Citation	Berben, L., Dobbels, F. (2012), An ecological perspective on medication adherence Western Journal of Nursing Research, 34(5), 635 - 653
Archived version	Post-print. Author manuscript: the content is virtually identical to the content of the published paper, but without the final typesetting by the publisher
Published version	http://dx.doi.org/10.1177/0193945911434518
Journal homepage	http://wjn.sagepub.com/
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IR	https://lirias.kuleuven.be/cv?u=U0015258 https://lirias.kuleuven.be/cv?u=U0005386

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An ecological perspective on medication adherence

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Abstract:

Adherence to a prescribed medication regimen is influenced not only by characteristics of the individual patient, but also by factors within the patient's environment, or so-called system level factors. Until now, however, health care system factors have received relatively little attention in explaining medication non-adherence. Ecological models might serve as a framework to help explain the influence of health care system factors on patient behavior (e.g., adherence). In an ecological model, different levels of factors influence patients' behavior, i.e. factors at the patient-level, micro- (provider and social support), meso- (health care organization), and macro (health policy) -levels. In order to understand medication adherence and implement interventions to improve medication adherence, factors at these different levels should be taken into consideration. This paper describes an ecological model comprised of the most important factors at the patient-, micro-, meso- and macro-levels.

Keywords: medication adherence, patient compliance, health care system ecological model

Introduction

Medication non-adherence is defined as “a deviation from the prescribed medication regimen sufficient to influence adversely the regimen’s intended effect” (Fine et al., 2009). In many patient populations non-adherence to medication regimens is a prevalent problem. On average, 25% (DiMatteo, 2004) to 50% (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008) of patients do not take their medications as prescribed.

Non-adherence to recommended medication treatment can have serious consequences, including poor clinical outcomes, higher (re)hospitalization rates, and increased health care costs (Blackburn, Dobson, Blackburn, & Wilson, 2005; Burman et al., 2008; Cherry, Benner, Hussein, Tang, & Nichol, 2009; DiMatteo, Giordani, Lepper, & Croghan, 2002; Dunbar-Jacob, Schlenk, & Caruthers, 2002; Haynes, et al., 2008; Ho et al., 2008; Ho et al., 2006; Kripalani, Yao, & Haynes, 2007; Pinsky et al., 2009; Simpson et al., 2006; Wei et al., 2002). A meta-analysis found that patients who were adherent were 26% more likely to have a good clinical outcome compared to patients who did not adhere to their overall treatment regimen, including medication taking (DiMatteo, et al., 2002). Non-adherence costs the US health care system an estimated \$100 billion annually in direct costs. Indirect costs exceed \$1.5 billion in lost patient earnings and \$50 billion in lost productivity (Peterson, Takiya, & Finley, 2003). In Germany, medical costs due to poor adherence are estimated to be up to 10 billion euro annually (Gorenoi, Schönermark, & Hagen, 2007). It can be assumed that the financial picture for the rest of Europe is similar. A recent study examining the economic costs associated with non-adherence to immunosuppressive medication post-renal transplant showed that patients who are persistently non-adherent were about \$21,600 more expensive to care for in the first three years after transplantation compared to patients with excellent adherence (Pinsky, et al., 2009).

Adherence to a medication regimen is a complex phenomenon influenced by the context in which a patient is expected to adhere to the prescribed medication including

relationships with family/friends and community and the social elements that influence his/her behavior. These influences often occur simultaneously and reciprocally.

Factors influencing adherence

Since adherence to a prescribed medication regimen is a fundamental prerequisite for the treatment to be effective, it is crucial to know which factors influence patients' adherence behavior, i.e., which factors are associated with poorer adherence. Modifiable factors can subsequently be targeted for intervention.

The World Health Organization (WHO) states that adherence is a multidimensional phenomenon, determined by the interplay of five dimensions (see Figure 1): (1) patient-related factors (e.g., self-efficacy, beliefs about the efficacy of medications, knowledge, and perceived barriers to adherence); (2) social and economic factors (e.g., social networks, family functioning and cost of medications); (3) therapy-related factors (e.g., symptom distress associated with side effects of the regimen, duration of treatment, and dose complexity); (4) condition related factors (e.g., co-morbidities, depression, and other psychiatric diagnoses such as substance abuse); and (5) health care system and health care team related factors (Sabaté, 2003).

