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How Do You Improve Compliance?

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ABSTRACT. Compliance, or adherence, as it relates to health care is the extent to which a person's behavior coincides with medical or health advice. Medication compliance is critical for all aspects of pediatrics, specifically in successful treatment, disease prevention, and health promotion. Compliance depends on the patient's and physician's committing to the same objectives. It is unfortunate that numerous studies and physician accounts reveal difficulties in achieving compliance with pediatric medication therapy. Medication compliance in pediatric patients ranges from 11% to 93%. At least one third of all patients fail to complete relatively short-term treatment regimens. Poor compliance places children at risk for problems such as continued disease, complicates the physician-patient relationship, and prevents accurate assessment of the quality of care provided. This article presents the issue in the context of its incidence of and barriers to compliance and provides general principles to improve compliance in pediatrics by improving communication and characteristics of the practice setting. A one-on-one relationship between physician and patient is needed for communication and improved compliance. *Pediatrics* 2005;115:e718–e724. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-1133; medication, compliance, adherence, prescription, education, physician-patient, dose, duration, palatability, practice, cost.

ABBREVIATION. AAP, American Academy of Pediatrics.

This article is based on reviews of medical literature concerning compliance issues, on information gathered by the American Academy of Pediatrics (AAP) Taskforce on Medication Compliance, the AAP Periodic Survey (no. 44), and personal clinical experiences of the authors.

As we begin the 21st century, the average medication compliance is ~50% in the pediatric population.¹ The range is from 5% to 15% for urban adolescent medication compliance to 85% to 95% for

suburban newborn immunization compliance. There are a host of factors that affect medication compliance, but key among them include social and economic circumstances, particularly health literacy, patient belief systems, patient education, acceptability and palatability of the medication, and adverse effects of the medication. The costs of noncompliance to the health care are not trivial. Although not pediatric specific, the National Pharmaceutical Council estimated that \$8.5 billion is unnecessarily spent annually on hospitalizations and physician visits caused by noncompliance to prescription regimens.² In pediatrics, it is necessary to deal with not only the issues of the patient but also the issues of the parent or other caregiver, which adds to the complexity of medication compliance.

Medication compliance was well reviewed by Jones³ in 1983, and little has changed since then in terms of medication issues. However, compliance issues are changing because dramatic shifts in the financing and organizing of health care already exert a negative effect on medication compliance. In response to increasing health care costs, particularly for prescription drugs, employers are instituting more restrictive formularies and shifting more of the costs to the employee through such innovations as multitiered copay systems. It remains to be seen whether parents who are faced with greater out-of-pocket prescription drug costs will decide to cut back on their children's use of medications.

Compliance is central to the pediatrician's ultimate concern: the health of the patient. Medication compliance is following a physician-prescribed regimen and duration of medication or schedule of immunizations. The health concern is that lack of compliance can produce inadequate or unsuccessful therapy¹; unnecessarily extended treatment; and cause additional physician visits, changed prescriptions, and, in the case of immunizations, increased susceptibility to diseases and their sequelae.

METHODS

Appropriate articles, studies, and reports were obtained through 3 Medline searches (www.ncbi.nlm.nih.gov/entrez/query.fcgi). The first search (limited to the previous 2 years) was for medication compliance, and the other searches (unbounded by time) included patient compliance, patient dropouts, or treatment refusal combined with 45 other terms including drug therapy (exploded) and specific formulations or methods of drug delivery. The searches identified >250 articles that were subsequently evaluated for clinical relevance and validity, and a second round involved whole article reviews. An additional search was conducted in December 2003 to update the final version of this article. In addition, data from an AAP Periodic Survey (no. 44)² on pediatricians' views on patient compliance with completing prescrip-

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tion regimens for acute and chronic illness were used. The survey was conducted from January to May 2000, and a total of 925 completed questionnaires were received, for a response rate of 56.7%. The data analysis was based on responses from 803 pediatricians who provide direct patient care. The resulting general principles addressed in this article are based on a combination of the literature review, the AAP survey, and professional opinion and consensus.

It is important to stress that reliability of data on compliance is subject to question, and it is likely that compliance is significantly lower than reported in many publications. For example, parent reporting of compliance has been documented to be grossly overrated. Elliott et al⁴ reported that mothers claimed 60% compliance with obtaining prescribed refills, but pharmacy records indicated that only 12% adhered to the schedule. The need for better data concerning compliance must temper interpretation of compliance issues. The authors of a recent review article⁵ pointed out shortcomings in many compliance studies and called for higher quality in future trials to better identify effective strategies. Others have called for standardized methods for measuring compliance.⁶

