls primarily to clinicians (physicians, nurses, staff), and it requires thorough patient and care giver education, more frequent patient contact, and the development of a patient-clinician partnership dedicated to the effective treatment of asthma. [References: 16]

Ramsey S. D. “**Suboptimal medical therapy in COPD: exploring the causes and consequences.**” *Chest*. (2000) **117**(2 Suppl): 33S-7S.

Effective outpatient management of COPD requires prescription of and adherence to appropriate therapies. Although practice guidelines for outpatient management of COPD are widely available, evidence suggests that these guidelines are not being implemented widely in clinical practice. Furthermore, several studies have shown that patient compliance with recommended therapy is poor. This paper discusses several reasons why implementation of practice guidelines and adherence with prescribed therapies may be poor. Potential clinical and economic consequences of suboptimal management are reviewed. Although the evidence suggests that improved compliance with guideline-recommended practice will improve symptoms and disease-specific quality of life, further work needs to be done to establish the cost-effectiveness of chronic therapies for COPD relative to other chronic conditions. Without such data, managed care organizations will be reluctant to allocate scarce resources toward expensive guideline implementation programs for individuals with this condition. [References: 27]

Spector S. “**Noncompliance with asthma therapy - Are there solutions?**” *Journal of Asthma* (2000) **37**(5): 381-388.

Compliance with medication is essential if treatment is to be effective. Noncompliance can include underuse, overuse, and erratic use of medication; underuse being the most frequently reviewed. Generally estimated to be around 10%-46%, noncompliance with asthma therapy is a serious problem and studies have shown that compliance with the mainstay of asthma treatment, inhaled corticosteroids, is low. Oral therapy offers better compliance with treatment, with many patients preferring tablets to inhalers. Different ways to monitor compliance include monitoring prescriptions, counting tablets, measuring levels of medication in blood or urine, and measuring canister weight, although none are fully effective. Contributing factors to noncompliance with treatment include side effects, lifestyle, social and economic factors, method of drug delivery, and dosing. The consequences of these include increased symptoms and asthma

exacerbations, both of which can lead to increased morbidity. To improve compliance, causal factors need to be addressed; there is a need to educate patients and those who support them about the disease and the importance of following the physician's recommendations. Various self-management programs have also been established to improve patient compliance at a relatively low cost. Difficulties with treatment may be addressed by simplifying the treatment regimen using oral therapy. A relatively new class of oral agents, the leukotriene modifiers, is being increasingly used in clinical practice.

Weinstein A. G. "**Asthma treatment and noncompliance.**" *Delaware Medical Journal.* (2000) **72**(5): 209-13.

**RATIONALE:** Noncompliance with asthma treatments is a common cause of hospitalization. Currently, physicians in the emergency department can only diagnose noncompliance with asthma therapy by asking patients if they have taken their medication (i.e., the HONOR SYSTEM). Patients frequently "overstate" their compliance and subsequently receive unnecessary supplemental medication (p.o. corticosteroid) as well as hospitalization. However, because their noncompliant behavior goes unrecognized, these individuals are at risk for recurrent emergency care and death. It is for these reasons that drug monitoring to identify compliance status should be available in the emergency department and in specialty clinics that care for chronic asthmatics. **RECOMMENDATIONS FOR ACTION:** 1) Develop drug monitoring systems and make them available. There are two electronic medication-monitoring devices with microprocessor technology available for metered-dose inhalers. These devices need further improvement in design, at a lower cost. Assays have been developed for oral and injectable medications recently approved by the FDA. These assays need to become commercially available. 2) Train health care providers to improve patient compliance. As noncompliance becomes more recognized, as a result of drug monitoring, educational and behavioral programs to improve compliance with treatment will need to be developed and disseminated.

Aziz A. M. and Ibrahim M. I. "**Medication noncompliance--a thriving problem**" *Medical Journal of Malaysia.* (1999) **54**(2): 192-9.

A study was conducted among out-patients attending the Melaka Tengah Health Clinic to determine their compliance status towards antihypertensive, antidiabetic and antiasthmatic drugs. A total of 585 patients were enrolled in this study. Assessment of compliance was carried out using pill-counting and house-to-house interviews 14 days from the date of medication dispensed at the counter. The noncompliance rate among the 464 successfully interviewed patients was 56%. The mean noncompliance percentage was 78.0 +/- 43.1% (range: -10.0-314.3%). Among the four variables of compliance studied, race was not seen as a determinant of compliance. The older age group and those taking two or more drugs were statistically significant to be a noncomplier. Females were highly likely not to comply with drug therapy. Patients who conform to their refill dates were not really drug compliers. Forgetting to take their drugs and inability to read instructions on drug labels were the main reasons given. Underdosing was more common than overdosing, with an estimated cost of RM20,261.00 of unused medications per year.

Cochrane G. M., Horne R. and Chanez P. "**Compliance in asthma.**" *Respiratory medicine* (1999)

93(11): 763-9.

Low rates of compliance with medication pose a major challenge to the effective management of most chronic diseases, including asthma. The high medical and social \*costs\* of \*non\*- \*compliance\*, and the apparent lack of effective methods for dealing with it, has stimulated renewed interest in this complex issue. Two broad categories of \*non\*- \*compliance\* have been identified, namely unintentional (or 'accidental') and intentional (or 'deliberate'). Unintentional \*non\*- \*compliance\* may result from poor doctor-patient communication or a lack of ability to follow advice. Intentional \*non\*- \*compliance\* occurs when the patient knows what is required but decides not to follow this to some degree. Healthcare professionals need to be aware of the various issues affecting compliance in all patients. The reasons for \*non\*- \*compliance\* are many and varied, and include factors such as complexity of the treatment regimen, administration route, patient beliefs about therapy and other psychological factors. Improvement in \*patient\* \*compliance\* with therapy will require better doctor-patient communication, improved patient education, the tailoring of therapy to the individual and possible novel strategies such as offering feedback to the patients on their level of compliance.

Leu S. and Eng K. **“Determination of unclaimed prescriptions at an outpatient department, Songklanagarind Hospital.”** *Journal of Pharmacy Practice* (1999) **12**(6): 433-440.

Unclaimed prescriptions are an initial indication of noncompliance. Although the patients receive the best treatment, they may fail to take their medicines. As a result, the illness may not be relieved and this can lead to hospitalization or use of emergency services. This study was conducted to determine the characteristics and reasons for unclaimed prescriptions in a 680-bed and tertiary care center from July to October 1997. Patients' data were collected from medical records and from questionnaires that asked for the reasons prescriptions were not claimed. During the four-month period, 695 unclaimed prescriptions were identified, accounting for approximately 0.67% of all prescriptions filled. Results showed that patients least likely to claim a prescription included women, those who visited the hospital during official hours, those who had chronic disease, and those who went to see internal medicine physicians. Three most common diseases were those involving respiratory system (8.6%), musculoskeletal system (6.3%), and genitourinary system (6.0%). More than half (56.5%) were treated with the essential drugs. Neuromuscular agent was the most frequent drug class of unclaimed prescriptions, followed by respiratory agent, dermatological agent, and vitamins and minerals. Of the 695 patients, 152 patients responded to the questionnaires. Sixty-one patients indicated that they had received their medications later on and, therefore, were excluded from the analysis. Thus, 61 questionnaires were analyzed. The most important reason patients did not claim their prescriptions was cost (22.0%). The next most frequently mentioned reasons were forgetfulness (12.1%), business (11.0%), and lack of communication (8.8%). These patients need to be counseled about the importance of taking their medicines. In addition, health care providers should develop strategies to improve patient compliance with their medications.

Schmier J. K. and Leidy N. K. **“The complexity of treatment adherence in adults with asthma: challenges and opportunities.[comment].”** *Journal of Asthma*. (1998) **35**(6): 455-72.

The therapeutic program for persons with asthma includes recommendations for altering the environment and a drug regimen designed to alleviate symptoms, minimize exacerbations, and improve quality of life. Unfortunately, patients can have difficulty adhering to these recommendations, which



contributes to treatment failure and increased costs. This paper provides a comprehensive review of the challenge of adherence in adults with asthma, including the costs and benefits, optimal adherence levels, assessment methods commonly used in research and practice, factors believed to predict poor adherence, and tested and untested strategies for improving adherence. Opportunities for further research are discussed throughout the paper. [References: 91]

Bender B., Milgrom H. and Rand C. **“Nonadherence in asthmatic patients: is there a solution to the problem?”** *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology* (1997) **79**(3): 177-85; quiz 185-6.

