Published in final edited form as:
J Behav Med. 2012 February ; 35(1): 47–62. doi:10.1007/s10865-011-9341-9.

The Role of Prospective Memory in Medication Adherence: A Review of an Emerging Literature

Jennifer B. Zogg[1], **Steven Paul Woods**[2], **John A. Sauceda**[3], **John S. Wiebe**[3], and **Jane M. Simoni**[4]

[1]Department of Pediatrics, University of Southern California, Keck School of Medicine, Los Angeles, California

[2]Department of Psychiatry, University of California, San Diego, School of Medicine, La Jolla, California

[3]Department of Psychology, University of Texas at El Paso, El Paso, Texas

[4]Department of Psychology, University of Washington, Seattle, Washington

Abstract

Although neurocognitive impairment is an established risk factor for medication non-adherence, standard neurocognitive tests developed for clinical purposes may not fully capture the complexities of non-adherence behavior or effectively inform theory-driven interventions. Prospective memory, an innovative cognitive construct describing one's ability to remember to do something at a later time, is an understudied factor in the detection and remediation of medication non-adherence. This review orients researchers to the construct of prospective memory, summarizes empirical evidence for prospective memory as a risk factor for non-adherence, discusses the relative merits of current measurement techniques, and highlights potential prospective memory-focused intervention strategies. A comprehensive literature review was conducted of published empirical studies investigating prospective memory and medication adherence. Overall, reviewed studies suggest that prospective memory is an important component of medication adherence, providing incremental ecological validity over established predictors. Findings indicate that prospective memory-based interventions might be an effective means of improving adherence.

Keywords

chronic disease treatment; medication adherence; episodic memory; neuropsychological assessment; review

Poor adherence is a serious threat to the success of long-term therapies for chronic disease (Dunbar-Jacob et al., 2000). In developed countries, an estimated 50% of patients suffering from chronic conditions like asthma, hypertension, diabetes and HIV/AIDS do not comply with regimens as prescribed (Sabaté, 2003). Suboptimal adherence can be associated with increased morbidity and mortality, poorer clinical outcomes, reduced quality of life, and higher long-term health costs, including hospitalizations and physician consultation (Osterberg & Blaschke, 2005). Many factors influence medication adherence, including patient characteristics, such as psychiatric conditions and beliefs; social and economic circumstances, for instance family support and access to health care; disease and treatment

Correspondence may be sent to: Jennifer B. Zogg, USC MCA, 1640 Marengo St., 3rd floor, Los Angeles CA 90033 Tel: 626-487-8215, zogg@usc.edu.

characteristics, including whether the disease is chronic or acute and the medication side-effect profile; and attributes of the health care system and service delivery, such as the doctor-patient relationship (Sabaté, 2003).

One patient characteristic that has received considerable attention is neurocognitive impairment, which a growing literature suggests increases the risk of non-adherence. Impairments in the domains of episodic memory, executive functions, and information processing speed have all been linked to lower rates of adherence. For example, Hinkin and colleagues (2002) identified a two-fold greater likelihood of non-adherence among HIV-infected participants who were neurocognitively impaired as compared to unimpaired people living with HIV. While these relationships are statistically significant and independent of psychiatric factors and disease severity, the associated small-to-medium effect sizes might suggest that standard clinical tests do not detect the full range of adherence-related neurocognitive deficits and that the predictive power of cognitive factors may yet be improved. Moreover, it may be argued that standard neurocognitive tests, many of which were developed not for research purposes but to detect clinical conditions, are limited in the extent to which they can directly inform theory-driven intervention strategies to promote medication adherence.

Researchers and clinicians might therefore benefit from the identification of novel cognitive predictors of adherence that can inform treatment recommendations. While no predictor alone explains the complex set of behaviors involved in adherence, emerging evidence suggests that prospective memory could represent an important piece of the puzzle. Prospective memory is defined as the neurocognitive capacity to successfully form, maintain, and execute an intention at a particular point in the future in response to a specific cue. Simply stated, prospective memory describes one’s ability to remember to do something at a later time. Examples of prospective memory include remembering to deliver a message to a friend, remembering to pay the monthly household bills, and, particularly pertinent to health researchers, remembering to take one’s medications. In this review, we aim to orient health researchers to the construct of prospective memory, summarize and critique the empirical evidence for prospective memory as a risk factor for medication non-adherence, discuss the relative merits of current measurement techniques, and highlight prospective memory-focused intervention strategies that may be particularly fruitful targets for future program development and research.

Theoretical Framework for Prospective Memory

The concept of memory for intentions can be traced back to Freud’s essays on psychopathology of everyday life (Freud, 1965); however, the modern cognitive construct of prospective memory was not subject to empirical investigation until the early 1970s and did not readily capture the imagination of cognitive psychologists until the publication of Einstein and McDaniel’s (1990) influential paper on prospective memory and aging. Current conceptual models of prospective memory place this construct broadly in the realm of episodic memory, which is an aspect of declarative memory involving the conscious recollection of events. Within this framework, prospective memory is contrasted with retrospective memory, which describes the ability to recall events from the past when explicitly prompted. Most standard clinical tests of memory are retrospective memory tasks that involve learning and recall of word lists, brief written passages, or figures, and these represent the bulk of tasks used in clinical research on the possible role of memory in medication non-adherence. Importantly, prospective memory and retrospective memory are theorized to be singly dissociable, such that retrospective memory is a necessary but insufficient condition for successful prospective memory (Kliegel et al., 2008). Evidence for their dissociability comes from neurocognitive (Gupta et al., 2010; Salthouse et al., 2004);

neurobiological (Woods et al., 2006); and everyday functioning (Woods, Iudicello et al., 2008) studies showing these constructs are separable, albeit related. Neuroimaging research to date suggests that prospective memory is primarily dependent on prefrontal systems, such as Brodmann's area 10 (Kliegel et al., 2008; Simons et al., 2006) and the dorsolateral prefrontal cortex, which may reflect the contribution of executive functions such as planning and cognitive flexibility. Prospective memory also relies on the integrity of the medial temporal lobe, specifically the hippocampal formation, which is critical to the retrospective memory encoding and consolidation aspects of prospective memory (McDaniel & Einstein, 2007; West, 2008).

Figure 1 displays a broad conceptual model of the component processes of prospective memory adapted from numerous sources (Carey et al., 2006; Kliegel et al., 2008). The first stage of the model involves the formation or encoding of the intention that is tied to a specific cue, which may involve either the passage of time (e.g., "I will take my medication every four hours") or a specific event (e.g., "I will take my medications after dinner"). Relative to other components of prospective memory, the encoding phase has received considerably less attention (McDaniel & Einstein, 2007). It is thought to involve generation of an action plan, organization, and binding of the cue-intention pairing. Several factors can influence the robustness of the cue-intention pairing, including their semantic relatedness (McDaniel et al., 1998; Woods et al., 2010).

The second phase is the delay between the formation of the intention and the occasion for its execution, which can range from several minutes to weeks. Attention is directed toward competing ongoing activities during the delay period, which prevent active continuous rehearsal of the cue-intention pairing, thereby separating the construct of prospective memory from traditional models of working memory (Baddeley, 2003). Although controversy exists regarding the primacy of strategic versus automatic processing (see Smith, 2008), monitoring the environment for cues during this delay period may be evidenced in both automatic/spontaneous processes and strategic ones, such as purposeful clock-checking behavior (McDaniel & Einstein, 2000).

The model's third stage requires the accurate detection and recognition of the cue and the self-initiated retrieval of the corresponding intention. This stage is widely considered the defining feature of prospective memory as it differentiates the construct from retrospective memory in which retrieval is based on an explicit prompt. Several features of the cue itself can influence detection and recognition (McDaniel & Einstein, 2000), including its salience (distinctive cues are more effective), centrality to the ongoing task (focal cues are more easily detected and recognized), and association with the intention (semantic relatedness is facilitative). Another important feature of the cue is whether it requires detecting the passage of time or the occurrence of an event. Generally speaking, time-based cues are more difficult to detect as they place greater demands on strategic monitoring (e.g., time estimation and retrieval processes), which are primarily supported by prefronto-striatal systems (McDaniel et al., 1999). Event-based tasks, on the other hand, are largely held to involve more automatic or spontaneous retrieval processes.

The final two stages of the component process model of prospective memory are the recollection and execution of the intention. The content of the intention is recalled from retrospective memory, which as noted is an essential element of successful prospective memory. The accuracy of the search and retrieval of the intention from retrospective memory at this stage may be affected by the complexity of its content, including the volume of information to be retrieved; its relationship to concurrently held intentions; and the number of competing intentions presently "online" (i.e., cognitive load). The execution of the intention, on the other hand, may be viewed as a relatively automatic process, at least in the absence of gross neurological deficits such as apraxia or aphasia. Once executed, the accuracy and completeness of the realized intention is evaluated (Cuttler & Graf, 2007), which is a particularly salient feature of tasks that occur repeatedly and according to a relatively established schedule (i.e., "habitual prospective memory"). This is arguably the case with adherence to many medication regimens (McDaniel et al., 2009).

For over a decade, researchers have pondered whether prospective memory might represent an important component of medication adherence (Ellis, 1998; Park & Kidder, 1996), yet only a very few empirical studies have examined this fundamental question. We summarize and critique these studies below, the central concern of which is whether self-reported or performance-based prospective memory operates as a meaningful predictor of non-adherence. The section is organized according to the chronic disease context in which the research was conducted. (Please see the Measurement section for descriptions of some of the assessment instruments referenced here.)