DISCUSSION

Shift in Physician-Patient Relationship

Changes in the organization of practice settings and payor/reimbursement systems have affected the practice environment. Pressures and organization issues impair continuity of patient contact and availability of time to spend with individual patients. Patients increasingly obtain information from a variety of sources. Pharmaceutical companies now advertise directly to consumers. The Internet facilitates immediate access to health care information that may be helpful in patient education, but it is often without context or understanding of the various clinical, psychological, and sociological factors that interact in the clinical setting. Internet-based information may be written by physicians but without knowledge of the individual patient. Therefore, the physician must now deal with more independent decisions by patients that may affect compliance and must learn to use increased access of patients to information to improve compliance.⁷

Consequences of Noncompliance

The efficacy of prescription drugs and medication regimens has been determined through clinical trials (although often not pediatric trials) and reinforced by clinical experience. In clinical trials, some of the failure to respond is attributable to noncompliance with the medication protocol among trial subjects. It is not surprising that in the less organized and poorly monitored environment of clinical practice, noncompliance with prescribed medication is an important contributor to failure of patients to respond or of less-than-expected response to treatment.⁸

As noted by Elliot et al,⁴ relying on parental reports to confirm compliance or to identify compliance problems is problematic. This underscores the thought that the body of research on medication compliance is inadequate in many regards and has not quantified the effect of noncompliance on health care. However, noncompliance is undoubtedly a major contributor to repeated office visits, changed and additional prescriptions, extended course of illness and treatment, and unnecessary use of health care resources. In the extreme, noncompliance with med-

ication can be the root cause of therapy failure (eg, transplant rejection, seizures, diabetic coma).

Barriers to Medication Compliance

Limited Time and Continuity of Physician-Patient Interaction

Many issues are central to enhancing compliance; chief among these include understanding the prescribed medication regimen, acceptance of the need for compliance, and continuity in response to questions that may arise during care management.⁹ In the spectrum of pediatric practice, from solo practitioner to the multipersonnel-directed medical home, time is needed to explain the treatment plan and the importance of compliance to the patient and family and to get feedback on their understanding and circumstances. For example, time is required to negotiate a best fit of medication; patient and family concerns; schedule restraints; and, most important, ability of patient, family, or caregiver to comply with the prescribed regimen.

However, time is becoming a scarce commodity for the practicing pediatrician. Pressure from practices and plans to address administrative and billing concerns along with the daily tasks of managing nonphysician staff all serve to reduce the amount of time that the pediatrician has to address the needs of the patient and the family during the clinical encounter. It is becoming increasingly important for the pediatrician to manage time effectively not only to meet diagnostic needs but also for patient education, development of a treatment plan, and choice of medication, all of which affect compliance.

Familiarity of the pediatrician and the office staff with the patient, family, and treatment program also are important elements relating to patient or family confidence, consistent response to questions or problems that may arise concerning compliance, and reinforcing follow-up to the treatment program. Continuity of care also can be lost in some settings as a consequence of an imposed change in attending physician or by the patient's presenting at different offices or care facilities.

Patient and Family Characteristics

Compliance must be addressed for both acute and chronic uses of medications. It is commonly stated but poorly documented that medication compliance is a larger problem with chronic courses of medication. Matsui¹ noted essentially equal rates of noncompliance in a review of reports of short- and long-term medication regimens. However, ongoing support to encourage compliance is especially important for the children who are on long-term regimens.¹⁰⁻¹³ To encourage compliance, the pediatrician should examine the organization of the practice to identify barriers and set in motion changes to overcome these obstacles.

Understanding on the part of patient and caregiver of the need and importance of following prescribed treatment has been identified as an important element in compliance. This takes on a special meaning in the pediatric context, given the unique communication triad (eg, provider-caregiver-patient).¹⁴ There

are environmental factors that affect this understanding, including health literacy, education, and culture. Liptak¹⁵ discovered that education and culture could strongly affect such understanding and the time and educational effort needed on a case-by-case basis. In fact, many of the disparities in health outcome that are based on cultural, ethnic, and socioeconomic factors may reflect to some extent disparities in the adoption and maintenance of healthy lifestyles and adherence to medical regimens. To bridge this potential communication gap, the pediatrician needs to assess the patient's knowledge level and determine whether misinformation or perspectives from outside sources, including the Internet, influence the patient and the family.

Certain types of psychopathology have been associated with noncompliance (eg, oppositional defiant disorder in adolescents).¹⁶ Patients with psychiatric comorbidities represent a significant challenge to primary care providers and may need assistance from mental health professionals. Similarly, culture and perspective on the causes of disease and the treatment of disease can have a large effect on attitude and desire to be compliant.⁴ These factors must be addressed in designing a treatment plan, educational efforts, and support activities, to at least some extent, if the pediatrician is aware of them. An understanding of the patient's and the family's cultural influences also is essential if compliance is to occur.^{17,18}

The caregiving environment also can have a large effect on compliance, including situations such as dysfunctional families with poor or no communication, the patient's being escorted to the pediatrician by someone other than the primary caregiver, a patient's having multiple caregivers who share information and coordinate the treatment regimen, or a patient's moving across different sites during a course of a week or a day, thus complicating availability of medication, coordination of treatment, and desire or ability to comply. An approach using social learning strategies was shown to improve compliance in an uncontrolled study of inner-city children who had asthma and faced many of these challenges.¹⁹

Pediatrician Characteristics

The subject of compliance is a serious one for most physicians. There are issues that are beyond the direct control of the physician, including palatability, dosage formulation, and costs. However, prescribing practices can help mitigate the influence of these issues on compliance for individual patients, including selecting medications that are most apt to enhance compliance, based on experience.