Until now, most efforts to understand the remarkably high rates of non-adherence have focused on patient-related, socio-economic, treatment-related and condition-related factors (Kidd & Altman, 2000; Sabaté, 2003). The following factors have been reported to be related to non-adherence: non-white ethnicity, poorer social support, poorer perceived health, poorer socio-economic status, complex treatment regimens, more co-morbidities, poverty, illiteracy, low levels of education, unemployment, unstable living conditions, younger age, and a negative view of medication taking (Bosworth, Oddone, & Weinberger, 2008; Sabaté, 2003). A meta-analysis in transplantation, however, showed that the factors examined to-date only explain a small portion of the variability in medication non-adherence (Dew et al., 2007). This

suggests that factors not immediately associated with the patient or the treatment but rather factors related to the health care system and the health care team may also explain variability in non-adherence. Health systems can be defined as “all organizations, people and actions whose primary intent is to promote, restore or maintain health” (de Savigny & Adam, 2009). However, the influence of health system level factors on patients’ non-adherence to medication regimens has not been examined to the same extent as patient-, socio-economic-, treatment- and condition-related factors (De Geest et al., 2010; N. H. Miller, Hill, Kottke, & Ockene, 1997; Sabaté, 2003).

Theoretical background

A number of theoretical approaches including the Health Belief Model (Rosenstock, 1974), Theory of Planned Behavior (Ajzen, 1991), Theory of Self Care Deficit (Orem, 2001) The transtheoretical model (Prochaska & DiClemente, 1984) and Social Learning Theory (Bandura, 1977) were proposed to describe factors influencing behaviors such as medication adherence (Alemi et al., 2000; Bosworth, et al., 2008). Social Cognitive Theory attempts to also explain social and environmental influences on an individual's behaviors. This theory proposes that the environment shapes behavior by making it more or less rewarding to behave in a certain way (Bandura, 1977). While these theories are useful in understanding the role of patient-related factors and his/her immediate social environment in adherence, they largely ignore the influence of health care system and health care team related factors on patient behavior (Bosworth, et al., 2008). Given that behavior is also influenced by factors from the system where patients lives and receives health care, theories that integrate system-level factors may more fully explain medication taking behavior (Dew, et al., 2007). Similarly, the importance of the system in promoting behavioral changes cannot be ignored (Alemi et al. 2000).

System thinking and the ecological model

The process of accounting for the influence of various people, circumstances and historical choices on the behavior that is to be modified is called system thinking or ecological thinking (Alemi, Pawloski, & Fallon, 2003; Alemi, Pawloski, Fallon, & Tinsley). The concept of ecology originates from public health and psychology (Glanz, Rimer, & Marcus Lewis, 2002; Glanz, Rimer, & Viswanath, 2008). In public health, environmental influences on diseases have been recognized for centuries (Glanz, et al., 2002). In education, it is acknowledged that predicting achievements of students requires not only consideration of student-related variables such as intelligence, motivation or self-efficacy, but also variables at the level of the teacher, school, and educational system (Morrison Gutman & Feinstein, 2008; Sellstrom & Bremberg, 2006). In social epidemiology, ecology has also received more attention in the past 30 years (Krieger, 2001). In 1994, Nancy Krieger proposed the ecosocial theory, a theory that “embraces population-level thinking and rejects the underlying assumption of biomedical individuals without discarding biology” (Krieger, 1994), pg 896.

Urie Bronfenbrenner (1977) was the first person who focused specifically on the multiple environmental levels influencing behavior (Bronfenbrenner, 1977, 1980). In Bronfenbrenner’s model, behavior is viewed as being affected by, as well as effecting, factors at multiple levels of the environment (Bronfenbrenner, 1977, 1980). These different levels can be divided into the patient-, the micro-, the meso-, and the macro-level (see Figure 2 and Table 1) (Kidd & Altman, 2000).

