ORIGINAL ARTICLE

Adherence to treatment in adolescents

Danielle Taddeo MD¹, Maud Egedy MD², Jean-Yves Frappier MD¹

D Taddeo, M Egedy, J-Y Frappier. Adherence to treatment in adolescents. Paediatr Child Health 2008;13(1):19-24.

Health care professionals must be alert to the high prevalence of low adherence to treatment during adolescence. Low adherence increases morbidity and medical complications, contributes to poorer quality of life and an overuse of the health care system. Many different factors have an impact on adherence. However, critical factors to consider in teens are their developmental stage and challenges, emotional issues and family dysfunction. Direct and indirect methods have been described to assess adherence. Eliciting an adherence history is the most useful way for clinicians to evaluate adherence, and could be the beginning of a constructive dialogue with the adolescent. Interventions to improve adherence are multiple - managing mental health issues appropriately, building a strong relationship, customizing the treatment regimen if possible, empowering the adolescent to deal with adherence issues, providing information, ensuring family and peer support, and motivational enhancement therapy. Evaluation of adherence at regular intervals should be an important aspect of health care for adolescents.

Key words: Adolescent; Adherence; Compliance; Treatment

naediatricians and other health care professionals are often faced with adolescents whom they suspect may not be following their treatment recommendations. Compliance involves following the doctor's orders or "the accurate observance by a patient of a prevention or treatment regimen set out by a health professional" (1). The term adherence has been used more in recent literature, and is defined as "the extent to which a person's behaviour, in terms of taking medications, following diets, or executing lifestyle changes, coincides with medical or health advice" (2). Although compliance and adherence are often used interchangeably, in the present article, adherence is used because it focuses on whether a person adheres to the regimen rather than passively follows the doctor's orders (3). It also implies partnership and cooperation between the patient and the caregiver.

Low adherence to any medical recommendation, such as a diet or a prescribed medication, is recognized in adult (4), paediatric and adolescent populations. It is reported both for prophylactic and preventive treatment (eg, oral contraception), and for medications to treat severe chronic health conditions such as diabetes, cystic fibrosis or organ transplant, thus possibly resulting in life-threatening consequences.

L'adhésion au traitement chez les adolescents

Les professionnels de la santé doivent être conscients de la forte prévalence de faible adhésion au traitement pendant l'adolescence. Cette faible adhésion accroît la morbidité et les complications médicales, contribue à une diminution de la qualité de vie et à une surutilisation du système de santé. De nombreux facteurs différents ont des répercussions sur cette adhésion. Cependant, les facteurs essentiels à envisager chez les adolescents sont leur étape de développement et les problèmes qu'ils affrontent, les défis émotionnels et le dysfonctionnement familial. Des méthodes directes et indirectes permettent d'évaluer l'adhésion. L'obtention des antécédents d'adhésion constitue le moyen le plus utile pour les cliniciens d'évaluer l'adhésion et peut déclencher un dialogue constructif avec l'adolescent. Il existe de multiples interventions pour améliorer l'adhésion, telles que la prise en charge convenable des troubles de santé mentale, l'établissement d'une relation solide, la personnalisation du schéma thérapeutique dans la mesure du possible, l'habilitation de l'adolescent à affronter les problèmes d'adhésion, la transmission d'information, la garantie du soutien de la famille et des camarades et la thérapie de mise en valeur de la motivation. L'évaluation de l'adhésion à intervalles réguliers devrait constituer un aspect important des soins aux adolescents.

SCOPE OF THE PROBLEM

Patient adherence is important for the success of any medical treatment. In a meta-analysis including paediatric and adult populations, DiMatteo et al (5) compared the results of medical treatment in patients who adhered to their treatment with those who did not, and reported a 26% reduction in poor treatment outcome. The odds of a good outcome if the patient is adherent are almost three times higher than the odds if the patient has low adherence (5).

Rates of adherence in the adolescent population vary widely, from 10% to 89%, for chronic illnesses (6-8). Bender et al (9) studied children with asthma, and reported that only 50% to 60% of them were taking prescribed doses of inhaled medications. In another study of 161 adolescents infected with HIV, Murphy et al (10) found that 83% of them were taking 'some' of their medications, but only 50% reported adherence to their entire medical regimen. Shemesh et al (11) reported an 'ideal adherence' rate after liver transplant in children and teens, ranging from 51.9% to 70.4%, depending on the method of assessment.