Characteristics of the practice setting and specific physician behaviors can further improve compliance. A first step is to have a well-organized practice setting. Although sophisticated and expensive high-technology solutions are beyond the reach of most physicians, there are low-tech solutions that can be used immediately. Physicians and their office staff can study and improve scheduling protocols and office or clinic operations to expedite appointments and follow-up, barring intervening medical emer-

gencies. Parents are most likely to be effective partners in communication and education if they are not distracted by restless children, their own time constraints, and the inherent unpleasantness of waiting. Conversely, the physician is likely to address compliance if he or she is not feeling the pressure of a crowded patient waiting room. Improved communication skills have been shown to shorten visit duration, improve patient response, and decrease needed follow-up care.²⁰

Availability and continuity of care also will promote compliance.¹⁵ Telephone availability 24 hours a day, 7 days a week is imperative to answer patients' and families' concerns and to reinforce effective administration of medication. Off-hours availability also can benefit compliance by keeping the door open to patients and families who otherwise may take the child to emergency departments or urgent care clinics, resulting in fragmented care. On-call arrangements staffed by a triage nurse or a physician who is unfamiliar with the patient's treatment plan requires additional time and information to assess the problem that parents may face in administering medications. Home visits are another tool, as is the growing use of online consultations. Numerous surveys show that many patients are interested in communicating with their physicians online, and more than 3 million already do so. Although reimbursement and malpractice issues are major barriers, online consultation can work to promote patient adherence.

Clinical experience has shown that within the office or clinic setting, the following steps take little time and can be revealing:

1. Ask explicitly about difficulties in administering medications to the child currently or in the past.
2. Ask about the amount of medication left in the bottle or container.
3. Consider the lifestyle of the family and the degree to which they can be expected to adhere to a specific treatment plan.
4. Do not prescribe complex regimens all at once; rather, institute 1 step at a time.
5. Encourage or specify telephone calls to iron out difficulties.
6. Try to avoid regimens that require school involvement, although this may be difficult with some psychotropic or antiretroviral medications.

Medication Factors

Duration, schedule, formulation, palatability, cost, and adverse effects of medication all are factors that contribute to compliance. Most trials on medication factors and compliance have been performed with adults, not children. Caution must be exercised in extrapolating findings from adult studies to children because of physical, developmental, attitudinal, and environmental differences. There is a paucity of studies of crushed tablets (a common practice in pediatrics) that may affect potency and compliance. Furthermore, ingesting a volume of fruit juice to mask the taste of a drug has potential to alter the bioavailability of the drug.²¹ The effects of flavoring agents

on pharmacokinetics and pharmacodynamics are largely untested.

Duration

There is good recent evidence that compliance decreases over the treatment period in medication for acute infection.²² Older work was notable for its failure to randomize and the use of different forms of medication (tablets vs suspension) in studies of children of different ages, detracting from the power of conclusions.^{23,24} These compliance results were confirmed, however, in a later study with treatment duration randomized.²⁵ Socioeconomic factors and comparisons of different antibiotics and durations of therapy^{26–28} may have confounded studies with similar findings. Compliance with long-term therapy also has been noted to decrease over time.^{29,30}

Complexity of Medication Schedule

A host of studies have examined the relationship between dosing schedules and compliance with the medication regimen.^{31–34} The general findings across all studies is that the simpler the schedule, the greater the likelihood of compliance. For example, compliance with oral medicine was better with twice daily versus 4 times a day,^{35,36} whereas several reports mentioned that parents prefer less dosing, particularly avoiding the middle of the day. Data support this notion in the primary care setting; however, an effect on compliance has not been noted consistently.^{26,37–44} A recent survey of caregivers for children with HIV failed to show a difference in compliance on the basis of the number of medications prescribed, although factors related to simplifying the medication regimen were cited by parents as a significant means to enhance adherence in this and another study.^{45,46}

Forms

Medications are administered in a variety of forms, including liquid, suspension, powder, tablet, capsule, topical creams, and topical patches. They may be administered by different routes, such as injection, oral rectal, inhalation (oral or nasal), or topical, in appropriate formulations.