Empirical data on prospective memory and medication adherence

HIV/AIDS

The majority of studies investigating prospective memory and adherence have been conducted in the context of HIV disease. Building on research showing that HIV-associated neurocognitive impairment is associated with increasing risk of non-adherence to antiretroviral medication (Hinkin et al., 2002), Woods and colleagues conducted a series of studies to determine whether prospective memory accounted for non-adherence behavior independently of known neurocognitive and other predictors. In the first of these studies to focus exclusively on medication taking (Woods, Moran, Carey et al., 2008), 87 HIV-positive adults were administered the laboratory-based Memory for Intentions Screening Test (Raskin, 2004) and a self-report measure of prospective memory (Prospective and Retrospective Memory Questionnaire; Smith et al., 2000). (A previous study evaluated prospective memory effects on instrumental activities of daily living, including a single item on medication adherence [Woods, Iudicello et al., 2008].) Participants also completed a self-reported measure of medication management. Hierarchical regression analyses indicated that objective and self-reported measures of prospective memory together explained unique variance in medication management after accounting for demographic, psychiatric, psychosocial and environmental, and other cognitive factors known to predict adherence (δR^2s = 0.37, 0.16, 0.06, 0.30, respectively). Conceptually, the observed pattern of prospective memory errors (i.e., omission or no-response errors) suggested that monitoring, cue detection, and possibly retrieval processes were more strongly related to failures of adherence than encoding or consolidation.

Although this was the first study to provide evidence for the incremental ecological validity of prospective memory in the context of medication adherence, the design was limited by an exclusive reliance on a self-report measure of medication adherence. In general, self-reported antiretroviral adherence estimates can be inflated by as much as 20% compared to electronic drug monitoring measures (Arnsten et al., 2001; Pearson et al., 2007; Wagner & Miller, 2004). Also, the measure of medication management tapped individuals' *beliefs* about medication taking and therefore may not necessarily have reflected actual adherence (Woods, Carey et al., 2007). Moreover, this assessment measured beliefs about medications in general rather than those specifically regarding antiretroviral therapies, which may involve barriers not necessarily germane to other medication regimens, such as regimen complexity and stigma.

These limitations were addressed in a subsequent study using an electronic medication event monitoring system to measure medication adherence (Woods et al., 2009). Participants ($N =$

79) were classified as adherent (> 90% correct doses) or non-adherent using the medication event monitoring system data and compared on laboratory and self-report measures of prospective memory, as well as neuropsychological, psychiatric, and psychosocial characteristics. Non-adherent individuals demonstrated worse prospective memory than adherent patients (Cohen's d = -0.54), and the loss-of-time error profile, wherein participants executed a correct intention but at the wrong time, reflected difficulties monitoring time concurrently with an ongoing task (Cohen's d = 0.69). Those committing errors on the laboratory measure of prospective memory were almost six times more likely to be classified as non-adherent than those with no errors. Follow-up logistical regression analyses indicated that impaired prospective memory performance was a unique and independent predictor of non-adherence relative to disease characteristics and other known neurocognitive and psychosocial predictors of adherence, such as depression and global cognitive impairment. That the strongest relationships between HIV-associated prospective memory impairment and medication management were observed for time-based trials converged with earlier evidence suggesting that HIV-associated prospective memory deficits arise more from problems monitoring the environment for cues during distracting activity and retrieving the appropriate intention in a timely manner than with consolidation of the intention in long-term memory (Woods, Iudicello et al., 2008; Carey et al., 2006, Woods, Moran, Carey et al., 2008).

Contrary to previous findings (Woods, Moran, Carey et al., 2008), neither self-reported prospective memory nor the semi-naturalistic performance-based prospective memory trial (for which participants were instructed to telephone researchers before 24 hours elapsed) predicted adherence. The authors suggested that the medication event monitoring system assessment may have been more sensitive to actual adherence behavior than self-report, which may have been associated with self-reported medication management in the previous study merely due to shared-method variance. On the other hand, medication event monitoring system-measured adherence was documented for only four weeks, perhaps not long enough to capture important trends in behavior such as drug holidays and weekly non-adherence patterns that would more accurately reflect actual adherence. External validity was limited because active drug users were excluded and the sample was predominantly male. Findings nevertheless showed that HIV-associated prospective memory impairment was independently and strongly correlated with the risk of objectively measured non-adherence to antiretroviral medication.

Contardo and colleagues (2009) were the first to measure the effects of prospective memory on HIV medication adherence while controlling for current substance use. Substance abuse is highly prevalent among people living with HIV (Berg et al., 2007) and has emerged as a reliable risk factor for antiretroviral non-adherence (Hendershot et al., 2009). Moreover, time-based prospective memory has been shown to predict risky sexual and injection practices among substance-dependent HIV-infected and uninfected adults (Martin et al., 2007). As in the Woods et al. study (2009), medication adherence was measured using medication event monitoring procedures and prospective memory using the Memory for Intentions Screening Test (N = 97). Factor loadings indicated that the Memory for Intentions Screening Test captured unique variance in cognitive processing relative to executive function and verbal learning, accounting for almost 50% of the variance in neuropsychological performance. A factor derived from several subscales, including 15-minute recall, event-based performance, and action responses, was the only one of the four retained neuropsychological factors to correlate significantly with adherence (r = 0.23). In contrast to findings from Woods et al. (2009), event-based task performance was associated with adherence whereas time-based performance was not. Other studies have reported conflicting findings on this point, possibly due to psychometric inequities between the measurement of time-based versus event-based prospective memory (e.g., Martin et al.,

2007) or small sample sizes (Carey et al., 2006; Martin et al., 2007). One reason for the discrepancy here might be that the participant groups in the two studies differed in ways that affected the nature of the relationship between prospective memory and adherence. That is, while the link between substance use and medication adherence is well documented (Hendershot et al., 2009), less explicit are the relationships among substance use and time-based versus event-based processes. Just as disease-or age-related cognitive compromise appears to differentially impact time-versus event-based prospective memory (e.g., Raskin et al., 2010), substance use may differentially impact the two in unexpected and unmeasured ways, confounding any observed effects of prospective memory on adherence. On the other hand, making a distinction between time- and event-based processes per se may be less explanatory than accounting for the cognitive complexity of time-versus event-based cues (Henry et al., 2004). For although time-based tasks appear to place a greater emphasis on self-initiated monitoring and retrieval than do event-based tasks (Einstein & McDaniel, 1990), the difficulty level of some event-based tasks, including of the ongoing activities, may place demands on strategic aspects of monitoring (Foster et al., 2009) and retrieval (Kliegel et al., 2008) that are comparable to those observed during time-based tasks.

Because no diagnostic information was provided clarifying the extent of substance dependence in this sample (self-report assessments indicated 39% used cocaine in the preceding 30 days and 17% used alcohol to intoxication), it is unclear whether prospective memory would similarly account for adherence behavior in other samples of HIV-positive substance users. In addition, error scores from the Memory for Intentions Screening Test were not reported, complicating comparisons to results from other studies. Error scores may provide insight into the cognitive mechanisms driving prospective memory performance. Errors may be coded as “no response” (i.e., omission); task substitutions (e.g., replacement of a verbal response with an action or vice-versa); loss of content (e.g., acknowledgment that a response is required to a cue but failure to recall the content); and loss of time (i.e., performing the intention later than intended after the target cue). Any of these may be recorded during any of the eight different Memory for Intentions Screening Test trials, each of which measures a unique combination of time-or event-based prospective memory, a two- or 15-minute delay period, and a verbal or behavioral response. These data enable the development of hypotheses regarding specific sources of prospective memory failures (e.g., Woods et al., 2009); for instance, omission errors are thought to represent a failure of cue detection and are considered to be a “true” prospective memory failure (e.g., Raskin et al., 2010). Task substitution errors (e.g., intrusions and perseverations) are presumed to reflect deficits in executive control and/or retrospective memory (e.g., Carey et al., 2006). Retrospective memory failure is possibly responsible for loss of content errors, and loss of time errors seem to be due to difficulty with strategic monitoring, time estimation, or impulsivity. When reported, this information provides an important opportunity for more finely tuned comparisons of prospective memory performance across studies.

Nevertheless, the fact that an association emerged between prospective memory and medication adherence despite the potentially confounding effects of substance use provided further support for the external validity of the relationship between prospective memory and non-adherence. Most recently, Zogg and colleagues (2010) demonstrated that the Memory for Intentions Screening Test summary score was the sole predictor of a naturalistic measure of compliance with general medical instructions after controlling for a host of potential confounders (X^2 =6.1, p = .01).

Rheumatoid arthritis

The first empirical study to evaluate the relationship between prospective memory and medication adherence was conducted in the context of rheumatoid arthritis. Hertzog and colleagues (2000) analyzed data from a larger study with 121 adult patients to determine whether self-reported memory complaints, including those related to prospective memory, were valid indicators of medication non-adherence. The Memory Functioning Questionnaire Frequency of Forgetting Scale-Prospective was used to measure prospective memory, and adherence was assessed both by medication event monitoring and self-report. The Memory Functioning Questionnaire prospective memory scale correlated with each of two self-reported adherence items (*rs* = -0.20 and -0.29) but not with objective adherence as measured using medication event monitoring. A performance-based semi-naturalistic measure of prospective memory (telephoning and leaving a message with an answering service every day for seven days) was unrelated to either self-report or objective measures of adherence. A latent factor summarizing self-reported prospective memory, retrospective memory, and working memory correlated 0.17 with objectively measured adherence, but this "memory complaint" factor was not modeled as a predictor of adherence in a structural equation model because it was more strongly correlated with free recall and depressive affect (squared multiple correlation = 0.33). More central to the point of this study, results suggested that patient reports of memory deficiencies specific to medication adherence (but not to general memory for future intentions such as assessed with the Memory Functioning Questionnaire) were likely to reflect actual adherence deficiency and should therefore be considered clinically relevant.