Patient-level factors comprise characteristics of the individual such as knowledge, self-efficacy, and attitudes. This level also incorporates the developmental history of the individual (McLeroy, et al., 1988). As previously noted, however, this level only explains a limited portion of the variability in non-adherence (effect sizes ranged from -0.06 to 0.15) (Dew, et al., 2007).

Micro-level factors encompass factors related to interpersonal or face-to-face relationships with health care professionals, as well as social support (Yach, 2002). An example is the quality of communication between the health care professionals and patients. A meta-analysis focusing on patient adherence to treatment recommendations and physician communication in diverse illness populations and settings found that the risk for non-adherence was 19% higher when there was poor communication with the physician (Zolnieriek & Dimatteo, 2009). Another aspect of patient – health care provider communication is language barriers. Evidence shows that language barriers have adverse effects on accessibility to care, the quality of care received, patient satisfaction, and patient health outcomes, including medication adherence (Bischoff, 2006; Bischoff, Perneger, Bovier, Loutan, & Stalder, 2003). In our recent systematic review, we also found that the degree of trust the patient has in the health care professional was one of the factors most consistently related to medication adherence (Berben et al., submitted).

Meso-level factors refer to the practice patterns or the characteristics of the health care organization where the patient is being treated (Yach, 2002). Examples of health care organization characteristics or practice patterns are the time available for consultation and interventions implemented in daily clinical practice to enhance patients' medication adherence. In contrast to interactions between individual clinicians and patients (a micro-level factor), the meso-level refers to characteristics of the entire health care organization. The Dialysis Outcome and Practice Patterns Study (DOPPS), a prospective, observational study conducted in hemodialysis centers in seven countries showed that center characteristics such as a larger size (> 60 patients) and a lower percentage of highly trained staff were related to worse dialysis adherence rates (Saran et al., 2003). In the Swiss HIV cohort study, the center where the patient was followed accounted for significant variability in adherence rates, with some centers having better rates than others (Glass et al., 2006). These differences may be related “center effects”, which refer to differences in outcome that cannot be explained

exclusively by identifiable differences in the patients treated by a given center or specific treatments utilized (Loberiza, Serna, Horowitz, & Rizzo, 2003).

Macro-level factors include the characteristics of the health care system in which a patient lives (Yach, 2002). This level includes local, state, and national laws and policies related to health such as insurance coverage and regulations on reimbursement for medication. Denhaerynck and colleagues showed significant differences in the prevalence of medication non-adherence between European and US kidney transplant patients and among European transplant patients from different countries (Denhaerynck et al., 2006). More specifically, US transplant patients had higher non-adherence rates than European transplant patients (19.3% vs. 13.2%) (OR= 1.78; 95% CI= 1.10, 2.89). Comparisons among European patients showed that non-adherence rates differed between Belgium (16%) and the Netherlands (14.1%) ($p=0.02$) and between Belgium and Switzerland (11.4%) ($p<0.001$) (Denhaerynck, et al., 2006). The meta-analysis of Dew et al. also reported higher rates of non-adherence in North American patients compared to European patients (Dew, et al., 2007). A possible explanation of the variations in adherence rates between different countries and continents could be differences in medication-related out-of-pocket expenses. For instance, the lifelong costs of immunosuppressive drugs are completely covered in certain countries (e.g., Belgium and the Netherlands), while in other countries immunosuppressive drugs are only partly reimbursed, or covered only for a limited time period. In addition, the latest report of the Commonwealth Fund, which focuses on access, cost and care experiences, found differences in insurance-related experiences between countries (Schoen et al., 2010). More specifically, the report surveyed eleven countries and found different systems of health care coverage leading to significant differences in access to care, cost burdens and problems with health insurance (Schoen, et al., 2010). They did not investigate the influence of these system factors on medication adherence. Similarly, Piette et al. reported that 23% of the 2,008 older chronically ill patients they examined reported medication non-adherence because of medication-related

costs (Piette, Heisler, & Wagner, 2006). In another study of patients with diabetes, Piette and colleagues showed that the patients' insurance status was related to cost-related medication underuse (Piette, Wagner, Potter, & Schillinger, 2004).