Studies that have evaluated forms of medication preference and compliance rates have been numerous, and their conclusions are different depending on the type of medication. Although 75% to 100% of children have been reported^{47–49} to express a preference for one form over another (eg, sprinkles vs syrup), only 1 of these trials measured compliance. From the parental perspective, earlier studies reported that parents prefer oral liquid to solid forms (eg, powder, tablets, capsules), but compliance was measured in only some studies.^{50–52} A recent randomized study of infants and toddlers with malaria demonstrated superior adherence to a regimen of crushed tablets when compared with syrup.⁵³ In a study of children with HIV, caregivers reported that it was easier to administer the tablet form of a medication than a large volume of powder.⁵⁴ The dosing interval was also changed at the same time, making it difficult to draw firm conclusions about the impact on compliance.

Asthma is a model of chronic disease that is

treated with different forms of medication. No difference in compliance was noted with 2 types of inhalers in adults and adolescents with asthma,⁵⁵ and mixed results have been reported comparing compliance with oral tablets versus inhalers, with more recent work favoring tablets.^{56–61}

Palatability

There are conflicting data concerning whether children can distinguish between different commercial preparations and, thus, whether palatability is important for compliance. Certainly, many have observed children refuse certain medications. One study of children 6 to 12 years of age showed clear dislike of 1 of 4 suspensions, but compliance was not measured.⁶² Other open-label and single-blind trials of paired antibiotic preparations found that children expressed preferences.^{63,64} One problem with palatability studies is the lack of a “gold standard” for taste, and another is that the usefulness of parental reports or facial hedonic scales in children who are younger than 6 years has been debated.⁶⁵ Some retrospective studies indicate that negative palatability (displeasing taste and rough texture) has a negative influence on compliance,^{41,43,66} and pleasing taste improves compliance.⁶⁷ A recent study of children with HIV noted that palatability factors related to ease of administration of certain medications, although there was no difference between study groups in terms of adherence.⁵⁴

The magnitude of the effect of palatability on compliance is not clear and deserves additional study to address possible changes with age of the patient and effects of impaired olfactory senses. Influences of culture and culinary background also may affect taste and texture perceptions.

Cost

Cost, in contrast to individual response to the drug or formulation, has an effect on access to medication. Studies have purported cost as a barrier to use⁶⁸ and public aid as a facilitating factor.⁶⁹ Surprising, a recent Canadian study cited cost as a factor in parents' unwillingness to fill a prescription that was given in the emergency department, but nearly 80% of patients had some form of prescription plan.⁷⁰ Cost also drives the decision to develop drug formularies that may restrict access to and availability of some useful medications, ignoring the importance of palatability, frequency of dosing, and efficacy to compliance.

Adverse Effects

Adverse effects from the medication seem to contribute to poor compliance, as an inverse relationship between adverse effects and compliance has been demonstrated,^{67,71,72} although this finding is not universal.¹⁶ They also contribute to the discontinuation of the medication.⁷³

Research activities may further elucidate compliance issues and develop tools and approaches to improve compliance. Congressional Report Language for the FY 2000 Appropriations bill urged the Office of Behavioral and Social Sciences Research and several other National Institutes of Health institutes to stress the need for all institutions to fund behavioral and social sciences research to improve

adherence to medical regimens. In fact, the National Institute of Child Health and Human Development instituted the behavioral pediatrics and health promotion research program. One component of this program is research on compliance issues. It encourages research to elucidate behavioral mechanisms involved in adherence to medical and behavioral regimens for children who have acute and chronic illness. This is a significant indication of the government's increasing interest in this topic. However, there are several things that clinicians can do to improve compliance today. These are enumerated below.

General Principles to Enhance Medication Compliance

1. Improve communication between physician and patient and/or family. The practice setting, time management, specific questions to patient and/or family, education, focused and written materials given to the patient and/or family, and an atmosphere of encouraging the expression of questions or concerns all contribute to improving communications and compliance.^{20,74} The physician must elicit responses from the patient/caregiver to ascertain the patient's objectives, as well as his or her understanding and willingness to comply, thus confirming effectiveness of communication. Electronic systems that manage patient records; track prescriptions; and provide educational, prescription, and treatment plan information can support compliance by providing information to the physician and to the patient/caregiver.
2. Modify or negotiate regimens. Physicians should forge a partnership with families to devise a regimen with which they are most likely to comply.¹⁵ Parents are likely to express preferences for (or difficulties with) certain schedules; also form and palatability should be considered individually with each patient, as multiple options frequently exist. Determine whether cost or other barriers will impede compliance.
3. Emphasize patient self-management of disease or illness. Taking ownership for managing one's condition results in increased motivation to understand the illness or treatment plan. Receptivity to education and heightened responsibility for ensuring compliance, including informing the physician of barriers or problems, stem from taking ownership. When the patient desires the objective of therapy, compliance is more likely.
4. Use the simplest effective regimen available. In some contexts, directly observed therapy may be necessary in the short term to enhance adherence⁷⁵ or for public health reasons, as in tuberculosis. Single-dose or few-dose regimens leave little opportunity for failed compliance. Once-a-day dosing reduces complications from multiple caregivers, dependence on schools, and schedule issues. Examples are single-dose antibiotics for otitis media, extended-release dosage forms that are emerging, and hormonal depot injections.
5. Use technology and devices. Novel technologies are available to enhance compliance. Examples