Measurement of adherence is challenging and reported rates vary according to the method of assessment. Teens may also have varying adherence levels within their treatment regimen. Johnson et al (12) studied a group of

Accepted for publication November 14, 2007

¹Adolescent Medicine Division, Sainte-Justine UHC, University of Montreal, Montreal; ²Adolescent Medicine, Quebec City, Quebec Correspondence and reprints: Dr Danielle Taddeo, Adolescent Medicine Division, University of Montreal, Sainte-Justine UHC, 3175 chemin Côte-Sainte-Catherine, Montreal, Quebec H3T 1C5. Telephone 514-345-4722, fax 514-345-4778, e-mail danielle.taddeo@ssss.gouv.qc.ca

adolescents with type 1 diabetes and found that 25% were neglecting insulin injections, 81% were not following their diet and 29% were not measuring their glucose level and were completing a daily diary with fictitious levels. This may suggest that adolescents have better adherence to treatments that have more immediate and potentially serious consequences if not followed, compared with recommendations that have less obvious benefits or are more intrusive to their lifestyle.

There are many repercussions of low adherence in teens, with obvious consequences for themselves, their families and the health care system. For chronic conditions, low adherence increases morbidity and medical complications (hospitalization), contributes to poorer quality of life (fatigue and school absenteeism) and an overuse of the health care system (unnecessary medical consults and investigations) (3). Low adherence increases health care costs and may lead a health care team to withhold treatment. In the case of organ transplantation, low adherence is a leading cause of graft rejection and may cause death (13).

UNDERSTANDING LOW ADHERENCE IN TEENS

Many different factors that potentially impact on adherence have been studied, such as demographic, familial, socioeconomic, personal, type of illness, therapeutic regimens and the relationship with health care professionals (14-48). Although some of the results are contradictory, factors that appear to have a positive impact on adherence are positive family functioning, close friends, internal locus of control, treatment with immediate benefits, parent's beliefs in seriousness of illness and efficacy of treatment, and physician empathy. Other factors that seem to have a negative impact on adherence are being an older adolescent, mental health issues with the caregiver, family conflicts, complex therapy, medication with side effects and denial of illness. Teens who are experiencing emotional, social, family or mental health problems struggle more with adhering to medical regimens; low investment in the treatment plan can be a sign of depression or other psychosocial problems during the teen years. Patient beliefs and attitudes are among the most studied predictors of adherence. The Health Belief Model (49) and other tools have identified many personal variables associated with adherence - the patient's perception of susceptibility to disease, of the severity of the illness and of the efficacy of the proposed therapy. Other factors include perceptions of obstacles to adherence, attitudes toward therapeutic regimens, parents' and other significant adults' or peers' perception of the therapeutic regimen, and the level of influence of these persons on the adolescent (50, unpublished data).

The other critical factor to consider when discussing adherence in teens is their developmental stage. Adolescence is a crucial time for physical, pubertal and cognitive maturation, in addition to psychosocial changes, including identity formation and the development of independent social relationships. During the teen years, the

20

child will move from complete dependence to a more autonomous lifestyle (51). Adolescents are expected to take increasing responsibility for their health and health care. This gradual and progressive process is without major turmoil and rebellion for most young people.

Cognitive changes include the transition from concrete thinking to more abstract thinking. Young teenagers will mainly believe what they can see or have experienced and, thus, they cannot fully appreciate the long-term or unseen consequences of not taking their medications. Formal operations enable adolescents to deal with hypothetical thinking and to analyze many different kinds of evidence to support an argument. The ability to engage in formal thinking is inconsistent at first, and at times of stress (such as an illness), adolescents may regress to more simple ways of problem solving. Despite their maturing skills, they may remain self-centred and feel invulnerable to consequences negative things happen only to others. This process explains the risk-taking behaviour and limit testing seen predominantly during adolescence in many domains sexuality, sports, driving and drug experimentation. Low adherence to treatment can be a way of testing limits. Even adults have difficulty adhering to preventive and healthpromoting advices such as diet, exercise, contraception, smoking prevention and helmet use. This is even more of a challenge for adolescents because they often have not yet fully developed risk assessment skills, impulse control or organizational abilities.