LEARNING OBJECTIVES: Reading this article will reinforce the reader's awareness of the relationship between adherence and treatment outcome, of the causes of \*nonadherence\*, of methods of measurement, and of steps toward successful intervention. DATA SOURCES: Articles on adherence to asthma therapy were reviewed. A MEDLINE database using subject keywords was searched from 1990 through 1997. STUDY SELECTION: Pertinent articles were chosen, with preferential presentation of results from controlled studies. RESULTS: There is no evidence of recent improvement in the rates of \*nonadherence\*, and patients continue on average to take about 50% of prescribed medication. \*Nonadherence\* assessment is most accurate when it can be measured objectively, and relies neither on patient report nor physician estimate. The consequences of \*nonadherence\* are measured in patient suffering, financial \*cost\*, and serious compromise of clinical trial outcomes. Underlying causes of \*nonadherence\* are traced to characteristics of the disease, treatment, patient, and caregiver system. CONCLUSION: Improved adherence will lead to improved disease control, but only if medical care systems encourage and support the allocation of sufficient resources to allow barriers to self-management to be discussed and solutions negotiated. Attempts to improve adherence outside of the caregiver-patient relationship are less likely to succeed. Special programs for difficult-to-manage patients are necessary to change behavior, although significant illness improvement and \*cost\* savings are likely to result.

Dennehy C. E., Kishi D. T. and Louie C. **“Drug-Related Illness in Emergency Department Patients.”** *American Journal of Health System Pharmacy* (1996) **53**: 1422-1426.

<Abstract> Drug-related illnesses (DRIs) associated with visits to a hospital emergency department (ED) were identified and classified, and the \*cost\* of these DRIs was analyzed in a 560-bed teaching hospital for October 1994. A pharmacist reviewed all ED log forms on file and from these forms and the medical record the following information was collected for patients with a documented or suspected DRI: medication and allergy history, drug involved in and cause of the DRI, diagnosis, \*patient\* \*compliance\*, serum drug concentrations, and length of hospital stay. Of 1260 ED log forms reviewed, 565 (45%) described patients receiving drugs before the ED visit. A total of 50 DRIs were discernible in 49 log forms (3.9% of all 1260 forms, and 8.6% of the 565 forms describing patients taking medications before the visit). \*Noncompliance\*, inappropriate prescribing, and ADRs accounted for 58%, 32%, and 10% of the DRIs, respectively. The drugs most frequently involved were albuterol, insulin, and warfarin. Thirty-three (66%) of the DRIs were considered to have been preventable; these DRIs accounted for an estimated \$391,342 in annual ED and hospital \*costs\*.

<Abstract2> 9

Weinstein A. G. “**Clinical management strategies to maintain drug compliance in asthmatic children**” *Annals of Allergy, Asthma, & Immunology*. (1995) **74**(4): 304-10.

OBJECTIVE: Noncompliance with asthma medication is a common cause of treatment failure and may lead to unnecessary hospitalization and emergency care. This publication reviews factors associated with compliance with treatment regimens in general as well as with recommended asthma medications. General strategies (educational, organization, and behavioral) are reviewed with emphasis in behavioral strategies. These include reminders, tailoring, and contracting. STUDY SELECTION: A case report follows regarding a 9-year-old boy with severe asthma who was treated in a short-term inpatient asthma rehabilitation center and followed for 3 years as an outpatient. Specific clinical management strategies and techniques to maintain theophylline compliance are presented. CONCLUSION: A systematic approach emphasizing the use of behavioral strategies and drug monitoring can be helpful in promoting compliance with a therapeutic regimen. This may lead to a reduction in pulmonary morbidity and medical costs. [References: 57]

Anonymous. “**Virginia asthma patient compliance pilot project. (Medicaid cost-control measure).**” *F-D-C Reports Prescription Pharmaceuticals and Biotechnology* (1994) **56**(45): T&G4.

## Urinary and Kidney Diseases

Chisholm M. A., Vollenweider L. J., Mulloy L. L., Jagadeesan M., Wynn J. J., Rogers H. E., et al. "**Renal transplant patient compliance with free immunosuppressive medications.**" *Transplantation* (2000) **70**(8): 1240-4.

**BACKGROUND:** \*Noncompliance\* with immunosuppressive medications after renal transplantation is believed to be a major cause of allograft rejection and graft loss, with the impressive \*costs\* of these agents considered a significant reason for \*noncompliance\*. Our purpose was to determine the compliance rates of renal transplant patients who received their immunosuppressant therapy free of charge and evaluate their patterns of compliance. **METHODS:** All patients who received a renal transplant and received their immunosuppressant medications at our institution for their first year posttransplant were included in the study. Compliance rate was calculated and serum immunosuppressant concentrations were obtained to validate compliance assessments. **RESULTS:** Eighteen patients were included in the study. Approximately 48% of noncompliant patients were found to have subtarget drug concentrations, although only 14% of compliant patients had subtarget levels ( $\chi^2=12.9$ ,  $P<0.001$ ). At 5 months posttransplant, 95% of the patients remained compliant; however, by 12 months posttransplant, only 48% of the patients remained compliant. The mean time to the first noncompliant month was 9.8 months (95% confidence intervals=8.60-11.0). **CONCLUSIONS:** Patients who received their immunosuppressants free of charge were generally compliant within their first year of transplantation, however, compliance tended to decrease over time. This suggests that drug \*cost\* alone does not explain noncompliant behavior. Intensive efforts to increase medication compliance before month 8 posttransplantation should be implemented.

Howard A. C., O'Brien D. A., Cleveland W. H. and Gordon S. "**Targeted intervention to improve compliance in an urban hemodialysis population.**" *Nephrology News & Issues*. (1999) **13**(2): 27, 31-4.

Noncompliance impacts the successful delivery of care to the "urban" ESRD population. It is our belief that noncompliance can be an extension of the dysfunctional coping mechanisms of patients who lack adequate psychosocial support. In this article, we have described a pilot program providing on-site, targeted intervention for patients identified at increased risk for poor clinical outcomes, based on failure to comply with the prescribed dialysis treatment prescription. This collaboration between our "nephrology practice," an outpatient "HD facility," and a "C-L psychiatry service" has resulted in extremely low no-show rates in an urban dialysis population. We have also discovered an opportunity for reducing hospitalizations. Targeted intervention can improve compliance and prove to be cost effective.

### **Miscellaneous Diseases and General Articles**

Ballinger M. “**Compliance Dwindles as Drug Costs Escalate - Pharm Companies Look Inward to Mitigate Inflation for Members.**” *Managed Healthcare Executive* (2002) **12**(1): 7, 10.

<Abstract> The prescribing and utilization of prescription drugs in the community setting are discussed, as well as issues on elevating drug \*costs\*, pharmacoconomics, \*noncompliance\* and health outcomes, and the pharmacist's role in \*patient\* \*compliance\*.

Cleemput I., Kesteloot K. and DeGeest S. “**A review of the literature on the economics of noncompliance. Room for methodological improvement.**” *Health Policy.* (2002) **59**(1): 65-94.

Therapeutic noncompliance is a major issue in health care, having important negative consequences for clinical outcome as well as for health-care costs. This paper reviews the literature on the economics of therapeutic noncompliance, identifies methodological shortcomings and formulates recommendations for future economic research in this area. Medication noncompliance was explored more extensively, as the majority of articles dealt exclusively with this aspect of therapy. Eighteen studies were assessed according to their definition and measurement of medication noncompliance, study design, and identification and valuation of costs and outcomes. Very diverse designs and often invalid methods for calculating costs were found. Medication noncompliance is often ill-defined and measured in an inaccurate way. The economic consequences of therapeutic noncompliance have rarely been investigated according to the standard principles of good economic evaluation. Six studies examined both costs and consequences of noncompliance in a cost-outcome description or a cost-benefits, cost-effectiveness or cost-utility analysis. Eight studies dealt with the economic value of compliance-enhancing interventions. In general, studies on the economic consequences of noncompliance lack methodological rigour and fail to meet qualitative standards. There is a clear need for more and better research on the impact of noncompliance, on the cost-effectiveness of interventions and the potential of compliance-enhancing interventions to improve patient outcomes and/or reduce health-care costs. [References: 73]

Erlen J. A. “**Adherence revisited: the patient's choice. (Ethics).**” *Orthopaedic Nursing* (2002) **21**(2): 79.