include insulin pumps, intranasal administration devices, needle-free delivery systems, and devices that count actuations of an inhaler or opening a bottle. Age-appropriate adaptations of currently used devices can also be useful.⁷⁶ Other interventions also may improve compliance, including pill counting,⁷² slide tapes,⁷⁷ and behavior management.^{78,79} Some interventions have been tried without noted benefit in compliance, including use of a measured dispensing device⁸⁰ and medicine calendar recording.⁸¹ Development of microassays with blood or urine for prescribed drugs would greatly assist in monitoring compliance.⁸²

6. Develop better communication skills. Incorporate into undergraduate and graduate physician education and in continuing medical education the development of skills to communicate with patients, to educate patients, and to negotiate with patients for treatment programs with increased likelihood of compliance. Communication skills are required to understand the needs and objectives of the patient. Communication with and education of patients and parents concerning the medical condition and the treatment are essential to enlist enthusiasm and provide understanding, which promote compliance. Physician education can improve the quality and efficiency of communication with parents.²⁰ This can and should be modeled to students, residents, and other physicians in the practice setting.

With respect to all the principles enumerated above, the overriding issue for improved compliance is the development of a one-on-one relationship with mutual respect between 1 doctor and 1 patient. Indeed, the ultimate responsibility and authority lies within this one-on-one relationship. On the basis of our review and practice experience, the closer the practice setting gets to this one-on-one relationship for diagnosis, therapy, and follow-up, the better compliance will become. As concerned physicians, our task is to advocate and foster implementation of this one-on-one practice setting.

CONCLUSIONS

Although one can anticipate technologic developments that will include gene insertions and modified gene regulation and advances in pharmaceutical technology that may diminish compliance problems in treating some diseases, the need to address the matters noted in this report remains and will remain of major significance. Medication compliance for treatment regimens for acute and chronic conditions is low. Few medications are available in pediatric dosage forms, and the rate of extemporaneous formulation is high. However, continued enforcement of the pediatric rule may increase the number of drugs in pediatric formulation, and research may develop new tools to improve compliance.

The goal is not strict and absolute compliance but rather improvements in therapeutic response, which will be achieved by improvement in compliance with prescribed therapy on the basis of effective commu-

nication between the physician and the patient/caregiver concerning the response, problems with following the regimen, or adverse reaction to a drug. Communication is essential to ensure that physician and patient are working toward mutually agreed-on objectives. Pediatricians must continue to advocate for better health and appropriate therapeutics for their patients. Good communication with patients and families, education in health matters, negotiation of treatments and treatment regimens, and adoption of responsibility by patients and families for the success of the therapy will stand long into the future as foundations of successful health care.