Adolescence is a time for development of self-concept and identity. 'Who am I' is a fundamental question teens struggle with, and the development of a medical condition during these formative years can derail this process. Teens may struggle to incorporate a medical condition into their evolving sense of self, which may appear to clinicians as denial of the illness, failure to recognize the seriousness of an illness or low adherence with treatment recommendations.

Moving toward independence from their parents, adolescents typically want to make their own choices and have a sense of control over their lives. Having a disease may make them feel powerless and they may try to gain control by not taking their medications, missing appointments or not following dietary restrictions. Sometimes, the parents may have developed an overprotective parenting style, which can delay the teen's ability to take responsibility for his or her treatment or cause frustration for the adolescent. Thus, low adherence can be a way of confronting the authority of parents and professionals.

Socially, teens want to be accepted by their peer group. Having a chronic disease poses challenges to socializing. In adolescents with diabetes, negative relationships with peers was related to poor outcome (52). Teens do not want to be different from their peers, which can lead to denial or hiding their illness from peers, thus making adherence very difficult. Occasionally, the teen may perceive direct or indirect benefits to low adherence. Possible benefits include reduced medication side effects, increased flexibility in their personal schedules and freedom from thinking about

their disease (albeit temporarily). Some other benefits to consider for low adherence may be financial (not having to pay for medication), cosmetic (reduced acne, hirsutism or weight gain), avoidance of responsibilities (such as school or chores) or attention seeking (from parents, peers or caregivers).

EVALUATING ADHERENCE WITH AN ADOLESCENT

There is no 'gold standard' to assess adherence to a medical regimen. Direct and indirect methods of measurement have been described, both of which have limitations and benefits. Information on adherence is more reliable when it comes from multiple sources including the teen, parents and other health care providers on the team (53,54).

Direct methods

The assessment of medication or metabolite blood levels (eg, for anticonvulsants or antirejection drugs) or the measurement of control of the disease (eg, measuring hemoglobin A1c for diabetes or ferritin for iron deficiency) constitutes objective evaluations of adherence. However, these methods are not available for most conditions, and they only reflect the general adherence to the treatment (high levels of hemoglobin A1c could reflect low adherence to diet and/or insulin administration) or only reflect adherence in the recent past. Pill counts and electronic monitoring devices have limited value. Direct methods pose the risk of interfering with the relationship between the adolescent and the health care professional.

Indirect methods

Eliciting an adherence history is the most useful way for clinicians to assess adherence, and could be the beginning of a constructive dialogue with the adolescent about adherence (50,53,55). Indirect and open-ended questions should begin the discussion. Knowledge of the treatment regimen is addressed with questions such as, 'Can you tell me when you take your medications? 'How many pills do you take?' The side effects and how the adolescent feels about the treatment are questioned – 'Does the medication have effects you do not like?' 'What do you hate the most?' This can be followed by questions about difficulties with remembering to take medication and about strategies the teen uses to remember to take his or her medications. The adolescents can be asked to evaluate their own adherence. Three questions can be asked - 'If 1 represents teens who never take their medication and 5 represents those who always take their medication, where would you see yourself?" 'When was the last time you forgot your medications and how often did you forget your medication this past week?' A significant correlation has been found between these three questions, especially medication forgotten in the two previous days and low overall adherence (50, unpublished data). The adolescents can also be asked whether parents remind them to take their medication; frequent reminders from parents can be a sign of low adherence (50, unpublished data).

Assessing rates of prescription refills can give an indication of adherence, but does not ensure the adolescent is ingesting the medication. Assessing the adolescent's clinical response is also an indirect method, but factors other than adherence can have an impact. This is quite difficult when the target symptom is subjective, such as a headache or depression. Measurable physiological parameters are sometimes monitored to assess adherence (such as blood pressure with antihypertensive drugs), but results can be affected by other factors such as poor absorption, underdosing or lack of response.

