Pharmacy Internet Navigation Skills in Older Adults with HIV Disease: Influence of Health Literacy and Association with Medication Management

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Abstract

A large portion of health-based Internet use for persons with HIV is focused on online pharmacies, which can provide a more anonymous, cheaper and easier alternative to purchasing medications. Pharmacy Internet navigation skills (INS) are an important component of successful online pharmacy use in HIV populations, which may be affected by a multitude of factors, including neuropsychological deficits and low health literacy. The current study aimed to: 1) examine whether health literacy modulates the effects of HIV on pharmacy INS speed and accuracy; and 2) evaluate whether pharmacy INS are related to medication management in persons with HIV disease. Study participants included 98 individuals with HIV infection and 36 seronegatives who completed measures of health literacy, medication management, cognition, and the Test of Online Pharmacy Skills (TOPS). In models adjusting for sociodemographics, neurocognition and internet use and anxiety, there were no main effects of HIV on TOPS and no interaction with health literacy. There was a main effect of health literacy, which showed medium effect size associations with TOPS speed/accuracy irrespective of serostatus. Within the HIV+ subsample, models adjusting for sociodemographics, neurocognition and internet use and anxiety showed no main effects of TOPS speed/accuracy on medication management and no interaction with health literacy. There was a main effect of health literacy, which showed medium effect size associations with medication management. Findings indicate that health literacy plays a major role in online pharmacy navigation but is not synergistic with HIV disease. Future studies are needed to further explore the role of various dimensions of health literacy in online pharmacy navigation in order to better identify possible targets for compensation and remediation.

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Introduction

Widespread availability of high-speed Internet and advances in web-based technology over the past 20 years have altered the ways in which individuals navigate their day-to-day world. Many people today use the Internet to complete at least some daily household (e.g. shopping), social, and health-related activities (e.g. appointment scheduling, pharmacy refills) (Ryan & Lewis, 2017). Individuals with medical and psychological disorders are increasingly using online tools to gather health information (e.g. symptoms, medication side effects) and manage their health care (e.g. check laboratory results, schedule appointments, communicate with providers, refill prescriptions) (Dorner, Schulte-Hermann, Zanini, Leichsenring, & Stefanek, 2014). Further, the Internet is becoming a fundamental tool for psychological and medical assessment, treatment delivery, and various supports to bolster daily functioning and quality of life (Wawrzyniak, Ownby, McCoy, & Waldrop-Valverde, 2013).

As of 2015, 80% of households in the U.S. reported using the Internet, with the most common uses including communication for work/school and searching for general information (Kekäläinen & Kokko, 2017); approximately two-thirds of Americans report using the Internet to search for health information (Ryan & Lewis, 2017; Nguyen, Mosadesgei, & Almario, 2017; Perrin, 2015; Zickuhr & Madden, 2012). Indeed, health-related searches comprise approximately 5% of all Internet searches (Eysenbach & Kohler, 2003). The individuals who are most likely use the Internet for health information are women, younger adults, and persons with higher levels of education, income, and Internet experience (Diaz et al., 2002; Rice, 2006). Additionally, those with chronic health conditions or individuals who are experiencing problems with their health status tend to utilize the Internet for health searches more often than their healthy counterparts (Bundorf, Wagner, Singer, & Baker, 2006; Houston & Allison, 2002).