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REFERENCES

- Matsui DM. Drug compliance in pediatrics. *Pediatr Clin North Am*. 1997;44:1-14
- Noncompliance With Medications: An Economic Tragedy With Important Implications for Health Care Reform*. Baltimore, MD: Task Force for Compliance; 1994
- Jones JG. Compliance with pediatric therapy. *Clin Pediatr (Phila)*. 1983; 22:262-265
- Elliott V, Morgan S, Day S, Mollerup LS, Wang W. Parental health beliefs and compliance with prophylactic penicillin administration in children with sickle cell disease. *J Pediatr Hematol Oncol*. 2001;23:112-116
- Newell SA, Bowman JA, Cockburn JD. A critical review of interventions to increase compliance with medication-taking, obtaining medication refills, and appointment-keeping in the treatment of cardiovascular disease. *Prev Med*. 1999;29:535-548
- Ellis S, Shumaker S, Sieber W, Rand C. Adherence to pharmacological interventions. Current trends and future directions. *The Pharmacological Intervention Working Group. Control Clin Trials*. 2000;21(suppl):218S-225S
- Donovan JL. Patient decision making. The missing ingredient in compliance research. *Int J Technol Assess Health Care*. 1995;11:443-455
- Cramer JA. Relationship between medication compliance and medical outcomes. *Am J Health Syst Pharm*. 1995;52(suppl 3):S27-S29
- Spath P. Continuity of care means better instruction on meds. *Hosp Peer Rev*. 2000;25:53-55
- Thompson SM, Dahlquist LM, Koenning GM, Bartholomew LK. Brief report: adherence-facilitating behaviors of a multidisciplinary pediatric rheumatology staff. *J Pediatr Psychol*. 1995;20:291-297
- Davis MC, Tucker CM, Fennell RS. Family behavior, adaptation, and treatment adherence of pediatric nephrology patients. *Pediatr Nephrol*. 1996;10:160-166
- Bell F. Post-renal transplant compliance. *J Child Health Care*. 2000;4:5-9
- Meyers KE, Thomson PD, Weiland H. Noncompliance in children and adolescents after renal transplantation. *Transplantation*. 1996;62:186-189
- Sanz EJ. Concordance and children's use of medicines. *BMJ*. 2003;327: 858-860
- Liptak GS. Enhancing patient compliance in pediatrics. *Pediatr Rev*. 1996;17:128-134
- Bernstein GA, Anderson LK, Hektner JM, Realmuto GM. Imipramine compliance in adolescents. *J Am Acad Child Adolesc Psychiatry*. 2000;39: 284-291
- Fadiman A. *The Spirit Catches You and You Fall Down: A Hmong Child, Her American Doctors, and the Collision of Two Cultures*. New York, NY: Farrar Straus & Giroux; 1998
- Galanti G. *Caring for Patients From Different Cultures: Case Studies From American Hospitals*. Philadelphia, PA: University of Pennsylvania Press; 1997
- Bartlett SJ, Lukk P, Butz A, Lampros-Klein F, Rand CS. Enhancing medication adherence among inner-city children with asthma: results from pilot studies. *J Asthma*. 2002;39:47-54
- Clark NM, Gong M, Schork MA, et al. Impact of education for physicians on patient outcomes. *Pediatrics*. 1998;101:831-836
- Dresser GK, Bailey DG, Leake BF, et al. Fruit juices inhibit organic anion transporting polypeptide-mediated drug uptake to decrease oral availability of fexofenadine. *Clin Pharmacol Ther*. 2002;71:11-20
- MASCOT Study Group. Clinical efficacy of 3 days versus 5 days of oral amoxicillin for treatment of childhood pneumonia: a multicentre double-blind trial. *Lancet*. 2002;360:835-841
- Bergman AB, Werner RJ. Failure of children to receive penicillin by mouth. *N Engl J Med*. 1963;268:1334-1338
- Charney E, Bynum R, Eldredge D, et al. How well do patients take oral penicillin? A collaborative study in private practice. *Pediatrics*. 1967;40: 188-195
- Schwartz RH, Wientzen RL, Pedreira F, Feroli EJ, Mella GW, Guandolo VL. Penicillin V for Group A streptococcal pharyngotonsillitis: a randomized trial of seven vs ten days' therapy. *JAMA*. 1981;246:1790-1795