Importantly, prospective memory per se was not the focus of this study, nor was there reason to expect impairment in prospective memory as a result of rheumatoid arthritis. As discussed in more detail below, deficits in prospective memory are more likely in conditions that affect the central nervous system (especially prefontal systems) and therefore might show stronger associations with non-adherence. The Memory Functioning Questionnaire is furthermore not a performance-based measure, and no information concerning its ecological or criterion-related validity as a measure of prospective memory was provided. At least for the purposes of this review, this is of particular concern considering that none of the items used to measure prospective memory specifically queried self-reported memory for intentions to take prescribed medications. Instead, they were concerned with respondents' complaints about their ability generally to remember to do things in the future (e.g., remember birthdays). Indeed, as indicated by the subheading "Metamemory" given in the paper for the items taken from the Memory Functioning Questionnaire to measure prospective memory, the items more likely measured respondents' perceptions of their tendency toward prospective memory failures rather than actual prospective memory failures. As described more fully below, there may be a discrepancy for some individuals between actual and expected prospective memory, such that high expectations for future prospective memory performance do not comport with prior evidence of impairment (Woods et al., 2011). Finally, the confounding effects of unmeasured variables, such as the use of external memory aids, could not be ruled out for the field-based seven-day call-in task.

Diabetes

Vedhara and colleagues (2004) provided evidence for a relation between medication adherence and habitual prospective memory using data from 48 adults taking medication for Type 2 diabetes. Although by definition habitual memory tasks are performed repeatedly and thus may become relatively automatic over time, they also can introduce the possibility of errors of commission (i.e., "repetition errors," when the intended activity is mistakenly repeated because an individual cannot remember whether it was originally performed) and errors of omission (a dose is missed because it was mistakenly thought to have been taken already). This is a particular challenge and potential hazard for older adults (e.g., Einstein et al., 1998), who may be more likely than younger adults to have medication prescriptions requiring systematic adherence. Consistent with traditional laboratory approaches to prospective memory measurement, a computer-based paradigm was used in which the memory task was embedded in a cognitively demanding ongoing activity (categorizing words presented on a computer screen into groups). Adherence was assessed using medication event monitoring. Correct execution of the prospective memory task was defined as pressing the space bar 30 seconds after the beginning of the trial over 20 trials containing 60 word categorization tasks each and implied no errors of omission or commission. Individuals who were more likely to correctly execute the prospective memory task were also more likely to take the correct number of doses (Cohen's $d = 0.65$) and miss fewer doses (Cohen's $d = -0.72$) than those who committed at least one error. While the number of omission and of commission errors on the habitual prospective memory task were not per se related to any indicator of medication adherence, results showed that overall prospective memory task performance was, at least as reflected by the total number of errors committed by participants. This is the only study to examine habitual prospective memory, a process likely to be of particular relevance to adherence to some medication regimens. Yet the small sample size was small, and considering the high variability observed with both the prospective memory and adherence measures, data may not have represented elderly diabetic people in general. The sole inclusion of elderly individuals also reduced generalizability. Furthermore, the authors did not consider covariates in their analyses, raising the possibility that other important psychiatric, social or environmental predictors of adherence were responsible for the findings.

Summary and limitations

The majority of these studies support the hypothesis that deficits in prospective memory increase the risk of suboptimal medication adherence across various clinical populations, age groups, types of prospective memory tasks (i.e., self-report and objective, time- and event-based), and study designs. The magnitude and reliability of these findings suggest that deficient prospective memory could be an important target for cognitive neurorehabilitation efforts to improve medication adherence. It is important to note, however, that this research has been impeded by several limitations. An over-reliance on self-report and a lack of attention to potentially important confounders has raised questions of response bias and vulnerability to Type 1 error. The presence of an actual intention to adhere to a medication regimen, for instance, has not been explicitly evaluated in the studies reviewed here. An important assumption about the effects of prospective memory is that the individual initially has formed a clear and strong intention, as deficits in prospective memory are unlikely to factor into non-adherence if the individual has no intention of taking a medication. Indeed, this is illustrated in the guiding conceptual framework displayed in Figure 1, which proposes that the first stage of prospective memory is the actual formation of the intention. It follows that interventions intended to improve prospective memory are likely to have the biggest impact among individuals who are motivated to take their medications and form an intention to do so. This is not inconsistent with attitude-behavior and health behavior models in which intention is a proximal predictor of behavior reflecting motivational components including, in the case of medication adherence, attitudes toward medications, beliefs about its efficacy, beliefs about one's own ability to comply with the regimen (i.e., perceived behavioral control), and the perceived value to important others of adherence (i.e., subjective norms) (cf. Fishbein & Ajzen, 1975; Ajzen, 1985, 1991). Accordingly, individuals with strong intentions may be more likely to form more structured and reliable plans for organizing their medication-taking than those who doubt the effects of their medicines or the need to take them.

Yet, as is evident both intuitively and empirically, having an intention to do something does not reliably translate into doing it. This implies that the presence of an intention may be a necessary but not sufficient condition for behavior change. Intention is estimated to account for up to 30% of the variance in social and health behaviors studied prospectively, whereas presumably 100% of participants who agree to change their behavior begin with good intentions (Sheeran & Orbell, 1999). This raises the possibility that other factors, such as neurocognitive functioning, exert effects on behavior independently of intention or in conjunction with it. Liu and Park (2004) for example, reported that intention strength was not associated with differences in blood glucose monitoring in elderly adults who either formed implementation intentions or did not, theorizing that automatic cognitive processes rather than intention strength explained differences in behavior. Woods and colleagues (Woods, Moran, Carey et al., 2008; Woods et al., 2009) observed that episodic memory, specifically prospective memory, explained unique variance in antiretroviral non-adherence beyond that accounted for by beliefs about one’s own ability to comply with the regimen (a motivational variable embodied in the concept of behavioral intention as construed by attitude-behavior models). Hall and colleagues showed that college students who intended to improve their physical activity and diet but who performed relatively worse on tests of executive function were less likely to improve either behavior than were their counterparts with stronger executive functioning. In these studies, executive function/intention interactions predicted physical activity ($\delta R^2 = 0.072$) and dietary choice ($\delta R^2 = 0.037$) independently of intention (Hall et al., 2008). Much work underscores the importance of considering the relationships among motivation, intention, and executive function in studies of the effects of prospective memory on non-adherence (e.g., Hall et al., 2006, 2008).

Research is also needed to further evaluate the conditions under which intentions are executed spontaneously; that is, without recall of the intention. Convincing evidence supports the view that forming an intention can, under certain circumstances, activate an automatic associative memory process by which retrieval of an intended action is reflexively triggered when an individual encounters a relevant event-based cue, whether or not the person is thinking about the intention at the time (Einstein & McDaniel, 2005). An opposing view contends that the only mechanism for intention retrieval is engaging in continuous monitoring of the environment for cues. Whether the individual is aware of it or not, monitoring is set in motion when an intention is formed, putting the person in “retrieval mode” until the cue is encountered. Whereas spontaneous retrieval relies only minimally on cognitive capacity, continuous monitoring taxes cognitive resources, such as attention and working memory, at the expense of the ongoing task (Smith, 2003). This is important because intentions that are retrieved under conditions encouraging spontaneous processing may be easier to execute, particularly for people with already reduced cognitive capacity, such as the elderly or those with conditions involving the central nervous system.

The known influence on adherence of structural factors, such as regimen complexity, homelessness, being busy or away from home, or the unavailability of medications, has yet to be considered in the context of prospective memory. Important social factors are also absent from the literature, for instance the degree of available social support and perceived stigma regarding medication taking. Most study designs are cross-sectional, leaving open the question of whether prospective memory effects persist over time or change relative to other changing influences, including the development of new habits. More fundamentally, the correlational nature of the research does not allow the conclusion that prospective memory impairment per se increases non-adherence, as unknown factors such as those reviewed here instead might have been responsible for impaired performance.

Well-controlled studies of prospective memory necessarily occur in the laboratory, but external validity is at issue if results do not generalize to longer durations of measurement than are possible in the lab. The delay between intention formation and execution, for example, is significantly shorter in laboratory-based designs than would be the case with “real world” medication adherence. Also, the nature of the distractions incorporated into lab-based prospective memory tests might not in fact approximate the nature of those encountered in daily living. On the other hand, semi-naturalistic assessments, while incorporating longer delay periods and "real-life" distractions, are likely to be confounded by unassessed environmental influences, such as participants' use of memory aids and family and social interaction.

Another important avenue for future research is the extent to which limited metacognitive awareness (i.e., a deficit in "meta-prospective memory") explains the relationship between HIV-associated prospective memory impairment and medication adherence (Woods et al., 2011). Research shows that individuals with HIV infection, for instance, may have high expectations of their future prospective memory performance despite prior evidence of impairment and consequently not employ otherwise effective compensatory strategies, such as pillboxes (Woods, Carey, Moran et al., 2007; Woods, Iudicello et al., 2008). The likely complex relationships among discrepancy of expected and actual prospective memory, the use of compensatory strategies, and functional outcomes are yet to be explored.