It has been estimated that more than half of persons enrolled in primary care use the Internet to find information about nutrition, side effects of therapies, and alternative medicines (e.g., Diez et al., 2002). Intriguingly, patients often rate the information they find online as equal to or better than information they obtain from their healthcare provider (e.g., Diez et al., 2002). In fact, 60-80% of persons who utilize the Internet to search for healthcare information choose not to discuss it with their provider (Russ, Giveon, Granek Catarivas & Yaphe, 2011). This is concerning given the sheer volume of websites that contain health information (Dearness & Tomlin, 2001), many of which are of questionable quality (Eysenbach, Powell, Kuss, & Sa, 2002). Therefore, using the Internet for finding health-related information involves a host of additional risks, including using inaccurate and potentially dangerous information about one’s health condition (e.g., Kunst, Groot, Latthe, Latthe, & Khan, 2002), especially for persons with lower health literacy (Mittman & Cain, 1999). On the other hand, there are confirmed benefits of utilizing the web as a resource to access health information. A survey of individuals using the Internet to find health information in the U.S. reported that half of the participants thought that the information they found online improved the way they take care of themselves and positively affected their decisions about healthcare (Fox & Rainey, 2002). In this way, utilizing online resources to find appropriate information can also potentially improve health outcomes. Thus, it is important to understand the mechanics of how people use the Internet for health-related purpose in order to develop proper supports that help to optimize its effective use.

Internet Navigation Skills (INS)

The extent to which the Internet can be used as a resource for healthcare depends, at least in part, on how well the individual can navigate the Internet. Internet navigation skills (INS) describe an individual's ability to effectively utilize online resources and can be measured through a variety of online tasks (see Woods et al., 2019). Although there are no currently validated theoretical models of INS, this construct is thought to comprise a variety of physical (e.g., visual perception, motor), neurocognitive (e.g., attention and working memory, semantic knowledge), and psychological (e.g., self-efficacy, technology-related anxiety) factors. General predictors of INS accuracy include education, with studies showing medium effect sizes for the association between INS accuracy and more years of education in clinical populations (e.g., Woods et al., 2016; Goverover et al., 2016). Older age is also related to worse performance (e.g. speed, accuracy) on performance-based Internet search tasks (Chevalier et al., 2015; Laberge & Scialfa, 2005; Czaja, Sharit, Ownby, Roth, & Nair, 2001; Woods et al., 2019). Additionally, technology-based anxiety may affect INS. Although studies show mostly null associations between INS performance and general anxiety or mood disorders (Goverover & DeLuca, 2015; Woods et al., 2016, 2017), two studies found that INS task accuracy is related to both state and trait computer-related anxiety (Woods et al., 2016, 2017). Moreover, time spent online is another important factor in predicting INS performance. Agree and colleagues (2015) show that an increase in daily Internet use is associated with better Internet search performance. Similarly, Woods et al. (2016) found that lower accuracy on INS pharmacy and medical records tasks were related to less frequent technology use.

Furthermore, neurocognitive function (i.e. cognitive function associated with specific pathways or loci within the brain and are affected by different disease processes;

Sharafkhaneh & Grogan, 2015) has been shown to play a major role in the individuals' ability to effectively navigate online resources. The average Internet user has likely experienced online frustrations such as forgetting log-in passwords or trouble with navigating websites that require specific browsers or devices to work, crash often, contain faulty links or have unclear instructions. For the average person, these issues can make Internet navigation more cumbersome and challenging, but it can severely complicate the lives of individuals with neurocognitive disorders and clinical populations. Indeed, neurocognitively impaired persons have high rates of self-reported problems independently navigating technology (Nygård, Pantzar, Uppgard, & Kottorp, 2012), including the Internet (Mayben & Giordano, 2007). This complex activity requires adequate motor abilities (e.g. operating a keyboard, mouse or touchscreen), visuospatial abilities (e.g. navigating the contents of a website), and executive functions (e.g. inhibition, multitasking). In a systematic review, Woods et al. (2019) described the results of 17 studies that examined the relationship between INS performance and neuropsychological functioning. They found consistent medium-to-large relationships between measures of episodic memory, executive functions, and visuospatial skills and INS performance (i.e. accuracy and speed, with reliably stronger findings for accuracy). They also found small-to-medium sized relationships between INS performance, motor skills, and information processing speed.