- Lauvau DV, Verbist L. An open, multicentre, comparative study of the efficacy and safety of azithromycin and co-amoxiclav in the treatment of upper and lower respiratory tract infections in children. *J Int Med Res*. 1997;25:285-295
- Hoppe JE, Wahrenberger C. Compliance of pediatric patients with treatment involving antibiotic suspensions: a pilot study. *Clin Ther*. 1999;21:1193-1201
- Hoppe JE, Blumenstock G, Grotz W, Selbmann HK. Compliance of German pediatric patients with oral antibiotic therapy: results of a nationwide survey. *Pediatr Infect Dis J*. 1999;18:1085-1091
- West RJ and Lloyd JK, Leonard JV. Long-term follow-up of children with familial hypercholesterolaemia treated with cholestyramine. *Lancet*. 1980;8200:873-875
- Martinez J, Bell D, Camacho R, et al. Adherence to antiviral drug regimens in HIV-infected adolescent patients engaged in care in a comprehensive adolescent and young adult clinic. *J Natl Med Assoc*. 2000;92:55-61
- Coutts JA, Gibson NA, Payton JY. Measuring compliance with inhaled medication in asthma. *Arch Dis Child*. 1992;67:332-333
- Gibson NA, Ferguson AE, Aitchison TC, Paton JY. Compliance with inhaled asthma medication in preschool children. *Thorax*. 1995;50: 1274-1279
- Campbell LM, Gooding TN, Aitchison WR, Smith N, Powell JA. Initial loading (400 mcg twice daily) versus static (400 mcg nocte) dose budesonide for asthma management. *Int J Clin Pract*. 1998;52:361-370
- Moncica I, Oh PI, ul Qamar I, et al. A crossover comparison of extended release felodipine with prolonged action nifedipine in hypertension. *Arch Dis Child*. 1995;73:154-156
- Beer S, Laver J, Benson L, et al. Comparison of serum theophylline levels in asthmatic children receiving sustained-release and rapid-release theophylline tablets. *Isr J Med Sci*. 1982;18:255-258
- Tinkelman DG, Vanderpool GE, Carroll MS, Page EG, Spangler DL. Compliance differences following administration of theophylline at six- and twelve-hour intervals. *Ann Allergy*. 1980;44:283-286
- Gerber MA, Spadaccini LJ, Wright LL, Deutsch L, Kaplan EL. Twice-daily penicillin in the treatment of streptococcal pharyngitis. *Am J Dis Child*. 1985;139:1145-1148
- Williams H, Jones ER, Sibert JR. Twice daily versus four times daily treatment with beclomethasone dipropionate in the control of mild childhood asthma. *Thorax*. 1986;41:602-605
- Rice TD, Duggan AK, DeAngelis C. Cost-effectiveness of erythromycin versus mupirocin for the treatment of impetigo in children. *Pediatrics*. 1992;89:210-214
- Khurana CM. Issues concerning antibiotic use in child care settings. *Pediatr Infect Dis J* 1995;14(suppl):S34-S38
- Dagan R, Shvartzman P, Liss Z. Variation in acceptance of common oral antibiotic suspensions. *Pediatr Infect Dis J*. 1994;13:686-690
- Gehanno P, Barry B, Bobin S, Safran C. Twice daily cefpodoxime proxetil compared with thrice daily amoxicillin/clavulanic acid for treatment of acute otitis media in children. *Scand J Infect Dis*. 1994;26:577-584
- al-Shammari SA, Khoja T, al-Yamani. Compliance with short-term antibiotic therapy among patients attending primary health centres in Riyadh, Saudi Arabia. *J R Soc Health*. 1995;115:231-234
- Pichichero ME, Hoeger W, Marsocci SM, Murphy AM, Francis AB, Dragalin V. Variables influencing penicillin treatment outcome in streptococcal tonsillopharyngitis. *Arch Pediatr Adolesc Med*. 1999;153:565-570
- Reddington C, Cohen J, Baldillo A, et al. Adherence to medication regimens among children with human immunodeficiency virus infection. *Pediatr Infect Dis J*. 2000;19:1148-1153
- Boni S, Pontali E, De Gol P, Pedemonte P, Bassetti D. Compliance to combination antiretroviral therapy in HIV-1 infected children. *Int J Antimicrob Agents*. 2000;16:371-372