Adherence to treatment is an age-old issue in the health care provider-patient relationship. Although findings show that adherence has the potential to increase the efficacy of a treatment, is that the only consideration when examining the ethical questions surrounding adherence? What if the competent adult patient chooses not to adhere? The purpose of this paper is to examine the patient's choice to not adhere to a prescribed therapy. The author uses a hypothetical case as a way to identify and to challenge the assumptions underlying traditional adherence models.

Kennedy J. and Erb C. “**Prescription noncompliance due to cost among adults with disabilities in the United States.**” *American Journal of Public Health.* (2002) **92**(7): 1120-4.

OBJECTIVES: This study estimated national prevalence rates of medication noncompliance due to cost and resulting health problems among adults with disabilities. METHODS: Analyses involved 25,805

respondents to the Disability Follow-Back Survey, a supplement to the 1994 and 1995 National Health Interview Surveys. **RESULTS:** Findings showed that about 1.3 million adults with disabilities did not take their medications as prescribed because of cost, and more than half reported health problems as a result. Severe disability, poor health, low income, lack of insurance, and a high number of prescriptions increased the odds of being noncompliant as a result of cost. **CONCLUSIONS:** Prescription noncompliance due to cost is a serious problem for many adults with chronic disease or disability. Most would not be helped by any of the current proposals to expand Medicare drug coverage.

Pomerantz J. M. “**Patient Noncompliance with Medication: Antidepressants.**” *Drug Benefit Trends* (2002) **14**(4): 22-23.

<Abstract> This article discusses the reasons for \*noncompliance\* with antidepressants, namely, the low efficacy of the drugs and the side effects associated with the drugs.

Schneeweiss S., Maclure M. and Soumerai S. B. “**Prescription duration after drug copay changes in older people: Methodological aspects.**” *Journal of the American Geriatrics Society* (2002) **50**(3): 521-525.

**OBJECTIVES:** Impact assessment of drug benefits policies is a growing field of research that is increasingly relevant to healthcare planning for older people. Some cost-containment policies are thought to increase noncompliance. This paper examines mechanisms that can produce spurious reductions in drug utilization measures after drug policy changes when relying on pharmacy dispensing data. Reference pricing, a copayment for expensive medications above a fixed limit, for angiotensin-converting enzyme (ACE) inhibitors in older British Columbia residents, is used as a case example. **DESIGN:** Time series of 36 months of individual claims data. Longitudinal data analysis, adjusting for autoregressive data. **SETTING:** Pharmacare, the drug benefits program covering all patients aged 65 and older in the province of British Columbia, Canada. **PARTICIPANTS:** All noninstitutionalized Pharmacare beneficiaries aged 65 and older who used ACE inhibitors between 1995 and 1997 (N = 119,074). **INTERVENTION:** The introduction of reference drug pricing for ACE inhibitors for patients aged 65 and older. **MEASUREMENTS:** Timing and quantity of drug use from a claims database. **RESULTS:** We observed a transitional sharp decline of 11% +/- a standard error of 3% (P = .02) in the overall utilization rate of all ACE inhibitors after the policy implementation; five months later, utilization rates had increased, but remained under the predicted prepolicy trend. Coinciding with the sharp decrease, we observed a reduction in prescription duration by 31% in patients switching to no-cost drugs. This reduction may be attributed to increased monitoring for intolerance or treatment failure in switchers, which in turn led to a spurious reduction in total drug utilization. We ruled out the extension of medication use over the prescribed duration through reduced daily doses (prescription stretching) by a quantity-adjusted analysis of prescription duration. **CONCLUSION:** The analysis of prescription duration after drug policy interventions may provide alternative explanations to apparent short-term reductions in drug utilization and adds important insights to time trend analyses of drug utilization data in the evaluation of drug benefit policy changes.

Atkinson W. “**Disease Management: A Win-Win Game Plan; Employers and insurers are working**

**together to lower costs associated with treating chronic diseases. (Health Care).(Statistical Data Included)."** *HRMagazine* (2001) **46**(12): 59(5).

Frangakis C. E. and Baker S. G. "**Compliance subsampling designs for comparative research: estimation and optimal planning.**" *Biometrics* (2001) **57**(3): 899-908.

For studies with treatment \*noncompliance\*, analyses have been developed recently to better estimate treatment efficacy. However, the advantage and \*cost\* of measuring compliance data have implications on the study design that have not been as systematically explored. In order to estimate better treatment efficacy with lower \*cost\*, we propose a new class of compliance subsampling (CSS) designs where, after subjects are assigned treatment, compliance behavior is measured for only subgroups of subjects. The sizes of the subsamples are allowed to relate to the treatment assignment, the assignment probability, the total sample size, the anticipated distributions of outcome and compliance, and the \*cost\* parameters of the study. The CSS design methods relate to prior work (i) on two-phase designs in which a covariate is subsampled and (ii) on causal inference because the subsampled postrandomization compliance behavior is not the true covariate of interest. For each CSS design, we develop efficient estimation of treatment efficacy under binary outcome and all-or-none observed compliance. Then we derive a minimal \*cost\* CSS design that achieves a required precision for estimating treatment efficacy. We compare the properties of the CSS design to those of conventional protocols in a study of patient choices for medical care at the end of life.

Hausman A. "**Taking your medicine: relational steps to improving patient compliance.**" *Health marketing quarterly* (2001) **19**(2): 49-71.

Patient \*non\*-*compliance* with physicians' instructions is a major problem that \*costs\* billions of dollars each year. This study supports a significant role for communication, both as a form of information exchange and social support, and participative decision-making in improving \*patient\* *compliance*. These results, based on structural equation modeling, also support the interaction of communication and participative decision-making positively affecting compliance. Results suggest that one-way communication from physician to patient and patient education will not solve compliance problems by themselves. Instead the solution revolves around open, bi-directional information exchange, active listening by both parties, and truly informed consent on the part of patients.

Hughes D. A., Bagust A., Haycox A. and Walley T. "**Accounting for noncompliance in pharmaco-economic evaluations.**" *Pharmacoeconomics*. (2001) **19**(12): 1185-97.

Noncompliance with prescribed drug regimens is a widespread phenomenon which results in decreased efficacy and is often associated with increased medical expenditures. Despite this, economic evaluations based on decision-analytic models rarely incorporate noncompliance to allow for the differences in compliance observed between controlled clinical trials and routine clinical practice. This review examines the issues relating to the measurement of noncompliance, and the clinical and economic consequences of noncompliant drug taking behaviour. In order to fully appreciate the clinical (and therefore the economic) consequences of noncompliance, a detailed understanding of the type of noncompliance, the

pharmacokinetic and pharmacodynamic properties of the drug and the pathophysiological processes of the diseases being treated is required. These are described in detail, and a classification of drug-disease combinations according to the potential economic impact of the varying forms of noncompliance is set out. Issues are raised to highlight the need for improved modelling of the impact of noncompliance, and to this end, recommendations are made for future analyses. The main points are that compliance should be defined clearly, distinguishing between the various forms of noncompliance, that the assumptions relating to the health status of noncompliers should be explicit and robust, and that sensitivity analysis should be applied appropriately to ascertain the impact of noncompliance on the cost-effectiveness of drug therapies.

[References: 47]

Hughes D. A., Bagust A., Haycox A. and Walley T. **“The impact of non-compliance on the cost-effectiveness of pharmaceuticals: a review of the literature.”** *Health economics* (2001) **10**(7): 601-15.

\*Non\*-compliance\* with drug therapies not only limits their effectiveness, but in some instances, is associated with grave clinical sequelae and substantial economic burden. It is important, therefore, to consider \*non\*-compliance\* in economic evaluations. A review of pharmacoeconomic evaluations, which have applied sensitivity analysis to \*non\*-compliance\* rates, was undertaken to evaluate the impact of \*non\*-compliance\* on the \*cost\*-effectiveness of different drug therapies. Although 22 evaluations satisfied the inclusion criteria, additional information was obtained from the authors of most studies, as the published details were inadequate. The majority of evaluations assumed altered effectiveness owing to reduced compliance in the absence of supportive clinical evidence. Because of the disparity in the nature of the outcomes, the measures of \*non\*-compliance\* and the time horizon of the studies evaluated, it was not possible to compare the magnitude of the impact of \*non\*-compliance\* among different drug-disease combinations. However, it was evident that \*non\*-compliance\* always results in a reduction in efficacy, but its impact on \*costs\* varied substantially. The importance of incorporating measures of compliance is highlighted, as failing to account for 'real world' compliance rates in pharmacoeconomic evaluations may lead to selection of sub-optimal treatment strategies. Copyright 2001 John Wiley & Sons, Ltd.