System thinking and adherence

As depicted in Figure 2, each level interacts with and dynamically influences the other levels. Paying attention to the impact of environment or system in promoting medication adherence is essential, as the system surrounding the patient is often a major reason for success or failure in changing behavior (Alemi, et al., 2000). Kidd and Altman (2000) emphasize the importance of taking environmental factors into account when trying to understand a patient's adherence to a medication regimen (Kidd & Altman, 2000). This need has also been recognized by others. In 1997, an expert panel of the American Heart Association recommended a multi-level approach to improve medication adherence (N. H. Miller, et al., 1997), and more recently, the American Society of Hypertension recommended a more ecological approach to improve adherence to antihypertensive medications (Hill, Miller, & DeGeest, 2010). In addition, policy reports from the WHO and clinical practice guidelines from the National Collaborating Center for Primary Care and Royal College of General Practitioners (UK) strongly advocate using a systems approach that transcends the patient level when dealing with the issue of poor medication adherence (Nunes et al., 2009; Sabaté, 2003).

However, as stated previously, most studies to date have examined how characteristics of the patient and the treatment regimen impact adherence, and largely ignored risk factors at the micro-, meso-, and macro-level. Incorporating a multi-level approach will provide stronger evidence regarding the unique impact of particular risk factors relative to others, as well as whether the combined effects of risk factors are additive or synergistic. The ecological model described in this paper could serve as the conceptual framework underlying these

studies. An example is Phillips' (Phillips, 2011) study which examined the effects of social context factors on adherence to antiretroviral therapy. Factors were examined at individual-level, interpersonal-level and social context-level. The only factor examined that was significantly related to adherences was homelessness. This study did not, however, examine the influence of health care system factors.

Multilevel adherence interventions

As factors at the different levels influence patient adherence, interventions aiming to improve patients' adherence can target the patient, the micro-level (i.e., the health care provider), the meso-level (i.e., the health care organization) and/or the macro-level (i.e., health care policy) (see Table 1). To date, however, most adherence intervention research, albeit also limited, has focused on interventions at the patient-level. Interventions targeting the patient can be classified as educational/cognitive, counseling/behavioral, or psychological/affective interventions (De Bleser, Matteson, Dobbels, Russell, & De Geest, 2009). *Educational/cognitive interventions* present information individually or in a group setting, delivering information about medication use and the importance of adherence verbally, in written form, and/or audio-visually. *Counseling/behavioral interventions* shape and/or reinforce behavior, empowering patients to participate in their own care, while positively changing their skill levels or normal routines. *Psychological/affective interventions* focus on patients' feelings and emotions or social relationships and social support (De Bleser, et al., 2009). In a meta-analysis investigating the efficacy of interventions used to improve medication adherence in older adults, Conn et al. (2009) reported that the intervention used most often to improve adherence was education. Despite a significant improvement in knowledge, however, these interventions did not improve adherence (Conn et al., 2009). Similarly, in "*Adherence to long-term therapies – evidence for action*" the WHO states that adherence interventions at the patient-level have usually focused on increasing knowledge,

i.e., patient education (Sabaté, 2003). Yet, evidence shows that knowledge alone is not enough to establish and maintain strong adherence behavior (Sabaté, 2003). Despite evidence supporting the limited effectiveness of educational interventions, this is the intervention that is still most commonly used in clinical practice. A survey of transplant and cardiovascular health care professionals also found that educational/cognitive interventions were used most frequently in clinical practice, even though their perceived effectiveness was low (Berben et al., 2011; Berben, Dobbels, Kugler, Russell, & De Geest, In Press). Evidence indeed indicates that counseling/behavioral and psychological/affective interventions are more effective in promoting long-term behavioral changes, such as medication adherence (Hillsdon, Foster, Cavill, Crombie, & Naidoo, 2005). Despite the evidence that these interventions are more effective in promoting behavioral changes than educational/cognitive, health care providers often lack the skills required to effectively deliver these interventions and health care organizations are not designed to promote their use (Sabaté, 2003).