Self-report questionnaires are generally efficient means of assessing adherence, although such methods have been reported to overestimate adherence by 30% (56); their accuracy may be affected by the wording of the questions. Different questionnaires have been adapted to several chronic conditions (the Treatment Adherence Rating Scale and the Pediatrics AIDS Clinical Trials Group) (57).

INTERVENTIONS TO IMPROVE ADHERENCE

Given the many factors that contribute to low adherence in adolescents, there is no simple intervention that will apply to every adolescent scenario. Based on current research, a number of strategies are helpful in improving adherence.

The first step is obviously to accurately identify and assess low adherence and to identify perceptions toward the treatment regimen and barriers to adherence. This needs to be accomplished without directly confronting the adolescent or being judgemental. Acknowledging the struggles they may have with adherence can facilitate building rapport with the teen, such as, 'many teens find it hard to remember to take their pills twice a day – is it hard for you?'

If an emotional or mental health problem has been identified, it should be managed appropriately. Anxiety and depression are prevalent in teenagers, but they are sometimes reluctant to talk about it. They both have strong hereditary components so it is important to take a family history both to help with the diagnosis and to understand the context in which the adolescent is living. Depression should always be considered in teens who have low adherence and present with a lack of motivation and loss of interest, especially if other areas in their lives are also affected. A consultation with a mental health professional may be useful for the diagnosis and treatment of emotional or mental health problems.

A strong relationship with the teenager is the foundation on which all other adherence-improving interventions rely, and the health care professional should work to improve communication and empower the adolescent. Teens prefer a physician who is nonjudgemental, honest and expresses concern, empathy and respect for the adolescent and their family (58). Interviewing teenagers alone is essential to building rapport and delivers the message that the physician believes in their capacity to take charge of their disease and its treatment. A true partnership requires collaboration in decision-making when different options are available.

In making decisions about treatment, the physician should determine the extent to which the teen and the family can cope with the regimen in terms of scheduling, side effects and costs (1). For example, prescribing a very complicated dosing regimen may be setting the teen up for failure if they have attention deficit-hyperactivity disorder or the family tends to be chaotic or disorganized. The physician also needs to anticipate side effects and needs to inform the teen. Unexpected side effects can seriously compromise adherence and the trust in the physician. The adolescent and his or her family should be assured that the dose will be reduced as much as possible to prevent or decrease side effects. It is important to listen to the adolescent, and to try to customize the regimen in accordance with the adolescent's wishes as much as possible. The teenager can be empowered by the health care providers affirming that although they may be the expert of the disease and its treatment, the teen is the expert of his or her own life and priorities. The physician can ask the teenager to suggest ways to improve their own adherence. Many teenagers with a chronic condition feel they do not have control over their life because of the disease. It can be helpful to look for other areas of the teen's life in which they can have control. Provided there are no safety issues, parents and physicians have to be ready to make compromises.

Educational interventions

Educational interventions can improve adherence (55). Teens and their family should receive specific information about the disease (course of illness and prognosis), the prescribed treatment (required doses, daily schedule and side effects) and the importance of the proposed treatment. Information should be delivered verbally, but is best if complemented with written material and references to Web sites or books on the disease. Repeated education is important for youth and families affected by chronic diseases. The physician should not forget to evaluate the adolescent's disease-related knowledge, especially if the disease has been diagnosed at a young age, when the information may have been directed to the parents. General principles shown to improve the patient's understanding include being friendly rather than businesslike, providing instructions clearly and concisely, stressing the importance of the suggestion, using short words and sentences (avoid medical jargon), repeating information as needed, checking for understanding of the information given, being careful to adapt information according to the adolescent's cognitive abilities, encouraging questions and finally, and more importantly, determining whether the adolescent and his or her family expectations have been addressed (59).

Organizational strategies

Organizational strategies (55) can also contribute to improve adherence. For example, clustering appointments for teens who have to see more than one health care provider at a visit can improve attendance, as can arranging appointments for teens at a time when they miss the least

amount of school and when transportation is easiest for the family. The medical regimen should be as simple as possible, once or twice daily prescription being easier than more frequent doses. Medications with long half-lives, depot (extended-release medications) and transdermal medications can be useful when low adherence is likely. New technologies such as alarms on watches, reminders through cell phones or personal digital assistants, and pill boxes with paging systems may be particularly appealing to teenagers.