Morgan T. M. **“The economic impact of wasted prescription medication in an outpatient population of older adults.”** *Journal of Family Practice*. (2001) **50**(9): 779-81.

The causes and costs of outpatient medication waste are not known. We report the results of a cross-sectional pilot survey of medication waste in a convenience sample of 73 New Hampshire retirement community residents aged 65 years or older. We used questionnaires and in-home pill counts to determine the annual occurrence of medication waste, defined as no intention to take leftover medicines prescribed within the past year. Mean individual annual cost of wasted medication was \$30.47 (range = \$0-\$131.56). Waste represented 2.3% of total medication costs. The main causes for waste included: resolution of the condition for which the medication was prescribed (37.4%), patient-perceived ineffectiveness (22.6%), prescription change by the physician (15.8%), and patient-perceived adverse effects (14.4%). Individual costs were modest, but if \$30 per person represents a low estimate of average annual waste, the US national cost for adults older than 65 years would top \$1 billion per year.

Billups S. J., Malone D. C. and Carter B. L. “**The relationship between drug therapy noncompliance and patient characteristics, health-related quality of life, and health care costs.**” *Pharmacotherapy*. (2000) **20**(8): 941-9.

The objectives of this study were to determine the relationship between drug therapy compliance and risk of hospitalization and economic outcomes, and to identify potential indicators of compliance. We used computerized prescription records from 1,054 patients at high risk for drug-related problems. We calculated a compliance ratio for a 12-month period and correlated it with health care use, demographic variables, drug-related variables, and scores for health-related quality of life. Univariate results suggested that increased age ( $p=0.05$ ), high number of chronic conditions ( $p<0.001$ ), and high number of concurrent drugs ( $p<0.001$ ) were positively correlated with compliance. That is, increased values for these variables were associated with better compliance. Using logistic regression, the odds of being noncompliant was 0.665 as the number of chronic conditions increased. Compliance was not a predictor of concurrent or future hospitalizations or mortality, nor was it a significant predictor of health care costs.

Dunbar-Jacob J., Erlen J. A., Schlenk E. A., Ryan C. M., Sereika S. M. and Doswell W. M. “**Adherence in chronic disease.**” *Annual review of nursing research* (2000) **18**: 48-90.

\*Nonadherence\* to treatment regimen is a prevalent problem of patients with chronic disorders. Approximately half of the patients with a chronic disease have problems following their prescribed regimen to the extent that they are unable to obtain optimum clinical benefit. This chapter reviews the state of knowledge regarding adherence to chronic disease regimens across the life span and demonstrates that the extent and nature of the adherence problems are similar across diseases, across regimens, and across age groups. Adherence to the commonly prescribed regimens is addressed, including pharmacological therapies, therapeutic diets, and therapeutic exercise. Randomized, controlled studies focusing on various educational, behavioral, cognitive, and affective interventions to improve adherence are included. Based on this review, further work is needed to better understand and improve adherence. New strategies for analysis and measurement will support these needed advances in the field of adherence.

Wurster M. W. “**Computerized patient management system improves compliance, efficiency and revenue in anticoagulation clinic.**” *Chest* (2000) **118**(4): 128S.

Anonymous. “**Poor compliance can be costly.**” *Drug & Therapeutic Perspectives* (1999) **14**(10): 14-16.

Fawell N. G., Cookson T. L. and Scranton S. S. “**Relationship between tablet splitting and compliance, drug acquisition cost, and patient acceptance.[erratum appears in Am J Health Syst Pharm 2000 Feb 15;57(4):392].**” *American Journal of Health-System Pharmacy*. (1999) **56**(24): 2542-5.



As managed care pharmacy continues to grow and medication costs increase, pharmacy managers are continually looking for ways to reengineer distributive services to provide the most cost-effective care. In an effort to save money, the San Diego Veterans Affairs Healthcare System (SDVAHS) and other health systems have implemented tablet-splitting programs targeted at high-cost and widely prescribed medications. Despite this growing practice, published research examining the effects on compliance rates, patient acceptance, and actual cost savings is lacking. A recent computer-assisted literature search revealed only one study of tablet splitting that addressed patient compliance and acceptance. In that study, patients taking lovastatin and using a tablet splitter were mailed a questionnaire to assess their impressions of tablet splitting. A majority of the patients found tablet splitters easy to use and reported that compliance was not hindered. However, compliance was subjectively evaluated through patients' responses to questions; actual tablet counts were not performed. Furthermore, actual cost savings (if any) were not determined.

Keeler E. B., Robalino D. A., Frank J. C., Hirsch S. H., Maly R. C. and Reuben D. B. **“Cost-effectiveness of outpatient geriatric assessment with an intervention to increase adherence.”** *Medical Care.* (1999) **37**(12): 1199-206.

**BACKGROUND:** Comprehensive geriatric assessment (CGA) can be effective in inpatient units, but such inpatient settings are prohibitively expensive. If similar benefits could be obtained in outpatient settings, CGA might be a more attractive option. **OBJECTIVES:** To assess the cost-effectiveness (CE) of an outpatient geriatric assessment with an intervention to increase adherence. **SUBJECTS:** Three hundred fifty-one community-dwelling, elderly subjects with at least one of four geriatric conditions. **MEASURES:** In addition to the measures of functioning, we collected data on the costs of the intervention itself and on the use of medical services in the 64 weeks after the intervention. **RESULTS:** The intervention, which prevented functional decline, cost \$273 per participant. The intervention group averaged three more visits than the control group in the first 32 weeks after the intervention, but only 1.2 extra visits in the next 32 weeks. We estimate that the costs of these additional medical services would be \$473 for the 5 years after the intervention, leading to a total cost per Quality Adjusted Life Year (QALY) of \$10,600. **CONCLUSIONS:** The CE of this program compares favorably with many common medical interventions. Whether investments should be made in health care resources on treatments that lead to modest improvements in the functioning of community-dwelling elderly people remains a societal decision.

Olshaker J. S., Barish R. A., Naradzay J. F., Jerrard D. A., Safir E. and Campbell L. **“Prescription noncompliance: contribution to emergency department visits and cost.”** *Journal of Emergency Medicine.* (1999) **17**(5): 909-12.

We randomly surveyed 100 patients in the acute care section of a large urban university hospital Emergency Department (ED) on 6 days with regard to the existence of and reasons for prescription noncompliance. Noncompliance was considered a major factor contributing to the ED visit if: (1) no medications had been taken for at least 48 h before the ED visit; (2) the medications, when previously taken, had routinely controlled the condition for which the patient was presenting to the ED; and (3) no other significant cause or illness was believed to have precipitated the ED visit. ED, admissions, and yearly medication costs were calculated for all patients. Noncompliance was found to be a contributing factor in the cases of 22 patients (22%). The most common medications involved were phenytoin and albuterol. Cost was the most common reason for noncompliance (11 [50%]). The average ED charge per noncompliant

patient discharged was \$576.61. Six noncompliant patients were admitted at an average cost of \$4,834.62. The average cost of a year's medication was \$520.72. Noncompliance with drug prescriptions is a significant contributor to ED visits and health care costs.

Scheen A. J. “[**Medication compliance**].” *Revue Medicale de Liege*. (1999) **54**(11): 854-8.

Compliance is defined as the extent to which a patient's behaviour coincides with medical or health advice. Medication compliance seems to be rather low as 30 to 60% of no or poor adherence to medical recommendation have been reported. Numerous factors may influence medication compliance among which patient's characteristics, disease particularities, drug treatment modalities or physician's attitudes. The consequences of medication non-compliance may not only be dangerous for patient's health, but also dramatically increase the financial cost for public health services. Thus, all energies should be devoted to improve drug compliance, including treatment optimization and simplification, patient's information and education, use of practical means that facilitate adherence to medical recommendation, the patient being responsible for his/her treatment.

Urquhart J. (1999). Pharmacoeconomic impact of variable compliance. Drug Regimen Compliance: Issues in Clinical Trials and Patient Management. J.-M. Métry and U. Meyer. Chichester, John Wiley: 119-145.