Finally, participants among whom deficient prospective memory might reasonably be hypothesized are limited to those experiencing conditions known to adversely affect the central nervous system. These include many neuromedical diseases such as HIV infection, cardiovascular disease, hypertension, cancer, and diabetes mellitus; psychiatric conditions including schizophrenia, mood and anxiety disorders, and substance use disorders; and neurological populations, for instance regarding traumatic brain injury, stroke, Parkinson's disease, and multiple sclerosis, in which researchers have already shown – or would predict – evidence of prospective memory impairment (e.g., Katai et al., 2003). Prospective memory may not be as readily applicable to adherence in the areas of preventive care, such as mammography and pap testing, or lifestyle issues like diet and exercise, unless the population in which these topics were under study included individuals at high risk for impairment, such as older adults.

Nevertheless, it is still possible that prospective memory may be relevant to adherence in conditions that are not traditionally associated with neurocognitive impairment; indeed, there is a growing literature regarding the importance of individual differences in executive functions to health behaviors among healthy adults (see Williams et al., 2009). In fact, it is possible that subtle differences in cognitive functions (e.g., executive and memory processes) in globally unimpaired persons may increase the risk of non-adherence (and other poor health behaviors). A vicious cycle may then ensue in which non-adherence exacerbates disease progression and therefore may further compromise neurocognitive function (e.g., Ettenhofer et al., 2010). Consideration of subtle individual differences in prospective memory in healthy populations likely requires sensitive assessment tools that are not confounded by ceiling effects and provide sufficient variability in scores.

Measurement—As researchers have begun to identify the mechanisms and functional impact of prospective memory in a variety of clinical and non-clinical populations, assessment has become an important area of inquiry. The most common laboratory measures of prospective memory are variations on a protocol introduced in the seminal paper by Einstein and McDaniel (1990). Participants are generally presented with a primary, ongoing computerized task (e.g., lexical decision-making), during which they must complete a secondary prospective memory assignment, such as pressing a certain key in response to a stimulus that appears on the computer screen. The parameters of the ongoing task, cue, and intention are manipulated to test specific hypotheses regarding the cognitive mechanisms of prospective memory. Einstein and McDaniel's original paper validated the paradigm in a sample of older adults, and it has since been adapted for use with a variety of clinical groups, as well as children (e.g., Kvavilashvili et al., 2001). While such methodology permits flexibility and control that advances basic research in the area, a lack of standardization and normative data have limited its utility for clinical settings. More recently, several clinic-friendly standardized instruments have been developed to assess prospective memory. Here we review the most commonly used self-report and performance-based measures available and provide guidance for their use in research contexts.

Performance-based assessments

The most widely published performance-based instrument is the Memory for Intentions Screening Test (Raskin et al., 2010), which is now marketed as a proprietary instrument. The 30-minute test presents eight trails comprised of either time-based or event-based tasks, verbal or behavioral responses, and delays of either two or 15 minutes. There is also an optional semi-naturalistic task for which participants are instructed to telephone the researchers no longer than 24 hours after the evaluation. High inter-scorer reliability (0.81-0.99) can be achieved (Raskin et al., 2011; Woods, Moran, Dawson et al., 2008), and although internal consistency reliability has been poor across the eight trials in healthy adults (α = 0.48-0.73), much better reliability (α = 0.89-0.93) has been observed across the six subscales (Raskin et al., 2011; Woods, Moran, Dawson et al., 2008). There are alternate forms of the Memory for Intentions Screening Test, which according to Raskin (2009) have been shown to correlate at 0.89. Evidence of criterion-related validity comes from a strong correlation (0.80) with the items from the Rivermead Behavioral Memory Test measuring prospective memory (Raskin, 2009). Studies of patients with HIV infection (Carey et al., 2006; Woods, Carey et al., 2007; Woods, Moran, Dawson, et al., 2008); Parkinson's disease (Raskin et al., 2011); and schizophrenia (Woods, Twamley et al., 2007) have consistently shown deficits on the Memory for Intentions Screening Test relative to healthy adults. Several studies demonstrate a link between test performance and adherence behavior (Contardo et al., 2009; Woods, Dawson et al., 2009; Woods, Iudicello et al., 2008; Woods, Moran, Carey et al., 2008; Zogg et al., 2010) and other everyday functioning outcomes (e.g., Twamley et al., 2008; Woods, Iudicello et al., 2008).

The first proprietary standardized measure of prospective memory was the Cambridge Prospective Memory Test (Wilson et al., 2005), a revised version of which is now available through PsychCorp Assessments. The test takes approximately 25 minutes to administer and includes both time-based and event-based items interspersed with ongoing tasks. The instructions, prompts, and scoring methodology are highly structured, and test takers are permitted (though not required or encouraged) to use note taking to keep track of tasks, a strategy associated with enhanced performance (Fleming et al., 2009). Data from 22 participants in the standardization sample who were rated by two examiners demonstrated a strong interrater Pearson *r* of 0.998, though rater agreement was not calculated. Meanwhile, some evidence of test-retest reliability was found in a sample of 20 participants whose scores correlated 0.64 (Kendall's tau b) when they took the same form of the test twice over a seven to ten day interval, though they exhibited a significant practice effect. The authors have developed parallel forms of the measure, and Wilson and colleagues (2005) present modest support (from 23 participants) for reliability across forms. However, sample sizes were too small (11-12 per group) to interpret the null results of significance tests between forms. Results of the Cambridge Prospective Memory Test were shown to correlate moderately with scores from the Rivermead Behavioral Memory Test, the only standardized memory test at the time to tap both retrospective memory and prospective memory (Wilson et al., 2005). Among patients with traumatic brain injuries, Cambridge Prospective Memory Test scores also correlated with length of post-traumatic amnesia and executive function tests (Fleming et al., 2009).

A novel approach to assessing prospective memory that has amassed a substantial literature is the Virtual Week strategy (Rendell & Craik, 2000), which does not yet have published normative standards and is not available for purchase. The Virtual Week is organized as a board game, with spaces on the board representing times of day. Players roll dice to move their tokens around the board once for each day of the week and draw cards requiring them to perform time-or event-based tasks. Tasks are also categorized as either regular (such as taking daily medication for a chronic illness) or irregular (such as returning a library book). The original procedure can last over an hour, although more recent variations have reduced the administration time to less than 30 minutes by including fewer “days” (Henry et al., 2007). Rendell and Henry (2009) report strong internal consistency for the Virtual Week items, ranging from 0.84-0.94 in healthy controls to a split-half coefficient of 0.74 in individuals with schizophrenia. They also summarize validity data from several clinical populations, including recreational drug users, patients with schizophrenia, and patients with multiple sclerosis. Although the Virtual Week paradigm was constructed in an effort to maximize ecological validity, Rendell and Craik (2000) noted important differences between scores on their measure and performance on more naturalistic prospective memory tasks. Specifically, they found that older adults demonstrated worse performance than younger participants on the Virtual Week but outperformed the younger group on real-life tasks.

Self-report assessments

In addition to performance-based tasks, there have been efforts to assess prospective memory retrospectively by self-report. The most widely used of these assessments is the Prospective and Retrospective Memory Questionnaire (Smith et al., 2000). This test was originally developed for work with Alzheimer’s disease patients and includes 16 items with a five-point Likert-type response format tapping both time- and event-based phenomena within short- and long-term intervals. Its tripartite hierarchical factor structure has been confirmed in a nonclinical sample, with alpha coefficients for the total scale and the eight-item prospective and retrospective subscales of 0.89, 0.84, and 0.80, respectively (Crawford et al., 2003). In the original study by Smith and colleagues (2000), the measure showed evidence of validity by distinguishing between Alzheimer’s patients and their caregivers and documenting hypothesized differences between prospective and retrospective memory complaints. However, the instrument was not completed by Alzheimer’s patients themselves but by their caregivers. The Prospective and Retrospective Memory Questionnaire has not correlated well with objective measures when applied to individuals with suspected prospective memory deficits, and scores appear to be significantly impacted by psychological distress (Woods, Carey, Moran et al., 2007; Zeintl et al., 2006).

The Prospective Memory Questionnaire was the first self-report measure available (Hannon et al., 1995). It was designed using an iterative rational-empirical approach with its 52 items originally derived from rational and theoretical bases. The instrument was refined through repeated empirical testing, including factor analysis. It uses a nine-point Likert-type response format to tap self-perceived memory performance for long-term episodic, short-term habitual, and internally cued tasks and identifies techniques that individuals use to enhance recall. The instrument has demonstrated strong internal consistency overall, with a coefficient alpha of 0.92, while subscale reliabilities ranged between 0.78 and 0.89 (Hannon et al., 1995). Two-week test-retest reliability was demonstrated with an $r = 0.88$ for the overall measure and correlations between 0.64 and 0.88 for the subscales. However, data on the criterion-related validity of the Prospective Memory Questionnaire have not been as promising; while there were significant correlations between scores and performance on prospective memory tasks, those correlations were modest, and prospective memory task performance was better predicted by both age and tests of attention and concentration.