Behavioural strategies and problem-solving skills

Behavioural strategies and problem-solving skills (18,55) can be suggested. Visual reminders, such as leaving the medication where it is sure to be noticed or leaving notes to themselves may be helpful. Many teens find it easier to remember if they pair taking medications with other well-established behaviours (such as eating meals, brushing teeth or putting on make-up). Working together with the teen to solve struggles with adherence gives the physician a chance to reinforce problem-solving skills.

Peer and family support

Peer and family support can also contribute to better acceptance of a treatment. Practical support from parents and emotional support from friends can do a great deal to assist youth who have special health care needs. Peer support groups or specific summer camps are resources that can enhance the adolescent's satisfaction, help them create new relationships with friends and reinforce their ability to manage their condition. The use of peer educators within a school has been shown to improve asthma knowledge and attitudes within schools (60). In adolescents with diabetes, working with peers has a positive impact (52). A family group approach has been used successfully to increase adherence to therapy in HIV-infected youth (61). Family closeness and cohesiveness must be supported and reinforced, as well as family problem-solving skills (1). At times, low adherence may be a marker for more serious family dysfunction (such as parental mental health problems, family violence, substance use, or child abuse or neglect). In these circumstances, improving adherence will be extremely challenging without addressing the other issues. Referral for family therapy or other services may be necessary, and consideration must be given to involving child protection authorities as appropriate.

Motivational enhancement therapy

There are some structured interventions that have been studied and have proven to be effective for those who have adherence problems. Motivational enhancement therapy (62) is based on a nonjudgemental approach characterized by warmth, respect and empathy, but also curiosity (interest in the adolescent's view), humility (eagerness to learn more about the adolescent's perspective), low investment (which involves the clinician exploring, accepting and trying to understand the adolescent's view rather than coercing them to change attitudes and behaviours) and flexibility. There is

acceptance that enhancing motivation takes time and occurs not through coercion or education, but by helping the adolescent focus on the reasons for his or her low adherence (55). Motivational enhancement therapy is also based on the youth's readiness to change. Faced with a necessity for change, the teen can be in five different stages of motivation - precontemplation (denial of any problem), contemplation (acknowledgement of a problem, but not of a need to change), preparation (acknowledgement of a need to change, but not ready yet), action (ready for help) and maintenance (wants help to maintain the changes). Over time, the teen may move between these different states, randomly and in a nonlinear fashion. The health care provider adapts the intervention according to the teen's stage. Different techniques can be useful - open-ended questions ('Can you tell me about the problems for you in following your treatment'), reflective listening ('So, one of your reason for not taking your pills is that they are too big'), affirmation ('It is normal to feel weak and tired with your illness; taking your medication will support you') and eliciting mixed feelings ('So, you do not like to take the pills at school, but you also have noticed that when you do not take the pills, you cannot concentrate). One of the most valuable techniques is to discuss the pros and cons of adherence with the teen and summarize the adolescent's perspectives aloud with them.

The Resilience Enhancement Adolescent Profile

The Resilience Enhancement Adolescent Profile (63,64), another specific intervention, is based on the Adolescence