Anonymous. “[**Mississippi Medicaid program targets drug therapy compliance**].” *Public Sector Contracting Report*. (1998) **4**(8): 120-2.

Can pharmacists serving as disease management and drug therapy counselors to patients help reduce Medicaid costs? Program administrators hope so as they launch a new effort in which pharmacists serve as providers of disease management services and are paid for having counseling sessions with recipients.

Balkrishnan R. “[**Predictors of medication adherence in the elderly**].” *Clinical Therapeutics*. (1998) **20**(4): 764-71.

As average life expectancy increases, so do the incidence of chronic diseases and the number of persons receiving long-term drug therapy. Thus elderly patients' noncompliance with medication regimens has the potential for sweeping medical and economic consequences and is likely to become increasingly important in the design of disease-management programs for this population. The author conducted a MEDLINE search of the English-language literature for the years 1962 to 1997 to identify articles concerning predictors of medication compliance in the elderly. A descriptive analysis of this literature indicated that there remains some uncertainty about the reasons for noncompliant medication-taking in the elderly. Clear associations have been established between elderly patients' medication adherence and race, drug and dosage form, number of medications, cost of medications, insurance coverage, and physician-patient communication. However, the findings are inconsistent with regard to the effects of patients' age, sex, socioeconomic status, living arrangement, comorbidities, number of physician visits, and knowledge,

attitudes, and beliefs about health. Until the results of further comprehensive studies are available, the current knowledge should be considered when designing and implementing disease-management programs for the elderly. [References: 24]

Basskin L. **“How to Identify the Reasons for Patient Noncompliance with Drug Therapy.”** *Formulary (1998)* **33**: 64-67.

<Abstract> The first of a series of articles regarding the problems of \*noncompliance\* with drug therapy, \*costs\* of \*noncompliance\*, reasons for \*noncompliance\* in designated patient populations, and development of an approach for managing \*noncompliance\*, are discussed.

Cline J. C., Foster A. C., Lee T. J. and Pait L. D. **“Unclaimed Prescriptions in an Outpatient Pharmacy within an Academic Medical Center.”** *ASHP Midyear Clinical Meeting (1998)* **33**(Dec): P-376E.

<Abstract> Failure to obtain prescribed medications contributes to \*patient\* \*noncompliance\*. Unclaimed prescriptions result in undesirable patient outcomes and unnecessary healthcare \*costs\*. The Wake University Baptist Medical Center Outpatient Pharmacy fills approximately 350 prescriptions daily with many prescriptions unclaimed each month. This study quantified and characterized the number of unclaimed prescriptions, characterized the patients for whom the prescriptions were written, and identified reasons for unclaimed prescriptions. For a three-month period, customer demographics, prescription type, administration frequency, prescription \*cost\*, and therapeutic category were recorded for unclaimed prescriptions. Letters were sent to customers to determine reasons for unclaimed prescriptions. The unclaimed prescription rate during this period was 1.9%. The reason most frequently given was forgetfulness. \*Cost\* was \$10.00 or less for 87% of unclaimed prescriptions.

Cramer J. A. **“Enhancing patient compliance in the elderly. Role of packaging aids and monitoring.”** *Drugs and Aging (1998)* **12**(1): 7-15.

Inadequate compliance with medications is a significant contributor to the costs of medical care in every therapeutic area. No matter how severe the consequence, there is no assurance that all patients will take their medications as prescribed. Elderly patients are a particular concern because of their common deficits in physical dexterity, cognitive skills and memory, and the number of medications that they are typically prescribed. To overcome problems of compliance in the elderly, healthcare providers are advised to prescribe a simple dosage regimen for all medications to be taken (preferably 1 or 2 doses daily), to help the patient select cues that assist them in remembering to take doses (time of day, meal-time, or other daily rituals), to provide devices to simplify remembering doses (medication boxes), and to regularly monitor compliance. A variety of compliance aids are available to help patients organise their medications (e.g. plastic boxes) or remember dose times (alarms). Medication packaged in standard pharmacy bottles should be identified with special labels, or dose charts can be provided to check the daily schedule. Single-unit doses, widely used in hospitals, may be cumbersome for elderly patients who have difficulty opening the foil-backed wrappers. Medication boxes with compartments that are filled weekly by the patient, family member or a home healthcare provider are useful organisers that simplify the patient's responsibilities for

self-administration. Microelectronic devices can provide feedback that shows patients whether they have been taking doses as scheduled. Some systems are also designed to notify patients within a day if doses were omitted. No system is optimal for all patients, but elderly patients deserve a comprehensive assessment of their needs to enhance medication compliance.

McCarthy R. **“The price you pay for the drug not taken.”** *Business & Health* (1998) **16**(10): 27.

Patient noncompliance with drugs prescribed by doctors and hospitals is alarmingly high as it is reported that around 50% of prescriptions are not taken. Around 10% of hospital admissions are caused by noncompliance. The chief cause for this attitude is stinting on drug \*costs\* and plain ignorance about the effect of prescribed drugs. One solution to this problem may come in the form of improved packaging of medicines and the easy availability of compliance monitoring equipment which reminds the patient about such details as medication time and amount to be taken.

Ennis K. J. and Reichard R. A. **“Maximizing drug compliance in the elderly. Tips for staying on top of your patients' medication use.”** *Postgraduate Medicine*. (1997) **102**(3): 211-3, 218, 223-4.

The old joke goes, "I finally got it all together, but now I forget where I put it." So it is for many older patients facing complicated disease management plans. They think they understand, but then the instructions blur or they forget if they took the medications or they become concerned that the drugs cost too much and decide to cut back. Taking care of themselves is suddenly just too complicated. Drs Ennis and Reichard look at the issues and present some strategies to improve compliance among the elderly. [References: 13]

Fogarty J. S. **“Reactance theory and patient noncompliance.”** *Social Science & Medicine*. (1997) **45**(8): 1277-88.

With surprising frequency, and to the considerable dismay of health care professionals, patients both subtly and overtly refuse to cooperate with medical treatment. Despite considerable empirical and theoretical attention, and an abundance of interventions designed to combat it, noncompliance continues. Its persistence is accompanied by considerable costs borne by patients and society alike. The theory of psychological reactance sheds new light on the phenomenon. Reactance theory proposes that a perceived threat to an individual's freedom generates a motivational state aimed at recapturing the affected freedom and preventing the loss of others. In a medical context, patients' perceptions of threats to their freedom or control may induce noncompliance. This theory permits integration of many of the seemingly disparate and/or contradictory findings, and may afford professionals new opportunities for improving patient compliance.

Murphy J. and Coster G. **“Issues in patient compliance.”** *Drugs* (1997) **54**(6): 797-800.

Patient compliance refers to the willingness and ability of an individual to follow health-related advice, to take medication as prescribed, to attend scheduled clinic appointments and to complete

recommended investigations. It is a major health issue, with outcomes related to levels of morbidity, mortality and cost utilisation. Poor compliance has been reported as the most common cause of nonresponse to medication, with evidence to show that patients who adhere to treatment recommendations have better health outcomes than those who do not adhere, even when taking a placebo. Evidence-based practice guidelines, founded on clinical, behavioural and educational concepts, provide a means of measuring outcomes related to health status, patient satisfaction and cost-benefit issues, and may help to ensure that responsibility for compliance is shared between the clinician and the patient.

Bloom D. L. **“Facing the next challenge of pharmaceutical care: patient noncompliance.”** *Medical interface* (1996) **9**(11): 67-72.

Medication misuse is a costly problem. Fixing the matter will not be easy because it means reshaping pharmaceutical care. Yet, the business reasons for undertaking such an action are compelling. Not only would MCOs and payers reduce expenditures, but drug companies, pharmacists, and pharmacy benefit managers could vitalize their positions in the marketplace. This article proposes how an integrated program might overcome \*noncompliance\*.

Bloom D. L. **“High-tech aids will reduce health care costs.”** *Managed Care Pharm Pract* (1996) **3**(2): 18-20.

Gifford-Jones W. **“A simple way to save the health care system \$9B. (patient compliance).”** *The Financial Post* (1996)(Oct 12, 1996): p36.

Haynes R. B., McKibbon K. A. and Kanani R. **“Systematic review of randomised trials of interventions to assist patients to follow prescriptions for medications.(Review Article).”** *The Lancet* (1996) **348**(9024): 383(4).