Everyday functioning capacity is another factor that has been associated with Internet navigation performance. INS paradigms represent important, but often disregarded simulated capacity measures of everyday functioning, which can provide a performance-based measurement of ADLs (e.g. online shopping, managing finances) in an ecologically relevant manner. Woods et al. (2017) found that INS accuracy was reliably related to performance on the University of California San Diego Performance-based Skills Assessment (UPSA-B; Mausbach, Harvey, Goldman, Jeste, & Patterson, 2007), which measures functional capacity for finances and communication. Importantly, the associations between INS accuracy on the shopping and banking tasks were related to the UPSA-B independent of relevant co-factors, such as neurocognitive impairment, depression, and disease severity (Woods et al., 2017). These findings serve as early evidence for the construct validity of INS as a modern measure of everyday functioning.

INS for Health-Related Activities

INS for health-related activities are especially important for clinical populations, who must often rely on the Internet for looking up information about medications (e.g. side effects), checking lab results, and managing their healthcare (e.g., scheduling doctor appointments, pharmacy refills) (Kalichman et al., 2005; Schnall et al., 2014). Despite the large role that health-based INS play in the daily lives of persons with medical conditions, not many findings are available on this topic. Most studies focusing on health information search tasks were conducted in healthy samples (e.g. Agree et al., 2015; Chevalier et al., 2015; Czaja et al., 2010; Sharit et al., 2008, 2015). However, these studies consistently report moderate sized relationships of INS for health-related activities with measures of visuospatial skills, processing speed, attention, executive functions, and language, which are all domains commonly affected in neuropsychological populations (Morgan & Ricker, 2018). Thus, these findings combined with the fact that individuals with chronic health conditions, are more likely to utilize Internet sources to look for health information on the Internet (Bundorf, Wagner, Singer, & Baker, 2006; Houston & Allison, 2002), serve as converging evidence for clinical populations being uniquely vulnerable to adverse downstream effects of low INS performance in health-related activities.

Pharmacies are one of the most utilized health-related sites on the Internet, with an average of 1.5 million individuals using online pharmacy sites per year. Similar to health search use, individuals who are experiencing problems with their health status and those who have more prescriptions, tend to utilize online pharmacies more often than their healthy counterparts. Additionally, online pharmacy users tend to be older and have higher health care expenditures and more medical comorbidities (Brown & Li, 2014). Despite the benefits of using online pharmacies (e.g. quick and convenient purchase of medications), there are also risks. The combination of older age and health problems in this population makes the users of online pharmacies uniquely vulnerable to the many dangers associated with participating in the Internet pharmacy market. There are at least 35,000 globally operated online pharmacies, 96% of which fail to adhere to regulatory and safety requirements and are therefore operating illegally (Mackey & Nayyar, 2016). These illicit pharmacies introduce a host of risk factors, including fraudulent health claims, illegal versions of drugs and other concerns which are termed 'digital iatrogenesis' in patient safety literature (i.e. 'preventable patient harm resulting from injury that occurs from use of information, services or products delivered or enhanced through the Internet and related technologies') (Mackey & Liang, 2014). Yet we know little about the INS of Internet pharmacy navigation skills, which may also be affected by a multitude of factors reviewed above, including health literacy.

Health Literacy and INS for Health-Related Activities

Health literacy has been defined as "the capacity to obtain, communicate, process, and understand basic health information and services to make appropriate health decisions" (The Patient Protection and Affordable Care Act, 2010; see Sorensen et al., 2012). It is estimated that between 30 to 50 percent of US adults have marginal or low health literacy (Paasche-Orlow et al., 2005). Low health literacy can lead to adverse health outcomes including poor health care management, declines in mental health, and increased risk of mortality (Mosher et al., 2012; Wolf, Gazmararian & Baker, 2005). Meanwhile, higher levels of health literacy are shown to be associated with fewer hospitalizations, better overall health, and a decrease in emergency care service use (Berkman et al., 2011).