The Comprehensive Assessment of Prospective Memory contains 39 items tapping both frequency and severity of failures of prospective memory in incidental activities of daily living, such as shopping and preparing meals, as well as basic activities of daily living, such as grooming and personal hygiene. Its internal consistency reliability is good, ranging from

0.79 for the ten-item basic activities of daily living scale to 0.92 for the 23-item incidental activities of daily living scale (Roche et al., 2002). Chau and colleagues (2002) published similar findings, reporting two-week test-retest reliability among 26 participants ranging from 0.74-0.77 for the subscales and the overall measure. However, they also showed an unexpectedly positive correlation with age. Moreover, scores on the Comprehensive Assessment of Prospective Memory among patients with brain injuries have not predicted performance on the Cambridge Prospective Memory Test nor the Memory for Intentions Screening Test (Fleming et al., 2009). Yet when patients' relatives were asked to report on patients' prospective memory performance using the Comprehensive Assessment of Prospective Memory, their ratings were lower than those of the patients and correlated significantly (0.38-0.46) with patients' scores on the Cambridge Prospective Memory Test and the Memory for Intentions Screening Test.

Methods for prospective memory assessment vary greatly in their costs and benefits to the researcher or clinician. Most performance-based tasks are time consuming (requiring at least one half hour to complete), and proprietary measures require financial investment. Lengthy assessment complete with distracter tasks is necessary to distinguish "prospective memory proper," in which the planned action is recalled to consciousness after an intervening activity, from simple vigilance, in which the planned action is retained in consciousness from its assignment to its completion (Uttl, 2008). The reliability and validity of performance-based instruments are generally strong enough for research purposes, and in many cases for clinical decision-making. Limiting the clinical utility of some of these measures is their lack of demographically adjusted norms. Research has shown that at least some aspects of prospective memory performance vary substantially with age, education and literacy. Currently, the only instruments with available normative data are the Cambridge Prospective Memory Test, which is normed by age and estimated premorbid IQ, and the Memory for Intentions Screening Test, which is normed by age and education. Self-report measures are faster to administer and generally available at no cost, qualities attractive to both clinicians and researchers. However, their predictive validity is substantially lower, especially in clinical populations. While the frequency of prospective memory complaints is itself an important target for research, self-report methods seldom correlate with objective methods among patients with prospective memory deficits and are heavily influenced by psychological distress (Woods, Carey, Moran et al., 2007). More promising results have been obtained by asking caregivers or relatives to report on patients' impairments, a strategy better suited to clinical practice. However, even in such cases, associations with empirical measures of prospective memory are moderate at best.

Given the emerging state of the science, it is premature to conclude that performance-based assessment is superior to self-report, but the extant literature in prospective memory (and other cognitive domains, including retrospective memory) generally supports that contention. Further research is needed to develop valid, reliable measures that can be administered feasibly in clinical settings. These efforts are critical to the development of intervention strategies intended to address prospective memory impairment as it relates to treatment non-adherence. Meaningful assessment strategies will enable researchers to identify people at risk for prospective memory-related non-adherence, specify component processes that might be driving deficits, and determine treatment options with the greatest chance of success. Assessment is also important for the development and conduct of randomized controlled clinical trials designed to determine whether prospective memory-based intervention strategies are likely to improve medication adherence.

Implications for intervention strategies

Medication non-adherence is difficult to treat, as evidenced by several meta-analyses showing modest and inconsistent treatment effects that tend not to persist over time or reliably improve clinical outcomes (Amico et al., 2006; Haynes et al., 2007; Simoni et al., 2006). Considering the incremental ecological validity of prospective memory as a predictor, it is reasonable to hypothesize that prospective memory-based interventions might be an effective means of improving adherence, especially for groups at risk for cognitive impairment (Wilson & Park, 2008). Findings from research among patients with traumatic brain injury suggest that prospective memory is amendable to targeted intervention efforts, particularly if the component processes of the prospective memory failures in each individual are taken into account (Raskin & Sohlberg, 2009). As described above, prospective memory failures may occur at the intention formation stage (i.e., the encoding phase); the delay period between intention formation and cue detection (i.e., the monitoring phase); and the cue detection and self-initiated retrieval stage (i.e., retrieval phase). The next section highlights potentially fruitful prospective memory-based intervention strategies presented according to their relevance to these stages. Although we recognize that there is considerable theoretical debate regarding the independence of these “stages’ and our clinical capacity to identify and isolate impairment at this level of cognitive resolution, they nevertheless provide a useful heuristic model around which to organize a discussion of possible treatment approaches.

Encoding

A variety of interventions may effectively improve prospective memory at the encoding stage. Faulty encoding may signal deficient organizational and planning abilities or inadequate binding of the cue-intention pairing. One general approach is to create stronger, more salient links in memory between a specific cue (or situation) and an intention (Woods et al., 2010; McDaniel & Einstein, 2000). Evidence-based strategies include errorless learning (Clare & Jones, 2008); spaced-retrieval techniques (McDaniel & Einstein, 2007; Camp et al., 1996); and implementation intentions (Gollwitzer & Brandstatter, 1997) (see Table 1 for brief descriptions and references). The most frequently researched of these is perhaps implementation intentions, which are self-regulatory plans of action specifying when, where and how to behave in future situations (Gollwitzer & Brandstatter, 1997). Individuals perform a single, brief cognitive manipulation to link specific cues (times and places) with specific responses (medication ingestion). Responding to a designated cue as intended over time strengthens the cue-response connection until encountering the cue spontaneously leads to the desired behavior. Evidence of effectiveness comes from several areas of health behavior research, including treatment adherence to blood glucose monitoring among aging adults (Liu & Park, 2004). Other laboratory work suggests that planning during the encoding phase can benefit prospective memory even when the experimenter does not specify plan content and that planning aids may particularly benefit older adults (Kliegel et al., 2007).

Monitoring

A different set of approaches is likely to address prospective memory difficulties during the monitoring stage. This stage is the delay and retention period between the formation and the execution of an intention during which an individual experiences ongoing distraction. Successful prospective memory requires the ability to engage in distracting activities, yet disengage periodically to evaluate the environment for appropriate time or event cues, while in the meantime keeping an intention activated. More frequent attempts to monitor, such as checking the clock when the task is time-based, result in better prospective memory (McDaniel & Einstein, 2007). Theoretically, inadequate strategic allocation of attentional resources would result in a breakdown of this process (Carey et al., 2006). Training in self-regulatory strategies might compensate for this executive dysfunction by enabling individuals to redirect attention or minimize distraction and interruption. Goal management training is one such approach. Individuals complete structured group exercises to learn how to control the effects of distraction and re-direct attention to activities necessary to achieve goals. The laboratory-based approach of goal management training has been effective in patients with traumatic brain injury and may generalize to naturalistic settings (Levine et al., 2000), where researchers have demonstrated its utility in conjunction with errorless learning and content-free cuing techniques, including the STOP! paradigm (Fish et al., 2007) (see Table 1).

Cue detection and retrieval

Several remedial strategies may compensate for deficiencies in the third stage of prospective memory, cue detection and retrieval. Detection of an appropriate cue is theorized to trigger an effortful and controlled search for a stored intention (i.e., self-initiated retrieval). Failure to notice cues and apprehend that related actions are planned may indicate a disorganized or inefficient manner of searching and retrieving information from episodic memory (this part of the process is distinguished from recognizing *what* needs to be done, which occurs in phase four according to the proposed model) (Carey et al., 2006). Research has suggested that reducing self-initiated retrieval demands by increasing the quality of the cue and, therefore, the probability it will be detected may be effective (McDaniel & Einstein, 2007; Carey et al., 2006). Cues that most reliably activate intended action have meaningful associations with intended actions (e.g., a pill bottle to prompt taking medication [Woods et al., 2010], are distinctive enough to attract attention (a pill bottle stored in the silverware drawer rather than in the medicine cabinet), and are centrally located (the silverware drawer is a focus of attention during breakfast time when the pill is to be taken). Furthermore, the use of external cues, such as pillboxes, may maximize habitual memory ability in older adults or others with compromised cognitive capacity by increasing the likelihood of accurately evaluating whether the intended dose already had been taken. Such an approach might help reduce the burden on cognitive capacity of ongoing activity and minimize errors of omission and commission (McDaniel & Einstein, 2007). To the extent that these errors among older adults are due to reduced output monitoring, performance is likely to improve with more complex prospective memory tasks requiring participants' full attention (i.e., "distinctive motor action'; McDaniel et al., 2009).

Electronic devices that prominently notify a patient when to take a medication have been extensively investigated as retrieval cues. For instance, Wilson and colleagues evaluated the use of alphanumeric pagers to prompt routine behaviors among people with memory and executive function deficits in a randomized controlled trial (Wilson et al., 2001) (see Table 1). Task completion improved up to 75% at eight-week follow-up, and prospective memory improvement was sustained in some patients even after the pager was removed. More elaborate devices delivering timed, detailed messages that variously include dosage, conditions under which the medication should be taken, and other information have also been tested, particularly among people living with HIV. Results from these studies have been mixed (Simoni et al., 2009) but appear more promising among participants with known memory impairment (Andrade et al., 2005). Where electronic devices are not available or are too complicated or invasive, verbal reminders from peers, family, significant others or caregivers may bolster prospective memory. Limited support for this approach comes from studies testing more generalized systems of peer-support in which investigators observed improvement in some measures of HIV medication adherence (Simoni et al., 2009; Simoni et al., 2007). Patients with severely impaired prospective memory may benefit from Directly Observed Therapy, wherein family, community members or medically trained personnel directly observe scheduled doses being taken over a period of time. Leveraging the advantages of social support and peer pressure but also requiring extensive resources, this approach has been effective in improving adherence to tuberculosis treatment (Volmink & Garner, 2007) and, among people living with HIV, appears to be feasible and easily adapted to many settings and target populations (Goggin et al., 2007). Although Directly Observed Therapy is not informed by prospective memory theory, it nevertheless may reduce the demands on cue detection and retrieval processes and in this way fits the general model.