Many patients may not adhere to medication protocols as prescribed, thereby limiting the full therapeutic benefit. A review of the medical literature revealed that complex efforts to improve patient adherence were only marginally effective. The techniques included counseling, access to information and more convenient care, reminders, family therapy, reinforcement techniques, self-monitoring, and additional supervision. It is important to develop further assistance to patients to maximize the effectiveness of treatment interventions.

Layug M. and Sandor G. K. **“The cost of non-compliance.”** *Ontario Dentist*. (1996) **73**(8): 27, 29-31.

Lexchin J. **“Costs of noncompliance disputed”** *Cmaj.* (1996) **155**(1): 11-2.

Scott L. **“Providers push for remedies to costly drug noncompliance.”** *Modern Healthcare.* (1996) **26**(16): 44-6, 48, 50.

About half of patients taking any drug don't follow instructions. It's a problem that costs billions of dollars annually. Health plans are working harder to improve compliance because of the high toll it exacts on patient health and their own pocketbooks.

Scott L. **“Doctors' Orders: Provider Push for Remedies to Costly Drug Noncompliance.”** *Modern Healthcare* (1996) **26**: 44-46.

<Abstract> The programs of various health plans to reduce \*noncompliance\* because of the danger to patients' health and high \*costs\* are described, including new disease management programs that try to avert serious medical problems in people with chronic conditions and a push by pharmacists to be paid for counseling patients on proper drug use. Indicators of high risk of \*noncompliance\*, medical conditions in which \*noncompliance\* is greatest, and the use of pharmaceutical care practice to reduce \*noncompliance\* are also discussed.

Anonymous. **“The EDI revolution; by linking data bases electronically, providers and payers are lowering costs while improving patient compliance and prescribing patterns.”** *Business & Health* (1995) **13**(3): S22(3).

DiMatteo M. R. **“Patient adherence to pharmacotherapy: the importance of effective communication.”** *Formulary.* (1995) **30**(10): 596-8, 601-2, 605.

Despite the potential of modern pharmacotherapy to control disease and enhance quality of life, two out of five patients fail to take their prescribed medication correctly. Research indicates that the two primary influencers of adherence are the patient's beliefs in the value of the regimen and the patient's ability to overcome practical barriers to adherence. The patient's perception of value--ie, the risks, benefits, and efficacy of therapy--influences his or her commitment to the medication regimen. Barriers to adherence include side effects, number and frequency of dosages, and cost. Communication between health care providers and patients is crucial to enhancing patient adherence to medication regimens.

Johnson J. A. and Bootman J. L. **“Drug-related morbidity and mortality. A cost-of-illness model.[comment].”** *Archives of Internal Medicine.* (1995) **155**(18): 1949-56.

BACKGROUND: Preventable drug-related morbidity and mortality represent a serious medical problem that urgently requires expert attention. The costs to society of the misuse of prescription medications, in terms of morbidity, mortality, and treatment, can be immense. To date, research has

primarily documented increased rates of hospitalization secondary to medication noncompliance and/or adverse drug effects. **OBJECTIVES:** To develop a conceptual model of drug-related morbidity and mortality, and to estimate the associated costs in the ambulatory setting in the United States. **METHODS:** A probability pathway model was developed to estimate the cost of drug-related morbidity and mortality in the United States. Pharmacist practitioners were surveyed to determine conditional probabilities of therapeutic outcomes owing to drug therapy. Health care utilization and associated costs owing to negative therapeutic outcomes were estimated. **RESULTS:** Drug-related morbidity and mortality was estimated to cost \$76.6 billion in the ambulatory setting in the United States. The largest component of this total cost was associated with drug-related hospitalizations. When assumptions of the model were varied, the estimated cost ranged from a conservative estimate of \$30.1 to \$136.8 billion in a worst-case scenario. **CONCLUSIONS:** The cost of drug-related morbidity and mortality in the ambulatory setting in the United States is considerable and should be considered in health policy decisions with regard to pharmaceutical benefits. Policies and services should be developed to reduce and prevent drug-related morbidity and mortality.

Urquhart J. (1995). The noncompliance tax: judging the costs of patient noncompliance and the economic value of intervening to improve compliance with crucial drug regimens. *Pharmacoeconomics*. D. Breimer, A. Broekmans, H. Leufkens and F. Rutten. Leiden, Boerhaave Commissie: 21-25.

Feldman J. A. and DeTullio P. L. “**Medication noncompliance: an issue to consider in the drug selection process.**” *Hospital Formulary*. (1994) **29**(3): 204-11.

Patient medication noncompliance is a major public health problem that represents a significant cost to our health care system. Health care professionals--through counseling programs, and the pharmaceutical industry--through various improvements in drug products, have helped to improve medication noncompliance. Yet, additional research needs to be conducted on noncompliant behavior and into methods to improve it. All health care professionals, particularly those involved in selecting and guiding drug therapy decisions, need to be made aware of the costs to the health care system that result from noncompliance. [References: 30]

Rudd P. “**Linking compliance to outcomes: clinical and economic ramifications.**” *Canadian Journal of Cardiology* (1994) **10**(7 Suppl.): 3-5.

Urquhart J. “**When Outpatient Drug Treatment Fails: Non-Complier or Non-Responder? Identifying Non-Compliers as a Cost-Containment Tool.**” *Clinical Research and Regulatory Affairs* (1994) **11**(1): 19-38.

<Abstract> A new method that electronically records the time and date of each dose of medicine by means of a microchip within the closure of a conventional drug package to determine whether a patient on drug therapy is a non-responder or a non-complier is described. What the medication event monitoring measures, getting and interpreting the data, 2 new quality controls on ambulatory care, patient accountability

for correct dosing, the \*cost\* -effective response to unsatisfactory compliance, and practical steps when poor compliance is the root problem are also discussed.

<Abstract2> 34

Berg J. S., Dischler J., Wagner D. J., Raia J. J. and Palmer-Shevlin N. **"Medication Compliance: Healthcare Problem"** *Annals of Pharmacotherapy* (1993) **27**(Sept Suppl): S5-S19.

<Abstract> A review of \*patient\* \*compliance\* and its effect on healthcare \*costs\*, including barriers to compliance, forms of \*noncompliance\*, programs to educate and assist patients, advances in pharmaceutical technology, and packaging for easier drug administration, compliance devices, and some recommendations to improve compliance, is presented. This article qualifies for 2 hours U.S. CE credit by the ACPE.

<Abstract2> 42

Erickson J. **"The cost of medication noncompliance."** *AAPPO journal : the journal of the American Association of Preferred Provider Organizations* (1993) **3**(2): 33-4, 38-40.

Mandelker J. **"Monitoring drug compliance can reduce total medical plan costs."** *Business & Health* (1993) **11**(6): 26.

Raynor D. K., Booth T. G. and Blenkinsopp A. **"Effects of computer generated reminder charts on patients' compliance with drug regimens."** *British Medical Journal* (1993) **306**(6886): 1158-1161.

Objective. To investigate whether a reminder chart improved patients' compliance with their drug regimen after discharge from hospital. Design - Patients were randomly allocated to one of four groups. Two groups received the reminder chart: one also received routine counselling from a nurse and the other received structured counselling from a pharmacist, which included an explanation of the reminder chart. The other two groups received only counselling, either from a nurse or from a pharmacist. Patients were visited about 10 days later: they were questioned about their drug regimen, and their compliance was measured by tablet counting. Setting. The pharmacy in a district general hospital and patients' homes. Patients. 197 patients being discharged from hospital who were regularly taking two or more drugs. Intervention. An individualised reminder chart, which listed each person's medicines and when they were to be taken and was automatically generated by a medicine labelling computer. Main outcome measures. Patient's compliance with and knowledge of their drug regimen. Main results. Of the patients who received the reminder chart, 83% (95% confidence interval 74% to 90%) correctly described their dose regimen compared with 47% (37% to 58%) of those without the chart ( $p < 0.001$ ). The mean compliance score was 86% (81% to 91%) in both groups not given the reminder chart; 91% (87% to 94%) in the group given the chart without an explanation; and 95% (93% to 98%) in the group given the chart and an explanation. A mean compliance score of  $>85\%$  was achieved by 63% (53% to 73%) of patients without a reminder chart and by 86% (78% to 93%) of those receiving the chart ( $p < 0.001$ ). Conclusions. An



automatically generated reminder chart is a practical and cost effective aid to compliance.

Smith D. L. **“Effect of Patient Noncompliance on Health Care Costs.”** *Medical Interface* (1993) **6**(Apr): 74-76.