Both health literacy and navigating the Internet for health information require the individual to be able to search for and understand the information they find, so it is reasonable to hypothesize that the two sets of skills would be associated with one another. The literature on the relationship between health literacy and INS is limited with only three studies published on the topic to date (Agree et al., 2015; Neter & Brainin, 2017; Woods et al., 2016). All three studies however, found a significant relationship between the online search task and health literacy. Performance-based tests of health literacy, including numeracy (average r= .47) and Newest Vital Sign (average r= .45) (Weiss et al., 2005), have medium-to-large associations with INS accuracy, even after controlling for age and education (Woods et al., 2019). In a sample of healthy adults (n=223), Agree et al. (2015) found that a word-reading measure of health literacy was associated with performance on a search task that required participants to answer a question about the seasonal flu, even after controlling for demographic (OR= 1.07 [1.01, 1.13]). Likewise, Neter & Brainin (2017) found a medium sized relationship between perceived electronic health literacy and performance on search tasks that were designed to measure different components of electronic health literacy in a sample of older adults (n=82). The authors concluded that older adults may make reasonable, though inaccurate, evaluations of their skill level. Lastly, Woods et al. (2016) found small to large-sized relationships between several measures of health literacy and performance on mock online health-related tasks, with the strongest relationships detected on tasks of numeracy and health literacy comprehension, in persons with HIV disease. Taken together, these findings provide early evidence for the association between health literacy and health-related INS performance.

INS for Health-Related Activities in HIV disease

This study will examine the effects of health literacy on INS in persons living with HIV disease. In the modern era of antiretroviral (ARV) medications, HIV has been transformed into a chronic, manageable disease with near-normal life expectancies for those who are retained in care (CDC, 2019). Approximately half of HIV-infected individuals use the Internet for healthcare purposes (Dorner et al., 2014; Thomas & Shuter, 2010), with nearly two-thirds of those reporting that the Internet is both useful and important for health-related decisions (Woods & Sullivan, 2019). Utilizing health-related Internet resources for tasks such as obtaining essential health information (e.g., medication information), managing healthcare (e.g., scheduling checkup appointments), accessing psychosocial support resources (e.g., social networking), and performing various household activities (e.g., managing finances), is associated with significantly better general health status in people with HIV disease (Kalichman et al., 2005; Schnall et al., 2014). Poor health-based INS can be a serious barrier to optimal daily functioning in HIV, especially for individuals from disadvantaged backgrounds who may have limited access to the Internet and may have difficulty with this sometimes-complicated technology (Woods et al., 2019). Indeed, two-thirds of persons living with HIV require assistance in using the Internet (Mayben & Giardino, 2007). Among HIV+ individuals, identifying as Black or Latinx, having low-to-moderate perceived financial stability, lower education, and history of incarceration are all associated with being less likely to use the Internet for health-related activities (Saberi & Johnson, 2015) Additionally, fewer years of education, less frequent Internet use, and lower health literacy are all associated with poor INS performance in HIV disease (Woods et al., 2016).

Due to high levels of medication burden and a host of medical comorbidities, persons living with HIV may be particularly likely to use online pharmacies. To that end, it has been reported that 40% HIV+ persons use online pharmacies as compared to only 10% of demographically similar seronegatives (Woods et al., 2016). Factors such as stigma, limited physical mobility, problems with transportation, and potentially lower cost may all contribute to increased online pharmacy use among persons with HIV. Studies also show that polypharmacy in very common in HIV, particularly in older HIV+ adults (Guthrie et al., 2010, Marzolini et al., 2011, Bastida et al., 2017). One major cause for the high rates of polypharmacy comes from the fact that ART medications are commonly used in combination (Guaraldi et al., 2011) and HIV-infected persons also experience high rates of cardiovascular and psychiatric comorbidities (Bastida et al., 2017) for which additional drugs are prescribed (e.g. statins, antihypertensives, antidepressants, antipsychotics; Marzolini et al., 2011, Greene et al., 2014, Tseng et al., 2013). Thus, it is important to understand the factors that lead to successful online pharmacy use in persons living with HIV disease.