REFERENCES

- DiMatteo MR. The role of effective communication with children and their families in fostering adherence to pediatric regimens. Patient Educ Couns 2004;55:339-44.
- 2. Haynes RB. Introduction. In: Haynes RB, Taylor DW, Sackett DL, eds. Compliance in Health Care. Baltimore: John Hopkins, 1979:1-7.
- Lemanek KL, Kamps J, Chung NB. Empirically supported treatments in pediatric psychology: Regimen adherence. J Pediatr Psychol 2001;26:253-75.
- Kane S, Huo D, Aikens J, Hanauer S. Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. Am J Med 2003;114:39-43.
- DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: A meta-analysis. Med Care 2002;40:794-811.
- 6. Alvin P, Frappier JY. La compliance thérapeutique. Dans, Michaud PA, Alvin P (sous la direction de), et Deschamps JP, Frappier JY, Marcelli D, Tursz A, eds. La santé des adolescents: approche, soins, prévention. Lausanne: Payot, Paris: Douin, Montreal: Presses de l'Université de Montréal, 1997.
- 7. Alvin P, Rey C, Frappier JY. Compliance thérapeutique chez l'adolescent malade chronique. Arch Pediatr 1995;2:874-82
- Michaud PA, Frappier JY, Pless IB. La compliance d'adolescents souffrant d'une maladie chronique. Arch Fr de Pediatr 1991;48:329-36.
- Bender B, Wamboldt FS, O'Connor S, et al. Measurement of children's asthma medication adherence by self-report, mother report, canister weight, and Doser CT. Ann Allergy Asthma Immunol 2000;85:416-21.
- Murphy DA, Wilson CM, Durako SJ, Muenz LR, Belzer M; Adolescent Medicine HIV/AIDS Research Network. Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA. AIDS Care 2001;13:27-40.

Resilience Model, and is a multidisciplinary approach developed for the adolescent with cancer and their family. Resilience is "a process for identifying and developing resources or strengths to manage stressors in order to gain positive outcome from the experience" in which emphasis is placed on positive health behaviours (65). Reinforcing resilience should be one of the components of health care in the professional's attempt to enhance adherence (Saewyc and Tonkin [pages 43-47]).

CONCLUSION

Paediatricians and other health care providers must be alert to the high prevalence of low adherence to treatment during the adolescent years. Evaluation of adherence should be an important part of health care at regular intervals.

Effective, nonjudgemental communication is essential in fostering adherence to health-promoting and preventive practices, and to the treatment of chronic health conditions in teens. Health care providers must be aware that the adolescent's and parent's perceptions of the illness and the treatment are important and affect adherence. The youth and their family need repeated information on what they have to do, and should always be invited and encouraged to ask questions. Explanations should be given in a way that is understandable, with language that is appropriate to the developmental level of the teen; visual aids should be used as required. Treatment-related problems (forgetfulness and side effects) should be discussed at regular intervals.

- Shemesh E, Shneider BL, Savitzky JK, et al. Medication adherence in pediatric and adolescent liver transplant recipients. Pediatrics 2004;113:825-32.
- Johnson SB, Kelly M, Henretta JC, Cunningham WR, Tomer A, Silverstein JH. A longitudinal analysis of adherence and health status in childhood diabetes. J Pediatr Psychol 1992;17:537-53.
- 13. Falkenstein K, Flynn L, Kirkpatrick B, Casa-Melley A, Dunn S. Non-compliance in children post-liver transplant. Who are the culprits? Pediatr Transplant 2004;8:233-6.
- McQuaid EL, Kopel SJ, Klein RB, Fritz GK. Medication adherence in paediatric asthma: Reasoning, responsibility and behaviour. J Pediatr Psychol 2003;28:323-33.
- Murphy DA, Sarr M, Durako SJ, Moscicki AB, Wilson CM, Muenz LR; Adolescent Medicine HIV/AIDS Research Network. Barriers to HAART adherence among human immunodeficiency virus-infected adolescents. Arch Pediatr Adolesc Med 2003:157:249-55
- Friedman IM, Litt IF, King DR, et al. Compliance with anticonvulsant therapy by epileptic youth. Relationships to psychosocial aspects of adolescent development.
 J Adolesc Health Care 1986;7:12-7.
- 17. Moreland EC, Tovar A, Zuehlke JB, Butler DA, Milaszewski K, Laffel LM. The impact of physiological, therapeutic and psychosocial variables on glycemic control in youth with type 1 diabetes mellitus. J Pediatr Endocrinol Metab 2004;17:1533-44.
- Wysocki T, Miller KM, Harvey LM, et al. Behavior therapy for families of adolescents with diabetes: Effects on directly observed family interactions. Behav Ther 1999;30:507-25.
- Koocher GP, McGrath ML, Gudas LJ. Typologies of nonadherence in cystic fibrosis. J Dev Behav Pediatr 1990;11:353-8.
- DeLambo KE, Ievers-Landis CE, Drotar D, Quittner AL. Association of observed family relationship quality and problem-solving skills