47. Cloyd JC, Kriel RL, Jones-Saete CM, Ong BY, Jancik JT, Remmel RP. Comparison of sprinkle versus syrup formulations of valproate for bioavailability, tolerance, and preference. *J Pediatr*. 1992;120:634–638
48. Tonstad S, Ose L. Colestipol tablets in adolescents with familial hypercholesterolaemia. *Acta Paediatr*. 1996;85:1080–1082
49. McCrindle BW, O'Neill MB, Cullen-Dean G, Helden E. Acceptability and compliance with two forms cholestyramine in the treatment of hypercholesterolemia in children: a randomized, crossover trial. *J Pediatr*. 1997;130:266–273
50. Kiyingi KS, Sime L. Compliance profiles of paediatric patients in an outpatient department. *P N G Med J*. 1992;35:95–100
51. Babiker MA. Compliance with penicillin prophylaxis by children with impaired splenic function. *Trop Geogr Med*. 1986;38:119–122
52. Goode M, McMaugh A, Crisp J, Wales S, Ziegler JB. Adherence issues in children and adolescents receiving highly active antiretroviral therapy. *AIDS Care*. 2003;15:403–408
53. Ansah EK, Gyapong JO, Agyepong IA, Evans DB. Improving adherence to malaria treatment for children: the use of prepacked chloroquine tablets vs. chloroquine syrup. *Trop Med Int Health*. 2001;6:496–504
54. Gibb DM, Goodall RL, Giacomet V, McGee L, Compagnucci A, Lyall H. Adherence to prescribed antiretroviral therapy in human immunodeficiency virus infected-children in the PENTA 5 trial. *Pediatr Infect Dis J*. 2003;22:56–62
55. Galant SP, van Bavel J, Finn A, et al. Diskus and diskhaler: efficacy and safety of fluticasone propionate via two dry powder inhalers in subjects with mild-to-moderate persistent asthma. *Ann Allergy Asthma Immunol*. 1999;82:273–280
56. Alessandro F, Vincenzo ZG, Marco S, Marcello G, Enrica R. Compliance with pharmacologic prophylaxis and therapy in bronchial asthma. *Ann Allergy*. 1994;73:135–140
57. Kelloway JS, Wyatt RA, Adlis SA. Comparison of patients' compliance with prescribed oral and inhaled asthma medications. *Arch Intern Med*. 1994;154:1349–1352
58. Edelman JM, Preston SR, Turpin JA, et al. Parent and child preference for montelukast, a leukotriene receptor antagonist, compared to inhaled cromolyn in asthmatic children ages 6 to 11 [abstract]. *Eur Respir J*. 1998;12(suppl 29):18s
59. Drazen JM, Israel E. Should antileukotriene therapies be used instead of inhaled corticosteroids in asthma? Yes. *Am J Respir Crit Care Med*. 1998;158:1697–1698
60. Maspero JF, Duenas-Meza E, Volovitz B, et al. Oral montelukast versus inhaled beclomethasone in 6- to 11-year-old children with asthma: results of an open label extension study evaluating long-term safety, satisfaction, and adherence with therapy. *Curr Med Res Opin*. 2001;17:96–104
61. Bukstein DA, Luskin AT, Bernstein A. "Real-world" effectiveness of daily controller medicine in children with mild persistent asthma. *Ann Allergy Asthma Immunol*. 2003;90:543–549
62. Matsui D, Barron A, Rieder MJ. Assessment of the palatability of anti-staphylococcal antibiotics in pediatric volunteers. *Ann Pharmacother*. 1996;30:586–588
63. Powers JL. Properties of azithromycin that enhance the potential for compliance in children with upper respiratory tract infections. *Pediatr Infect Dis J*. 1996;15(suppl):S30–S37
64. Powers JL, Gooch WM III, Oddo LP. Comparison of the palatability of the oral suspension of cefdinir vs. amoxicillin/clavulanate potassium, cefprozil and azithromycin in pediatric patients. *Pediatr Infect Dis J*. 2000;19(suppl):S174–S180
65. Sjøvall J, Fogh A, Huitfeldt B, Karlsson G, Nylen O. Methods for evaluating the taste of paediatric formulations in children: a comparison between the facial hedonic method and the patients' own spontaneous verbal judgement. *Eur J Pediatr*. 1984;141:243–247
66. Iwai N. Drug compliance of children and infants with oral antibiotics for pediatric use. *Acta Paediatr Jpn*. 1997;39:132–142
67. Wandstrat TL, Kaplan B. Pharmacoeconomic impact of factors affecting compliance with antibiotic regimens in the treatment of acute otitis media. *Pediatr Infect Dis J*. 1997;16(suppl):S27–S29
68. Isenalumhe AE, Oviawe O. Polypharmacy: its cost burden and barrier to medical care in a drug-oriented health care system. *Int J Health Serv*. 1988;18:335–342
69. Gardner TL, Dovey SM, Tilyard MW, Gurr E. Differences between prescribed and dispensed medications. *N Z Med J*. 1996;109:69–72
70. Matsui D, Joubert GI, Dykxhoorn S, Rieder MJ. Compliance with prescription filling in the pediatric emergency department. *Arch Pediatr Adolesc Med*. 2000;154:195–198
71. Dolgin MJ, Katz ER, Doctors SR, Siegel SE. Caregivers' perceptions of medical compliance in adolescents with cancer. *J Adolesc Health Care*. 1986;7:22–27
72. Cromer BA, Steinberg K, Gardner L, Thornton D, Shannon B. Psychosocial determinants of compliance in adolescents with iron deficiency. *Am J Dis Child*. 1989;143:55–58
73. Erhardt LR. The essence of effective treatment and compliance is simplicity. *Am J Hypertens*. 1999;12(suppl):105S–110S
74. Delgado PL. Approaches to the enhancement of patient adherence to antidepressant medication treatment. *J Clin Psychiatry*. 2000;61(suppl 2):6–9
75. Gigliotti F, Murante BL, Weinberg GA. Short course directly observed therapy to monitor compliance with antiretroviral therapy in human immunodeficiency virus-infected children. *Pediatr Infect Dis J*. 2001;20:716–718
76. Watt PM, Clements B, Devadason SG, Chaney GM. Funhaler spacer: improving adherence without compromising delivery. *Arch Dis Child*. 2003;88:579–581
77. Williams RL, Maiman LA, Broadbent DN, et al. Educational strategies to improve compliance with an antibiotic regimen. *Am J Dis Child*. 1986;140:216–220
78. Pelco LE, Kissel RC, Parrish JM, Miltenberger RG. Behavioral management of oral medication administration difficulties among children: a review of literature with case illustrations. *J Dev Behav Pediatr*. 1987;8:90–96
79. Reimers TM, Piazza CC, Fisher WW, Parrish JM, Page TJ. Enhancing child compliance with nebulized respiratory treatment. A case study. *Clin Pediatr (Phila)*. 1988;27:605–608
80. Ellison RS, Altemeier WA. Effect of use of a measured dispensing device on oral antibiotic compliance. *Clin Pediatr (Phila)*. 1982;21:668–671
81. Kurokawa T, Minami T, Kitamoto I, Mizuno Y, Maeda Y, Takaki S. Compliance in epileptic children in Japan. *Epilepsy Res Suppl*. 1988;1:147–151
82. Palanduz A, Gultekin D, Erdem E, Kayaalp N. Low level of compliance with tuberculosis treatment in children: monitoring by urine tests. *Ann Trop Paediatr*. 2003;23:47–50

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