<Abstract> The effect of \*patient\* \*noncompliance\* on health care \*costs\* is discussed, including \*costs\* to third-party payers, how to increase \*patient\* \*compliance\*, \*cost\*-savings of patient education programs, and reasons for \*patient\* \*noncompliance\*.

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Donovan J. L. and Blake D. R. **“Patient non-compliance: Deviance or reasoned decision-making?”** *Social Science & Medicine* (1992) **34**(5): 507-513.

A large quantity of research concerning issues of patient compliance with medications has been produced in recent years. The assumption in much of this work is that patients have little option but to comply with the advice and instructions they receive. Studies have shown, however, that between one third and one half of all patients are non-compliant, but different authors cite different reasons for this high level of non-compliance. In this paper, the concept of compliance is questioned. It is shown to be largely irrelevant to patients who carry out a 'cost-benefit' analysis of each treatment, weighing up the costs/risks of each treatment against the benefits as they perceive them. Their perceptions and the personal and social circumstances within which they live are shown to be crucial to their decision-making. Thus an apparently irrational act of non-compliance (from the doctor's point of view) may be a very rational action when seen from the patient's point of view. The solution to the waste of resources inherent in non-compliance lies not in attempting to increase patient compliance per se, but in the development of more open, co-operative doctor-patient relationships.

Easterbrook P. **“Patient Compliance in Medical Practice and Clinical Trials [Book Review].”** *The Lancet* (1992) **340**(8826): 1023.

McNally D. L. and Wertheimer D. **“Strategies to reduce the high cost of patient noncompliance.”** *Maryland Medical Journal*. (1992) **41**(3): 223-5.

The documented low rate of compliance can result from ineffective communication by the pharmaceutical and medical profession, and poor comprehension of prescription instructions by the public. Presented are several examples of how pharmacists can assist physicians in improving and monitoring their patients' compliance behavior. Strategies to enhance communication through the written prescription are offered.

Mezey G. and Acsai M. **“The influence of compliance and non-compliance on the thrifty drug**

**therapy. (One of the influencing factors of the calculations concerning production cost and return). [Hungarian].”** *Gyogyszereszet* (1992) **36**(11): 669-672.

Anonymous. **“Special report: the value of pharmaceuticals. Misused or unused prescriptions may cost your health plan plenty.”** *Business & Health*. (1991) [VALUE]: 17-8.

Medication noncompliance is seriously affecting patient well-being, health care costs, and the national economy. The health consequences of noncompliance include prolonged illness, uncontrolled chronic disease, hospitalization, disability, and death.

Craghead R. M. and Wartski D. M. **“Evaluative Study of Unclaimed Prescriptions .”** *Hospital Pharmacy* (1991) **26**: 616-617.

<Abstract> An evaluative study of patient \*non\*-\*compliance\* through unclaimed filled prescriptions was conducted on 20,962 new prescriptions transmitted by computer from the prescriber directly to the pharmacy from 26 general and specialty clinics and 5 troop medical clinics associated with an Army medical center. Patients were considered non-compliant if the prescriptions went unclaimed after 5 days. A total unclaimed rate of 1.6% was determined. Through the managed care system there was no monetary \*cost\* to the patient and generally no waiting time for prescription pick-up. A break-down by clinic of origin and type of medications contributing to the compliance failure was also determined. Conclusions are made on the correlation between compliance failure, clinic type and drug category.

Hussar D. A. **“Improving Patient Compliance.”** *National Association of Retail Druggists Journal* (1991) **113**: 39-44.

<Abstract> \*Patient\* \*compliance\*, including common \*types of noncompliance\*, the therapeutic regimen factors that affect compliance, such as multiple drug therapy, frequency of administration, duration of therapy, adverse effects, \*cost\* of medication, administration of medication, and the taste of medications, is discussed. Ways to improve compliance, including patient education, compliance aids, and monitoring therapy by the patient and pharmacist, are included. This article qualifies for one hour U.S. CE credit by the ACPE.

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Pollner F. **“Difficult patients: too important to ignore. (Cover Story).”** *Medical World News* (1991) **32**(3): 34(7).

Anonymous. **“Underuse of prescription medicine costing U.S. billions, OSU says. (Oregon State University).”** *PR Newswire* (1990)(May 23): 0523SE007.

Col N., Fanale J. E. and Kronholm P. **“The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly.”** *Archives of Internal Medicine.* (1990) **150**(4): 841-5.

We interviewed 315 consecutive elderly patients admitted to an acute care hospital to determine the percentage of elderly hospital admissions due to noncompliance with medication regimens or adverse drug reactions, their causes, consequences, and predictors. Eighty-nine of the elderly admissions (28.2%) were drug related, 36 due to noncompliance (11.4%), and 53 due to adverse drug reactions (16.8%). One hundred three patients had a history of noncompliance (32.7%). Factors statistically associated with a higher risk of hospitalization due to noncompliance were poor recall of medication regimen, seeing numerous physicians, female, medium income category, use of numerous medications, and having the opinion that medications are expensive. Factors associated with an increased risk of an admission due to an adverse drug reaction were use of numerous different medications, higher medication costs, receiving Medicaid, and not receiving any home services. In conclusion, many elderly admissions are drug related; noncompliance accounting for a substantial fraction of these. Elders at high risk of being noncompliant are identifiable using a variety of criteria. Economic factors were important in predicting admissions due to noncompliance as well as adverse drug reactions.

Conlan M. F. **“R.Ph. counseling can reduce cost of noncompliance. (to employee benefit plans).”** *Drug Topics* (1990) **134**(13): 38.

Wade J. C. **“Ethical and economic aspects of noncompliance and overtreatment.”** *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne* (1990) **142**(3): 204-5.

Burgess M. M. **“Ethical and economic aspects of noncompliance and overtreatment.”** *CMAJ : Canadian Medical Association journal* (1989) **141**(8): 777-80.

Physicians have an ethical responsibility for \*cost\*-saving within the current medical care delivery system. \*Noncompliance\* and overtreatment are among the causes of excessive health care expenses. An effective means of improving compliance and avoiding unwanted or fruitless treatment is improved physician-patient communication. Improved communication is also the most ethical means of avoiding these expenses. The educated participation of patients in treatment decisions and of the public in health policy formation is ethically and economically preferable to bureaucratic responses and user fees. The public must be made aware of the \*costs\* and limited benefits of medical treatments and of the effects of lifestyle on health. The medical encounter must become more supportive and educational. Medical school curricula must emphasize patient involvement, which must be reinforced to medical students and residents by staff physicians' genuine concern and effort. Quality assessments and assurance should include evaluation of communication, patient satisfaction, use of follow-up and duplication of services.

Smith D. L. "**Compliance packaging: a patient education tool.**" *American Pharmacy*. (1989) **NS29**(2): 42-5, 49-53.

As a direct response to the profound negative impact that the high rate of noncompliance is having on therapeutic efficacy and total health-care costs, some pharmaceutical manufacturers have taken steps to develop compliance packaging for some products prescribed for ambulatory patients. The purpose of compliance packaging is to serve as a patient-education tool for health professionals and to make it easier for patients to remember to take their medications correctly at home. The ideal compliance package will be developed according to patient-education guidelines. Compliance packaging holds promise as a significant patient-education tool when health professionals combine it with personalized patient counseling and well-written medication instructions. Well-controlled cost-effectiveness studies are needed to determine the impact of compliance packaging on reducing total health-care costs.

Fincham J. E. "**Patient Compliance in the Ambulatory Elderly: Review of the Literature.**" *Journal of Geriatric Drug Therapy* (1988) **2**(4): 31-52.

<Abstract> A review of literature pertaining to \*noncompliance\* in the elderly is presented, including general problems of drug utilization, incidence of \*noncompliance\*, specific predictors of elderly \*noncompliance\*, the impact of communication between patient and pharmacist, methods to improve compliance and the \*cost\* effective nature of compliance interventions.

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Plant A. and Gross P. "**Economic Costs of Noncompliance with Medications in Australia.**" *Australian Journal of Pharmacy* (1988) **69**: 129-134.

<Abstract> Economic and health \*costs\* of drug \*noncompliance\*, and the impact on hospital admissions and pharmacy finances, are briefly discussed.

Urquhart J. and Chevalley C. "**Impact of Unrecognized Dosing Errors on the Cost and Effectiveness of Pharmaceuticals.**" *Drug Information Journal* (1988) **22**(3): 363-378.