- with treatment adherence in older children and adolescents with cystic fibrosis. J Pediatr Psychol 2004;29:343-53.
- Ruggiero L, Javorsky DJ. Diabetes self-management in children. In: Goreczny AJ, Hersen M, eds. Handbook of Pediatric and Adolescent Psychology. Massachusetts: Allyn & Bacon Inc, 1999:49-70.
- 22. Davis CL, Delamater AM, Shaw KH, et al. Parenting styles, regimen adherence, and glycemic control in 4- to 10-year-old children with diabetes. J Pediatr Psychol 2001;26:123-9.
- Chaney JM, Peterson L. Family variables and disease management in juvenile rheumatoid arthritis. J Pediatr PsychoI 1989;14:389-403.
- La Greca AM, Bearman KJ, Moore H. Peer relations of youth with pediatric conditions and health risks: Promoting social support and healthy lifestyles. J Dev Behav Pediatr 2002;23:271-80.
- Brownbridge B, Fielding D. An investigation of psychological factors influencing adherence to medical regime in children and adolescents undergoing hemodialysis and CAPD. Int J Adolesc Med Health 1989;4:7-18.
- Tebbi CK, Cummings KM, Zevon MA, Smith L, Richards M, Mallon J. Compliance of pediatric and adolescent cancer patients. Cancer 1986;58:1179-84.
- 27. Feinstein S, Keich R, Becker-Cohen R, Rinat C, Schwartz SB, Frishberg Y. Is noncompliance among adolescent renal transplant recipients inevitable? Pediatrics 2005;115:969-73
- Abbott J, Dodd M, Gee L, Webb K. Ways of coping with cystic fibrosis: Implications for treatment adherence. Disabil Rehabil 2001;23:315-24.
- Tamaroff MH, Festa RS, Adesman AR, Walco GA. Therapeutic adherence to oral medication regimens by adolescents with cancer. II. Clinical and psychological correlates. J Pediatr 1992;120:812-7.
- 30. Beratis S. Non compliance with iron chelation therapy in patients with beta-thalassaemia. J Psychosom Res 1989;33:739-45.
- Christiaanse ME, Lavigne JV, Lerner CL. Social aspects of compliance in children and adolescents with asthma. J Dev Behav Pediatr 1989;10:75-80.
- 32. Farrell SP, Hains AA, Davies WH, Smith P, Parton E. The impact of cognitive distortions, stress, and adherence on metabolic control in youths with type 1 diabetes. J Adolesc Health 2004;34:461-7.
- 33. Hentinen M, Kyngäs H. Compliance of young diabetics with health regimens. J Adv Nurs 1992;17:530-6.
- Passero MA, Remor B, Salomon J. Patient-reported compliance with cystic fibrosis therapy. Clin Pediatr (Phila) 1981;20:264-8.
- Ho J, Bender BG, Gavin LA, O'Connor SL, Wamboldt MZ, Wamboldt FS. Relations among asthma knowledge, treatment adherence and outcome. J Allergy Clin Immunol 2003;III:498-502.
- Shaw RJ, Palmer L, Blasey C, Sarwal M. A typology of nonadherence in pediatric renal transplant recipients. Pediatr Transplant 2003;7:489-93.
- Lemanek KL, Trane ST, Weiner RE. Asthma. In: Goreczny AJ, Hersen M, eds. Handbook of Pediatric and Adolescent Health Psychology. Massachusetts: Allyn & Bacon Inc, 1999:141-58.
- 38. Rogers AS, Miller S, Murphy DA, Taney M, Fortune T. The TREAT (Therapeutic Regimens Enhancing Adherence in Teens) program: Theory and preliminary results. J Adolesc Health 2001;29S:30-8.
- Carpenter CC, Cooper DA, Fischl MA, et al. Antiretroviral therapy in adults: Updated recommendations of the International AIDS Society – USA Panel. JAMA 2000;283:381-90.
- Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybeck TR. The effect of prescribed daily dose frequency on patient medication compliance. Arch Intern Med 1990;150:1881-4.
- 41. Horne R, Weinman J. Self-regulation and self-management in asthma: Exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventive medication. Psychol Health 2002;17:17-32.
- Murphy DA, Sarr M, Durako SJ, Moscicki AB, Wilson CM, Muenz LR; Adolescent Medicine HIV/AIDS Research Network. Barriers to HAART adherence among human immunodeficiency virus-infected adolescents. Arch Pediatr Adolesc Med 2003;157:249-55.