In order to be able to utilize counseling/behavioral and psychological/affective interventions effectively, health care professionals need the required competencies, necessitating interventions at the micro-level. More specifically, training and education in the utilization of these interventions need to be included in basic education programs as well as in ongoing professional education and training. Health care curricula need to be revised to include competencies in adherence enhancing interventions.

An example of an intervention targeting the micro-level is training health care professionals in the use of effective, patient-centered communication methods and behavioral management, including interventions to support patients in their medication adherence (National Council on Patient Information and Education (NCPPIE), 2007; Sabaté, 2003). A highly effective strategy that fosters a collaborative partnership with the patient and supports self-management is motivational interviewing. Motivational interviewing can be defined as “a client-centered, directive method for enhancing the intrinsic motivation to change by

exploring and resolving ambivalence” (J. H. Miller & Moyers, 2002; W. R. Miller & Rollnick, 1991). It is based on promoting a belief in the need to change and developing confidence to make the change (W. R. Miller & Rollnick, 2002; Paradis, Cossette, Frasure-Smith, Heppell, & Guertin). A meta-analysis of 72 randomized controlled trials using motivational interviewing as an intervention showed a significant and clinically relevant effect in 75% of the studies (Rubak, Sandbaek, Lauritzen, & Christensen, 2005). Even in consultations of only 15 minutes, motivational interviewing has been shown to be effective (Rubak, et al., 2005). A number of studies have examined the influences of motivational interviewing on medication adherence. Although most of them did not report statistically significant results, all studies showed a trend towards having better adherence in the intervention group compared to the control group (DiIorio et al., 2008; DiIorio et al., 2003; Golin et al., 2006; Holstad, DiIorio, Kelley, Resnicow, & Sharma, 2011; Parsons, Golub, Rosof, & Holder, 2007).

Interventions targeting the health care organization (meso-level interventions) mainly focus on changing practice patterns. More specifically, they promote continuity of care including informational continuity, management continuity, and relationship continuity (Guthrie, Saultz, Freeman, & Haggerty, 2008). They also focus on the skill mix and competencies of health care teams (De Bleser, et al., 2009; De Geest, et al., 2010). One example of changing practice patterns which has been shown to result in better adherence to treatment recommendations is the implementation of chronic illness management (Busse, Blümel, Scheller-Kreinsen, & Zentner, 2010). Chronic illness management refers to a model of care that combines the following building blocks: (1) continuity of care; (2) partnerships with patients, families and communities; (3) support for patients in improving their self-management; (4) attention to preventive measures; (5) decision-making support for health care professionals; and (6) availability of clinical information systems (Bodenheimer, Wagner, & Grumbach, 2002; Epping-Jordan, Galea, Tukuitonga, & Beaglehole, 2005; Pruitt

& Epping-Jordan, 2005; Yach, 2002). Evidence shows that improving patients' self-management support is the building block most strongly related to improved adherence to treatment regimens (Busse, et al., 2010).

An example of an intervention targeting the macro-level is changes in medical insurance coverage for prescription drugs in the US. Madden and colleagues investigated the impact of Medicare prescription drug coverage (Part D) on cost-related medication non-adherence (Madden et al., 2008). A principle goal of the implementation of Medicare Part D was to increase economic access to medications, especially among vulnerable poor and chronically ill populations (Madden, et al., 2008). The authors demonstrated that the implementation of Medicare Part D was associated with a significant decrease in the prevalence of cost-related medication non-adherence (from 15.2% in 2004 to 11.5% after Part D implementation in 2006) (Madden, et al., 2008). Along the same lines, the Affordable Care Act (Oberlander, 2009) will provide immunosuppressive drug coverage for kidney transplant recipients and undoubtedly has the potential to decrease cost-related non-adherence. Immunosuppressive drugs for kidney transplant recipients are currently only covered for the first 36 months post-transplant (California Health Advocates, 2009).

It needs to be mentioned that it might be challenging to distinguish patient focused interventions from interventions at the micro-, meso-, or macro-level of the health care system as all interventions eventually have the same goal: improving patients' adherence to their medication regimen. What differentiates them is the target of the intervention. For example, teaching health care providers methods to improve their communication with patients (e.g., motivation interviewing) would be considered a micro-level intervention. On the other hand, when a clinician utilizes motivational interviewing to improve patient adherence it is a patient-level intervention.