Given the inherent conceptual and logistical complexities in assessing prospective memory, it is recommended that clinicians, clinical researchers and others interested in assessing or addressing prospective memory consult with a neuropsychologist or other cognitive assessment expert for guidance regarding test and methods design, implementation, and interpretation.

Conclusion

A growing body of empirical evidence supports the hypothesis that prospective memory may play an important role in medication adherence when an individual forms an intention to adhere. Particularly compelling are data showing that prospective memory impairment may be associated with medication non-adherence independently of well-established risk factors, including standard neurocognitive assessments, psychiatric comorbidities, psychosocial and environmental features, and demographics. Yet despite an emergent literature supporting its ecological validity, prospective memory is rarely assessed in clinic or research settings, even among populations at high risk for impairment. Measurement challenges and time constraints represent formidable obstacles, and research is needed to develop valid, clinic-friendly, standardized measures of self-reported and performance-based prospective memory that are normed on relevant demographics. This work could improve the clinical prediction of non-adherence, an endeavor of potentially critical importance to the delivery of care to groups for whom non-adherence has been directly linked to morbidity and mortality (Bangsberg et al., 2001, 2007). Better assessment may also advance the development of comprehensive, adherence-specific theoretical models that in turn will inform much-needed intervention efforts. Given the growing number of studies identifying impaired prospective memory as an impediment to medication adherence, these will be valuable efforts, furthering our understanding of the role of prospective memory in patient non-adherence and leading to novel ways to treat this pervasive clinical challenge.

Acknowledgments

This critical review was supported in part by National Institute of Health R01 MH73419 to Dr. Woods and National Institute of Health R34 MH084674 to Dr. Simoni. None of the authors has a financial relationship with the organizations that sponsored this research.

References

Ajzen, I. From intentions to actions: A theory of planned behavior. In: Kuhl, J.; Beckmann, J., editors. Action control: From cognition to behavior. Springer-Verlag; Berlin: 1985. p. 11-39.

Ajzen I. The theory of planned behavior. Organisational Behavior and Human Decision. 1991

Amico KR, Harman JJ, Johnson BT. Efficacy of antiretroviral therapy adherence interventions: A research synthesis of trials, 1996-2004. Journal of Acquired Immune Deficiency Syndrome. 2006; 41:285–297.

Andrade ASA, McGruder HF, Wu AW, Celano SA, Skolasky RL Jr. Selnes OA, Huang IC, McArthur JC. A programmable prompting device improves adherence to highly active antiretroviral therapy in HIV-infected subjects with memory impairment. Clinical Infectious Diseases. 2005; 41(6):875–882. [PubMed: 16107989]

Arnsten JH, Demas PA, Farzadegan H, Grant RW, Gourevitch MN, Chang CJ, Buono D, Eckholdt H, Howard AA, Schoenbaum EE. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: Comparison of self-report and electronic monitoring. Clinical Infectious Diseases. 2001; 33:1417–1423. [PubMed: 11550118]

Baddeley A. Working memory: Looking back and looking forward. Nature Reviews Neuroscience. 2003; 4(10):829–839.

Bangsberg DR, Hecht FM, Charlebois ED, Chesney M, Moss A. Comparing objective measures of adherence to HIV antiretroviral therapy: electronic medication monitors and unannounced pill counts. AIDS and Behavior. 2001; 5:275–281.

Bangsberg DR, Kroetz DL, Deeks SG. Adherence-resistance relationships to combination HIV antiretroviral therapy. Current HIV/AIDS Reports. 2007; 4:65–72. [PubMed: 17547827]

Berg CJ, Michelson SE, Safren SA. Behavioral aspects of HIV care: adherence, depression, substance use, and HIV transmission behaviors. Infectious Disease Clinics of North America. 2007; 21:181–200. [PubMed: 17502235]

Burgess, PW.; Dumontheil, I.; Gilbert, SJ.; Okuda, J.; Scholvnick, ML.; Simons, JS. On the role of rostral prefrontal cortex (Area 10) in prospective memory. In: Kliegel, M.; McDaniel, MA.; Einstein, GO., editors. Prospective Memory: Cognitive, Neuroscience, Developmental, and Applied Perspectives. Taylor & Francis Group/Lawrence Erlbaum Associates; New York, NY: 2008. p. 235-260.

Camp, CJ.; Foss, JW.; Stevens, AB.; O'Hanlon, AM. Improving prospective memory task performance in persons with Alzheimer's disease. In: Brandimonte, M.; Einstein, GO.; McDaniel, MA., editors. Prospective Memory: Theory and Applications. Lawrence Erlbaum; Mahwah, NJ: 1996. p. 351-367.

Carey CL, Woods SP, Rippeth JD, Heaton RK, Grant I, the HNRC Group. Prospective memory in HIV-1 infection. Journal of Clinical and Experimental Neuropsychology. 2006; 28:536–548. [PubMed: 16676475]

Chau LT, Lee JB, Fleming J, Roche N, Shum D. Reliability and normative data for the Comprehensive Assessment of Prospective Memory (CAPM). Neuropsychological Rehabilitation. 2007; 17:707–722. [PubMed: 17852758]

Clare L, Jones RSP. Errorless learning in the rehabilitation of memory impairment: A critical review. Neuropsychology Review. 2008; 18(1):1–23. [PubMed: 18247118]

Contardo C, Black AC, Beauvais J, Dieckhaus K, Rosen MI. Relationship of prospective memory to neuropsychological function and antiretroviral adherence. Archives of Clinical Neuropsychology. 2009; 24:547–554. [PubMed: 19648150]

Crawford JR, Smith G, Maylor EA, Della Sala S, Logie RH. The Prospective and Retrospective Memory Questionnaire (PRMQ): Normative data and latent structure in a large non-clinical sample. Memory. 2003; 11:261–275. [PubMed: 12908675]

Cuttler C, Graf P. Sub-clinical compulsive checkers' prospective memory is impaired. Journal of Anxiety Disorders. 2007; 21:338–352. [PubMed: 16860532]

Dunbar-Jacob J, Erlen JA, Schlenk EA, Ryan CM, Sereika SM, Doswell WM. Adherence in chronic disease. Annual Review of Nursing Research. 2000; 18:48–90.

Einstein GO, McDaniel MA. Normal aging and prospective memory. Journal of Experimental Psychology: Learning, Memory, and Cognition. 1990; 16:717–726.

Einstein GO, McDaniel MA. Prospective memory, multiple retrieval processes. Current Directions in Psychological Science. 2005; 14(6):286–290.

Einstein GO, McDaniel MA, Smith RE, Shaw P. Habitual prospective memory and aging: Remembering intentions and forgetting actions. Psychological Science. 1998; 9:284–288.

Ellis, J. Prospective memory and medicine-taking. In: Myers, LB.; Midence, K., editors. Adherence to Treatment in Medical Conditions. Harwood Academic Publishers; Amsterdam, Netherlands: 1998. p. 113-131.

Ettenhofer ML, Foley J, Castellon SA, Hinkin CH. Reciprocal prediction of medication adherence and neurocognition in HIV/AIDS. Neurology. 2010; 74(15):1217–1222. [PubMed: 20220123]

Fish J, Evans JJ, Nimmo M, Martin E, Kersel D, Bateman A, Wilson BA, Manly T. Rehabilitation of executive dysfunction following brain injury: 'Content-free' cueing improves everyday prospective memory performance. Neuropsychologia. 2007; 45:1318–1330. [PubMed: 17084422]

Fishbein, M.; Ajzen, I. Belief, attitude, intention and behavior: An introduction to theory and research. Addison-Wesley; Reading, MA: 1975.

Fleming J, Kennedy S, Fisher R, Gill H, Gullo M, Shum D. Validity of the Comprehensive Assessment of Prospective Memory (CAPM) for use with adults with traumatic brain injury. Brain Impairment. 2009; 10:34–44.

Foster ER, McDaniel MA, Repovš G, Hershey T. Prospective memory in Parkinson disease across laboratory and self-reported everyday performance. Neuropsychology. 2009; 23:347–358. [PubMed: 19413448]

Freud, S. Psychopathology of Everyday Life. Norton; New York, NY: 1965.

Goggin K, Liston RJ, Mitty JA. Modified directly observed therapy for antiretroviral therapy: a primer from the field. Public Health Reports. 2007; 122(4):472–481. [PubMed: 17639650]

Gollwitzer PM, Brandstatter V. Implementation intentions and effective goal pursuit. Journal of Personality and Social Psychology. 1997; 73:186–199.

Gupta S, Woods SP, Weber E, Dawson MS, Grant I. Is prospective memory a dissociable cognitive function in HIV infection? Journal of Clinical and Experimental Neuropsychology. 2010; 32(8): 898–908. [PubMed: 20425662]

Hall PA, Elias LJ, Crossley M. Neurocognitive influences on health behavior in a community sample. Health Psychology. 2006; 25(6):778–782. [PubMed: 17100506]

Hall PA, Fong GT, Epp LJ, Elias LJ. Executive function moderates the intention-behavior link for physical activity and dietary behavior. Psychology and Health. 2008; 23(3):309–326.

Hannon R, Adams P, Harrington S, Fries-Dias C, Gipson MT. Effects of brain injury and age on prospective memory self-rating and performance. Rehabilitation Psychology. 1995; 40:289–298.

Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews. 2007; 2:CD000011.

Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: Review and meta-analysis. Journal of Acquired Immune Deficiency Syndrome. 2009; 52:180–202.

Henry JD, MacLeod MS, Phillips LH, Crawford JR. A meta-analytic review of prospective memory and aging. Psychology and Aging. 2004; 19:27–39. [PubMed: 15065929]

Henry JD, Rendell PG, Kliegel M, Altgassen M. Prospective memory in schizophrenia: Primary or secondary impairment? Schizophrenia Research. 2007; 95:179–185. [PubMed: 17630257]

Hertzog C, Park D, Morell RW, Martin M. Ask and ye shall receive: Behavioural specificity in the accuracy of subjective memory complaints. Applied Cognitive Psychology. 2000; 14:257–275.

Hinkin CH, Castellon SA, Durvasula RS, Hardy DJ, Lam MN, Mason KI, Thrasher D, Goetz MB, Stefaniak M. Medication adherence among HIV+ adults: Effects of cognitive dysfunction and regimen complexity. Neurology. 2002; 59:1944–1950. [PubMed: 12499488]

Katai S, Maruyama T, Hashimoto T, Ikeda S. Event based and time based prospective memory in Parkinson's disease. Journal of Neurology, Neurosurgery, and Psychiatry. 2003; 74:704–709.

Kliegel, M.; Jager, T.; Altgasen, M.; Shum, D. Clinical neuropsychology of prospective memory. In: Kliegel, M.; McDaniel, MA.; Einstein, GO., editors. Prospective Memory: Cognitive, Neuroscience, Developmental, and Applied Perspectives. Taylor & Francis Group/Lawrence Erlbaum Associates; New York, NY: 2008. p. 283-308.

Kliegel M, Martin M, McDaniel MA, Einstein GO, Moor C. Realizing complex delayed intentions in young and old adults: The role of planning aids. Memory & Cognition. 2007; 35(7):1735–1746.

Kvavilashvili L, Messer D, Ebdon P. Prospective memory in children: The effects of age and task interruption. Developmental Psychology. 2001; 37:418–430. [PubMed: 11370916]

Levine B, Roberston IH, Clare L, Carter G, Hong J, Wilson BA, Duncan J, Stuss DT. Rehabilitation of executive functioning: An experimental-clinical validation of goal management training. Journal of the International Neuropsychological Society. 2000; 6:299–312. [PubMed: 10824502]

Liu LL, Park DC. Aging and medical adherence: the use of automatic processes to achieve effortful things. Psychology and Aging. 2004; 19:318–325. [PubMed: 15222825]

Martin EM, Nixon H, Pitrak DL, Weddington W, Rains NA, Nunnally G, Grbesic S, Gonzalez R, Jacobus J, Bechara A. Characteristics of prospective memory deficits in HIV-seropositive substance-dependent individuals: preliminary observations. Journal of Clinical and Experimental Neuropsychology. 2007; 29:496–504. [PubMed: 17564915]

McDaniel MA, Bugg JM, Ramuschkat GM, Kliegel M, Einstein GO. Repetition errors in habitual prospective memory: Elimination of age differences via complex actions or appropriate resource allocation. Aging, Neuropsychology, and Cognition. 2009; 16:563–588.

McDaniel, MA.; Einstein, GO. Prospective Memory: An Overview and Synthesis of an Emerging Field. Sage Publications, Inc.; Thousand Oaks, CA, US: 2007.

McDaniel MA, Einstein GO. Strategic and automatic processes in prospective memory retrieval: A multiprocess framework. Applied Cognitive Psychology, New Perspectives in Prospective Memory. 2000; 14(SpecIssue):S127–S144.

McDaniel MA, Glisky EL, Guynn MJ, Routhieaux BC. Prospective memory: A neuropsychological study. Neuropsychology. 1999; 13:103–110. [PubMed: 10067781]

McDaniel MA, Guynn MJ, Einstein GO, Breneiser J. Cue-focused and reflexive-associative processes in prospective memory retrieval. Journal of Experimental Psychology. 2004; 30:605–614. [PubMed: 15099129]

McDaniel MA, Robinson-Riegler B, Einstein GO. Prospective remembering: Perceptually driven or conceptually driven processes? Memory and Cognition. 1998; 26:121–134.

Nieuwkerk PT, Sprangers MA, Burger DM, Hoetelmans RM, Hugen PW, Danner SA, van Der Ende ME, Schneider MM, Schrey G, Meenhorst PL, Sprenger HG, Kauffmann RH, Jambroes M, Chesney MA, de Wolf F, Lange JM. Limited patient adherence to highly active antiretroviral therapy for HIV-1 infection in an observational cohort study. Archives of Internal Medicine. 2001; 161(16):1962–1968. [PubMed: 11525698]

Osterberg L, Blaschke T. Adherence to medication. New England Journal of Medicine. 2005; 353:487–497. [PubMed: 16079372]

Park, DC.; Kidder, DP. Prospective memory and medication adherence. In: Brandimonte, M.; Einstein, GO.; McDaniel, MA., editors. Prospective Memory: Theory and Application. Lawrence Erlbaum; Mahwah, NJ: 1996. p. 369-390.

Pearson CR, Simoni JM, Hoff P, Kurth AE, Martin DP. Assessing antiretroviral adherence via electronic drug monitoring and self-report: An examination of key methodological issues. AIDS and Behavior. 2007; 11:161–173. [PubMed: 16804749]

Raskin SA. Memory for Intentions Screening Test (abstract). Journal of the International Neuropsychological Society. 2004; 10(Suppl 1):110. [PubMed: 14751013]

Raskin SA. Memory intentions screening test: Psychometric properties and clinical evidence. Brain Impairment. 2009; 10:23–33.

Raskin, S.; Buckheit, C.; Sherrod, C. Memory for Intentions Test (MIsT). Psychological Assessment Resources, Inc.; Lutz, FL: 2010.

Raskin SA, Sohlberg MM. Prospective memory intervention: A review and evaluation of a pilot restorative intervention. Brain Impairment. 2009; 10:76–86.

Raskin S, Woods SP, Poquette A, McTaggart AB, Sethna J, Williams RC, Tröster AI. A differential deficit in time-based prospective memory in Parkinson's disease. Neuropsychology. 2011; 25(2): 201–209. [PubMed: 21090895]

Rendell PG, Craik FIM. Virtual and actual week: Age-related differences in prospective memory. Applied Cognitive Psychology Special Issue: New Perspectives in Prospective Memory. 2000; 14:S43–S62.

Rendell RG, Henry JD. A review of virtual week for prospective memory assessment: Clinical implications. Brain Impairment. 2009; 10:14–22.

Roche NL, Fleming JM, Shum DHK. Self-awareness of prospective memory failure in adults with traumatic brain injury. Brain Injury. 2002; 16:931–945. [PubMed: 12443545]

Sabaté, E. Adherence to long-term therapies: Evidence for action (ISBN 92 4 154599 2). World Health Organization; Geneva, Switzerland: 2003.

Salthouse TA, Berish DE, Siedlech KL. Construct validity and age sensitivity of prospective memory. Memory and Cognition. 2004; 32:1133–1148.

Sheeran P, Orbell S. Implementation intentions and repeated behaviour: augmenting the predictive validity of the theory of planned behavior. European Journal of Social Psychology. 1999; 29:349–369.

Simoni JM, Huh D, Frick PA, Pearson CR, Andrasik MP, Dunbar PJ, Hooton TM. Peer support and pager messaging to promote antiretroviral modifying therapy in Seattle: a randomized controlled trial. Journal of Acquired Immune Deficiency Syndrome. 2009; 52(4):465–473.

Simoni JM, Pantalone DW, Plummer MD, Huang B. A randomized controlled trial of a peer support intervention targeting antiretroviral medication adherence and depressive symptomatology in HIV-positive men and women. Health Psychology. 2007; 26(4):488–495. [PubMed: 17605569]

Simoni JM, Pearson CR, Pantalone DW, Marks G, Crepaz N. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load: A meta-analytic review of randomized controlled trials. Journal of Acquired Immune Deficiency Syndrome. 2006; 43:S23–S35.

Simons JS, Schölvinck ML, Gilbert SJ, Frith CD, Burgess PW. Differential components of prospective memory? Evidence from fMRI. Neuropsychologia. 2006; 44:1388–1397.

Smith RE. The cost of remembering to remember in event based prospective memory: Investigating the capacity demands of delayed intention performance. Journal of Experimental Psychology: Learning, Memory, and Cognition. 2003; 29:347–361.

Smith, RE. Connecting the past and the future: Attention, memory, and delayed intentions. In: Kliegel, M.; McDaniel, MA.; Einstein, GO., editors. Prospective Memory: Cognitive, Neuroscience, Developmental, and Applied Perspectives. Taylor & Francis Group/Lawrence Erlbaum Associates; New York, NY: 2008. p. 29-52.

Smith GV, Della Sala S, Logie RH, Maylor EA. Prospective and retrospective memory in normal ageing and dementia: A questionnaire study. Memory. 2000; 8:311–321. [PubMed: 11045239]

Twamley EW, Woods SP, Zurhellen CH, Vertinski M, Narvaez JM, Mausbach BT, Patterson TL, Jeste DV. Neuropsychological substrates and everyday functioning implications of prospective memory impairment in schizophrenia. Schizophrenia Research. 2008; 106:42–49. [PubMed: 18055178]

Uttl B. Transparent meta-analysis of prospective memory and aging. PLoS One. Feb 20.2008 3(2):e1568. [PubMed: 18286167]

Vedhara K, Wadsworth E, Norman P, Searle A, Mitchell J, Macrae N, O'Mahony M, Kemple T, Memel D. Habitual prospective memory in elderly patients with Type 2 diabetes: Implications for medication adherence. Psychology, Health, and Medicine. 2004; 9(1):17–27.