- 43. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97.
- Soliday E, Hoecksel R. Health beliefs and paediatric emergency department after-care adherence. Ann Behav Med 2000;22:299-306.
- Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res 1999;47:555-67.
- 46. Nevins TE. Non-compliance and its management in teenagers. Pediatr Transplant 2002;6:475-9.
- 47. Korch BM, Fine RN, Negrete VF. Noncompliance in children with renal transplants. Paediatrics 1978;61:872-6.
- 48. Asadi-Pooya AA. Drug compliance in children and adolescents with epilepsy. Seizure 2005;14:393-5.
- Bond GG, Aiken LS, Somerville SC. The health belief model and adolescents with insulin-dependent diabetes mellitus. Health Psychol 1992;11:190-8.
- Frappier JY, Otis J, Alvin P, Campos Z. Factors associated with medication compliance in adolescents with chronic diseases. Clin Invest Med 1995;Suppl 18:A33.
- 51. Hamilton J, Daneman D. Deteriorating diabetes control during adolescence: Physiological or psychosocial. J Pediatr Endocrinol Metab 2002;15:115-26.
- Helgeson VS, Reynolds KA, Escobar O, Siminerio L, Becker D. The role of friendship in the lives of male and female adolescents: Does diabetes make a difference? J Adolesc Health 2007;40:36-43.
- 53. Jay S, Litt IF, Durant RH. Compliance with therapeutic regimens. J Adolesc Health Care 1984;5:124-36.
- Dolezal C, MeIIins C, Brackis-Cott E, Abrams EJ. The reliability of reports of medical adherence from children with HIV and their adults caregivers. J Pediatr Psychol 2003;28:355-61.
- Rapoff MA. Assessing and enhancing adherence to medical regimens for juvenile rheumatoid arthritis. Pediatr Ann 2002;31:373-9.
- Gaebel W. Towards the improvement of compliance: The significance of psycho-education and new antipsychotic drugs. Int Clin Psychopharmacol 1997;12 Suppl 1:S37-42.
- 57. Van Dyke RB, Lee S, Johnson GM, et al; Pediatric AIDS Clinical Trials Group Adherence Subcommittee; Pediatric AIDS Clinical Trials Group 377 Study Team. Reported adherence as a determinant of response to highly active antiretroviral therapy in children who have human immunodeficiency virus infection. Pediatrics 2002;109:e61.
- D'Angelo S, Lask B. Approaches to problems of adherence.
 In: Bluebond Langner M, Lask B, Angst DB. Psychosocial Aspects of Cystic Fibrosis. London: Arnold Press, 2001.
- 59. Rapoff MA. Adherence to Pediatric Medical Regimens. New York: Kluwer Academic/Plenium, 1999.
- Shah S, Peat JK, Mazurski EJ, et al. Effect of peer led programme for asthma education in adolescents: Cluster randomised controlled trial. BMJ 2001;322:583-5.
- Lyon ME, Trexler C, Akpan-Townsend C, et al. A family group approach in increasing adherence to therapy in HIV-infected youths: Results of a pilot project. AIDS Patient Care STDS 2003;17:299-308.
- 62. Lask B. Motivating children and adolescents to improve adherence. J Pediatr 2003;143:430-3.
- Clarke-Steffen L, Kupst MJ. The Adolescent Resilience-Model and interventions to promote resilience-critique. J Pediatr Oncol Nurs 2004;21:300-4.
- Nelson AE, Haase J, Kupst MJ, Clarke-Steffen L, Brace-O'Neill J. Consensus statements: Interventions to enhance resilience and quality of life in adolescents with cancer. J Pediatr Oncol Nurs 2004;21:305-7.
- 65. Haase JE, Heiney SP, Ruccione KS, Stutzer C. Research triangulation to derive meaning-based quality of life theory: Adolescent resilience model and instrument development. Int J Cancer Suppl 1999;12:125-31.