Methodological implications

In order to enable stronger conclusions regarding the unique impact of particular risk factors relative to others and whether the combined effects of a series of risk factors are additive or synergistic, assessment of the full range of risk factors for non-adherence, including factors at the micro-, meso-, and macro-level of the health care system is essential. The model presented in this paper was adapted from the ecological model proposed by Bronfenbrenner. Researchers are also strongly encouraged to use a theoretical framework such as the one we described in this paper to underpin the selection of patient-related as well as the system-related variables. The use of such a framework will guide the selection of factors to be examined, ensure that all important factors are included and contribute to building scientific understanding related to the complex phenomena of medication adherence. To increase the likelihood that associations found between a factor and adherence really reflects a true relationship between medication adherence and the factor examined, it is suggested that research shift away from cross-sectional, descriptive studies and toward prospective studies using multivariable analyses techniques. Methodological approaches including how to handle interactions between variables at different levels have already been used in educational studies (Singer, 1998). Multi-country, multi-center studies will permit investigators to comprehensively examine factors across all system levels and add to our understanding of their contribution to medication adherence in specific disorders such as HIV/AIDS or transplantation.

The use of a consistent definition and method of measuring adherence will facilitate comparison of findings across studies. Past research examining factors associated with adherence used varying definitions of and methods to measure adherence, making comparisons across studies challenging (ABC project, 2011; Chesney, 2006; Fine, et al., 2009). Furthermore, authors are encouraged to report effect sizes for the relationship between the factors examined and adherence to facilitate ability to compare findings across studies and perform meta-analysis.

Given that the current evidence base on adherence enhancing interventions is weak, there is also an absolute need for more intervention research, and in particular studies focusing on the micro-, meso-, and macro-levels. Interventions focusing on systems level factors need to be developed and tested in relation to medication adherence. Within these studies, factorial designs examining multi-level interventions are recommended to disentangle the effect of the different components of the intervention.

Conclusion

Patients' adherence to their medication regimens is not only influenced by patient-level factors but also by factors at the micro-, meso-, and macro-levels of the health care system. However, to date the latter three levels have not been examined to the same extent as patient-level factors. In order to be able to fully tackle medication non-adherence, taking these factors at the micro-, meso- and macro-level into account is essential. Furthermore, interventional research aiming to improve patients' medication adherence should not only address the patient-level, but should also focus on interventions targeting the micro-, meso-, and macro-levels of the health care system.

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Figure 1: Five interacting dimensions affecting adherence (Sabaté, 2003)

Figure 2: Framework for the review: the ecological model of Bronfenbrenner et al. (adapted) (Bronfenbrenner, 1977, 1980)

Table 1: Risk factors and interventions of medication non-adherence on the patient, micro-, meso-, and macro-level of the healthcare system

Level	Risk Factors	Interventions
Patient / Treatment	<ul style="list-style-type: none"> - Poor socio-economic status - Depression - Low education literacy - Cognitive dysfunction - Costs of medication - Higher co-morbidity - Living alone - Complex regimen - Side effects - Poor knowledge - Lack of motivation - Low self-efficacy - Health beliefs/attitudes 	<ul style="list-style-type: none"> - Educational/cognitive interventions - Counseling/behavioral - Psychological/effective intervention
Micro	<ul style="list-style-type: none"> - Trust in the health care provider - Communication style - Quality of the patient- health care provider relationship 	<ul style="list-style-type: none"> - Learning healthcare to use effective patient-centered communication methods and behavioral management
Meso	<ul style="list-style-type: none"> - Time available for consultation, - Specialty care/case management - Treatment team skill mix - Drug access, dispensing of drugs - Center of case satisfaction with clinic - Access of clinic 	<ul style="list-style-type: none"> - Continuity of care - Skill mix of health care team - Competencies of the health care team
Macro	<ul style="list-style-type: none"> - Insurance coverage - Regulations regarding reimbursement of drugs - Continent/country 	<ul style="list-style-type: none"> - Increase reimbursement of drugs - Public health care coverage for all inhabitants