Volmink J, Garner P. Directly observed therapy for treating tuberculosis. Cochrane Database Systematic Review. 2007; 4:CD0033431–30.

Wagner G, Miller LG. Is the influence of social desirability on patients' self-reported adherence overrated? Journal of Acquired Immune Deficiency Syndrome. 2004; 35:203–204.

West, D. The cognitive neuroscience of prospective memory. In: Kliegel, M.; McDaniel, MA.; Einstein, GO., editors. Prospective Memory: Cognitive, Neuroscience, Developmental, and Applied Perspectives. Taylor & Francis Group/Lawrence Erlbaum Associates; New York, NY: 2008. p. 261-2820.

Williams PG, Suchy Y, Rau HK. Individual differences in executive functioning: implications for stress regulation. Annals of Behavioral Medicine. 2009; 37:126–140. [PubMed: 19381748]

Wilson BA, Shiel A, Foley J, Emslie H, Groot Y, Hawkins K, Watson P. Cambridge Test of Prospective Memory (CAMPROMPT). San Antonio: Pearson Assessment. 2005

Wilson BA, Emslie HC, Quirk K, Evans JJ. Reducing everyday memory and planning problems by means of a paging system: A randomized control crossover study. Journal of Neurology, Neurosurgery, and Psychiatry. 2001; 70:477–482.

Wilson, EA.; Park, D. Prospective memory and health behaviors: Context triumphs cognition. In: Kliegel, M.; McDaniel, MA.; Einstein, GO., editors. Prospective Memory: Cognitive, Neuroscience, Developmental, and Applied Perspectives. Taylor & Francis Group/Lawrence Erlbaum Associates; New York, NY: 2008. p. 391-410.

Woods SP, Dawson M, Weber E, Grant I, The HIV Neurobehavioral Research Center Group. The semantic relatedness of cue-intention pairings influences prospective memory failures in older adults with HIV infection. Journal of Clinical and Experimental Neuropsychology. 2010; 32(4): 398–407. [PubMed: 19763997]

Woods SP, Dawson MS, Weber E, Gibson S, Grant I, Atkinson JH, The HIV Neurobehavioral Research Center Group. Timing is everything: Antiretroviral nonadherence is associated with impairment in time-based prospective memory. Journal of the International Neuropsychological Society. 2009; 15:42–52. [PubMed: 19128527]

Woods SP, Moran LM, Carey CL, Dawson MS, Iudicello JE, Gibson S, Grant I, Atkinson JH, The HIV Neurobehavioral Research Center Group. Prospective memory in HIV infection: Is "remembering to remember" a unique predictor of self-reported medication management? Archives of Clinical Neuropsychology. 2008; 23:257–270. [PubMed: 18243645]

Woods SP, Moran LM, Dawson MS, Carey CL, Grant I, The HIV Neurobehavioral Research Center Group. Psychometric characteristics of the Memory for Intentions Screening Test. Clinical Neuropsychology. 2008; 22:864–878.

Woods SP, Morgan EE, Marquie-Beck J, Carey CL, Grant I, Letendre SL, The HIV Neurobehavioral Research Center. Group Markers of macrophage activation and axonal injury are associated with prospective memory in HIV-1 disease. Cognitive and Behavioral Neurology. 2006; 19:217–221. [PubMed: 17159619]

Woods SP, Twamley EW, Dawson MS, Narvaez JM, Jeste DV. Deficits in cue detection and intention retrieval underlie prospective memory impairment in schizophrenia. Schizophrenia Research. 2007; 90:344–350. [PubMed: 17175138]

Woods SP, Carey CL, Moran LM, Dawson MS, Letendre SL, Grant I, The HIV Neurobehavioral Research Center Group. Frequency and predictors of self-reported prospective memory complaints in individuals infected with HIV. Archives of Clinical Neuropsychology. 2007; 22:187–195. [PubMed: 17289343]

Woods SP, Iudicello JE, Moran LM, Carey CL, Dawson MS, Grant I, The HIV Neurobehavioral Research Center Group. HIV-associated prospective memory impairment increases risk of dependence in everyday functioning. Neuropsychology. 2008; 22:110–117. [PubMed: 18211160]

Woods, SP.; Weber, E.; Grant, I.; The HNRP Group. Inaccurate self-predictions of prospective memory performance in HIV infection: Evidence for a meta-memory deficit. Paper to be presented at the 5th International Conference on Memory; York, England. Aug. 2011

Zeintl M, Kliegel M, Rast P, Zimprich D. Prospective memory complaints can be predicted by prospective memory performance in older adults. Dementia and Geriatric Cognitive Disorders. 2006; 22:209–215. [PubMed: 16899998]

Zogg JB, Woods SP, Weber E, Iudicello JE, Dawson MS, Grant I, The HIV Neurobehavioral Research Center Group. HIV-associated prospective memory impairment in the laboratory predicts real-world failures on a semi-naturalistic measure of health care compliance. The Clinical Neuropsychologist. 2010; 24:945–962. [PubMed: 20661839]

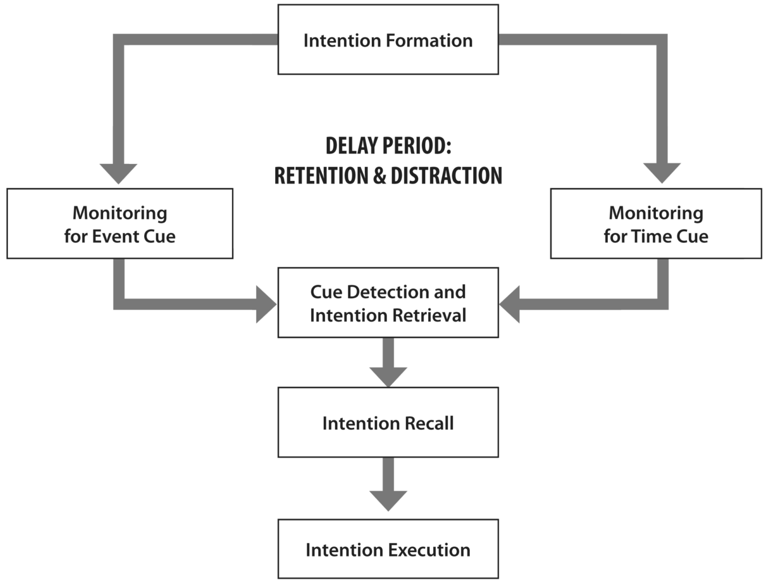

Figure 1.
Conceptual model of the component processes of prospective memory

Table 1

Evidence-based Intervention Strategies

Intervention	Description	Reference(s)
Errorless learning	Participants learn stimulus-response connections (an environmental cue, such as a pill bottle, followed by a semantically-related behavioral response, such as ingesting a dose of medication) in a context of high likelihood of success so that the possibility of errors and associated negative affect is reduced.	Clare & Jones, 2008
Spaced-retrieval techniques	Individuals practice repeatedly retrieving an intention with increasingly longer delays between each retrieval effort. An instructor asks the memory-impaired person to report what he or she is supposed to do that day, and upon receiving an answer (the correct intention), asks again after a specified interval (e.g., 20 seconds).	Camp, et al., 1996; McDaniel & Einstein 2007
Implementation intentions	Self-regulatory plans of action specifying when, where, and how to behave in future situations. Individuals perform a single, brief cognitive manipulation to link specific cues (i.e., times and places) with specific responses (medication ingestion).	Gollwitzer &Brandstatter, 1997; Liu& Park, 2004
Planning aids	General planning techniques (e.g., a flow chart) and/or specific planning strategies (e.g., targeting plan content) are provided in the intention formation phase to facilitate delayed realization of intended actions.	Kliegel et al., 2007
Goal management training	Individuals learn to control the effects of distraction and re-direct attention to goal-directed activities. Through exercises and activities completed in group settings, participants learn goal steps, link them to an intended action, then practice pausing several times per day to monitor and evaluate goal progress.	Levine et al., 2000
“STOP!” paradigm with goal management training	Through goal management training, participants link the cue phrase “STOP!” with pausing current activity and reviewing stored goals. Patients receive the content-free phrase as an electronic text message repeatedly and randomly throughout the day. Goal intentions are activated despite a lack of information about the prospective memory task itself.	Fish et al., 2007
Distinctive motor action	Individuals are instructed to take their medications while placing a hand on their head, crossing their arms, or performing some other unusual or silly action. This can mitigate errors of commission observed among older adults during habitual memory tasks by facilitating output monitoring (i.e., by requiring individuals to commit their full attention to the task).	McDaniel et al., 2009
Electronic reminder devices	A pager or other electronic device is programmed to notify a patient when to take medication, in some cases delivering timed, detailed messages that may include dosage, a description of the conditions under which medication should be taken, and other information.	Andrade et al., 2005; Simoni et al., 2009; Wilson et al., 2001
Verbal reminders from others	Explicit verbal reminders from peers, family, significant others or caregivers.	Simoni et al., 2009
Directly Observed Therapy	Family or community members or medically trained personnel directly observe scheduled doses being taken over a period of time.	Volmink & Garner, 2007; Goggin et al., 2007