<Abstract> The effects of \*patient\* \*noncompliance\* with drug regimens on drug efficacy and \*costs\*, patterns of \*noncompliance\* with prescribed regimens, and devices and packaging for encouraging and monitoring compliance are described and discussed. The potential effects of \*noncompliance\* on \*cost\* benefit analyses of different therapeutic regimens were outlined. Particular patterns of interruptions by patients in chronic drug therapy, called drug holidays, were discussed in additional detail, including the clinical and pharmacokinetic effects and \*costs\*. The need for improved monitoring methods to prevent drug holidays is also discussed.

Vandereycken W. and Meermann R. "**Chronic illness behavior and noncompliance with treatment: pathways to an interactional approach.**" *Psychotherapy & Psychosomatics*. (1988) **50**(4): 182-91.

The increasing cost of medical overconsumption is partially due to the physicians' neglect in everyday clinical practice of the intrinsic gratification of the sick role in our society. Many health care providers do not seem to realize that their intervention as experts in the patient's personal life inevitably implies they are becoming part of the ongoing learning history of that individual. Chronic somatic complaining and partial or complete refusal to follow therapeutic advice have to be viewed, first and foremost, as a symptom of a dysfunctional interaction between the patient and his/her immediate environment of which the clinician became a significant member. Management of chronic illness behavior and non-compliance with treatment requires both a functional analysis and a strategy inspired by an interactional perspective on the attitudes and behaviors of at least three parties involved in health care: doctor, patient, and family. [References: 45]

Anonymous. "**Noncompliance Results in Annual Loss of \$13 to \$15 Billion.**" *American Pharmacy* (1987) **VNS27**(Sept): 20.

<Abstract> Some of the factors that affect \*patient\* \*compliance\* with prescription drug therapy, and the effects of \*noncompliance\* on health care \*costs\* in the United States were summarized.

Enlund H. and Poston J. W. "**Impact of Patient Noncompliance on Drug Costs.**" *Journal of Social and Administrative Pharmacy* (1987) **4**(3): 105-111.

<Abstract> An investigation is made of the influence of \*patient\* \*noncompliance\* and irrational prescribing on the economics of drug use. Problems with compliance research are examined and examples are given of how \*noncompliance\* may contribute to gains or losses in the \*cost\* benefit analysis of drug treatment.

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Morse M. L. "**Drug Utilization Review: Implications for Patient Compliance.**" *US Pharmacist* (1987) **12**(Oct. Suppl.): 12-14.

<Abstract> Drug utilization review, focused on the issues of drug induced disease (a form of \*noncompliance\*) rather than for the sole purpose of saving money on the drug component of a prescription charge, is discussed. The goal of drug utilization review is stated to be the prevention of the exacerbation of disease caused by improper drug use and \*noncompliance\*. Detection of drug induced disease will offer the pharmacist a chance to become involved in a most important \*cost\* containment role.

Cluff L. E. "**Patient compliance: changing patterns of disease and health care costs.**" *Hospital formulary* (1985) **20**(4): 503-4, 507, 510.

Most of the drugs in our therapeutic armamentarium are effective and have contributed significantly to the health of Americans. Whereas \*patient\* \*compliance\* relating to prescribed medications has always been an issue, the impact of \*patient\* \*compliance\*--or \*noncompliance\*--on health care expenditures has added a new dimension to the controversy. Because of the growth of chronic care, physicians need to

prescribe long-term drug therapy that patients will administer themselves. Patients must be motivated to ensure compliance with treatment regimens that health care professionals prescribe or dispense.

Insull W. "**Management of adherence to prescribed medication.**" *Advances in experimental medicine and biology* (1985) **183**: 349-60.

\*Nonadherence\* is a major problem for long-term use of drugs affecting lipid metabolism. Effective programs for comprehensive management of adherence are available. Their administration and operation can be readily integrated within the usual operations of both large and small clinical trials. The programs are subject to quality control and, hence, can be administered effectively. The \*cost\* of a comprehensive adherence program is approximately 10% of the conventional \*cost\* of clinical trials, varies according to the nature and number of adherence tests, and is probably totally recovered through resultant economies. All of the elements of the adherence program can be adapted to private practice. The relative risks of \*nonadherence\* to drugs affecting lipid metabolism are estimated from analyses of four regimen characteristics.

Murphy D. "**Promoting Compliance Pays Off.**" *American Pharmacy* (1985) **VNS25**(Jan): 19, 22-24.

<Abstract> The \*costs\* to patients, the public and pharmacies of therapeutic \*noncompliance\*, and potential savings and effectiveness of various patient education and monitoring programs designed to improve compliance were discussed.

Smith M. "**Cost of Noncompliance and the Capacity of Improved Compliance to Reduce Health Care Expenditures.**" *Illinois Pharmacist* (1985) **47**(Oct.): 13, 27.

<Abstract> The \*cost\* of \*noncompliance\* and the capacity of improved compliance to reduce health care expenditures were addressed.

Cowen M. E., Jim L. K., Boyd E. L. and Gee J. P. "**Some possible effects of patient noncompliance.**" *JAMA : the journal of the American Medical Association* (1981) **245**(11): 1121.

Becker M. H. and Maiman L. A. "**Strategies for enhancing patient compliance.**" *Journal of Community Health*. (1980) **6**(2): 113-35.

Patient noncompliance is a substantial obstacle to the achievement of therapeutic goals. This paper reviews a number of practical interventions with demonstrated efficacy in enhancing patient adherence, including (1) improving patients' levels of information concerning the specifics of their regimens, reinforcing essential points with review, discussion, and written instruction, and emphasizing the importance of the therapeutic plan, (2) taking clinically appropriate steps to reduce the cost, complexity, duration, and amount of behavioral change required by the regimen and increasing the regimen's convenience through "tailoring"

and other approaches, (3) obtaining a compliance-oriented history of the patient's prior experiences and present health beliefs and, where necessary, employing strategies to modify those perceptions likely to inhibit compliance, (4) improving levels of patient satisfaction, particularly with the provider-patient relationship, (5) arranging for the continued monitoring of the patient's subsequent compliance to treatment, (6) increasing staff awareness of the magnitude and determinants of the noncompliance phenomenon and attempting to develop an "active influence orientation" in each member of the health care team, (7) using such techniques as patient-provider contracts to involve the patient in therapeutic decisions and in the setting of treatment objectives and creating incentives (through rewards and reinforcements) for achieving these objectives, (8) arranging for as much continuity of provider (and other staff) as possible, (9) establishing methods of supervising the patient, including involvement of the patient's social support network, and (10) involving fully the assistance of all available health care providers, assigning specific roles and responsibilities for activities directed at improving adherence to treatment.

### **Women's and Men's health**

[Rozenberg S, Vandromme J, Kroll M, Twagirayezu P, Vyankandondera J.](#)

[Compliance with hormone replacement therapy]  
Rev Med Brux. 1995 Jul-Aug;16(4):295-8. French.

[Rozenberg S, Vandromme J, Kroll M, Pastijn A, Liebens F.](#)

Compliance to hormone replacement therapy.  
Int J Fertil Menopausal Stud. 1995;40 Suppl 1:23-32. Review

[Epstein LH.](#)

The direct effects of compliance on health outcome.  
Health Psychol. 1984;3(4):385-93. Review.

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**ISPOR Medication Compliance**

Joyce A. Cramer  
Associate Research Scientist  
Department of Psychiatry  
Yale University  
School of  
950 Campbell Ave. (G7E)  
West Haven, CT 06516-2770  
Tel: 203-937-3894  
Fax: 203-937-3468  
e-mail: [joyce.cramer@yale.edu](mailto:joyce.cramer@yale.edu)

**ISPOR Medication Compliance  
Bibliography Group**

Jasmanda H. Wu  
Associate Director, Outcomes Research  
Ortho-McNeil Janssen Scientific Affairs, L.L.C.  
1125 Trenton-Harbourton Road  
Titusville, NJ 08560-0200  
Tel: 609-730-7718  
Fax: 609-730-2411  
e-mail: [jwu2@omjus.jnj.com](mailto:jwu2@omjus.jnj.com)

Sue Capon  
Staff Liaison to  
Special Interest Groups  
ISPOR  
Tel: 609-219-0773, ext. 21  
e-mail: [scapon@ispor.org](mailto:scapon@ispor.org)