However, there has been one study to date that has examined online pharmacy skills in HIV. In 2016, Woods et al. reported online pharmacy task data for 19 HIV+ individuals with HIV Associated Neurocognitive Disorders (HAND), 27 HIV+ individuals without HAND and 21 seronegatives. Participants completed the Test of Online Pharmacy Skills (TOPS), which requires the participant to log into a simulated, experimenter-controlled online pharmacy after completing a brief version of the Medication Management Test-Revised (MMT-R; see Scott et al., 2011). They are then instructed to refill an existing prescription, request to fill a new prescription, activate a pick-up reminder on a cellular phone, and check for possible drug interactions for their new prescription. TOPS was scored for total items completed (i.e. accuracy), errors (e.g. log-in failures), and time to completion. The study groups did not differ in TOPS error rates or time to completion, and the accompanying effect sizes for these analyses were small. However, the HAND group demonstrated significant, large effect size differences in TOPS accuracy relative to the other two study groups; in fact, none of the HAND participants received a perfect accuracy score on the TOPS. The study showed medium to large associations between poorer TOPS performance and lower scores on clinical measures episodic memory and executive dysfunction. In the full HIV+ sample, lower TOPS accuracy was associated with higher HIV RNA in plasma ($r = -0.47$), less frequent technology use, including daily Internet use (average $d = .95$) and fewer years of education ($r = 0.49$).

Moreover, a series of simple univariable correlational analyses showed that poorer performance on the online pharmacy task was moderately associated (range of $r = 0.4 - 0.55$) with lower scores on well-validated measures of health literacy within the HIV+ sample, including the Expanded Numeracy Scale, TOFHLA Reading Comprehension, MMT-R, and the Newest Vital Sign. These results suggest that online health-related behaviors are at least partly dependent on both basic (e.g., numeracy) and higher-order (e.g., understanding and appraisal of health-related information) aspects of health literacy. As noted above, low health literacy is a major barrier for HIV+ populations and affects 20–40% of individuals living with HIV infection (Kalichman & Rompa, 2000). Furthermore, low health literacy is shown to be associated with medication nonadherence (Jones et al., 2013; Kalichman, Ramachandran, & Catz, 1999), lower engagement in health care (Jones et al., 2013), and worse HIV disease outcomes (Kalichman & Rompa, 2000). Thus, low health literacy may amplify the risk of poorer online pharmacy accuracy in the setting of HIV disease.

There is ample theoretical and empirical evidence to support independent adverse effects that HIV disease and low health literacy have on functional outcomes such as INS performance. To my knowledge, however, there are no studies to date that have looked at health literacy as a possible moderator for health-related INS performance in the context of HIV disease. Based on my review of the literature to date, I hypothesize that HIV disease and low health literacy will have a synergistic relationship in affecting INS performance. This is in line with the "resource substitution theory," which hypothesized that resources have more beneficial effects among people with fewer alternative resources (Mirowsky & Ross, 2003). Resource substitution implies a moderating pattern, such that one resource (e.g., multimorbidity strain due to HIV disease) becomes increasingly prominent at lower levels of another critical resource (e.g., lower levels of health literacy). Likewise, the "syndemic theory" speculates that when multiple adverse conditions co-occur and synergistically interact, they produce a worse overall health outcome than if each of the conditions were experienced separately (Singer et al., 2006). Thus, it is plausible that the effects of HIV on pharmacy INS would be amplified among persons with low health literacy.

Pharmacy INS and Medication Adherence in HIV Disease

One of the most important benefits of Internet use in HIV populations is its association with greater confidence in adhering to ARV medications (Kalichman, Benotsch, Weinhardt, Austin, & Luke, 2002). Kalichman et al. (2005) reported that HIV+ individuals who used the Internet for health-related purposes were significantly less likely to be nonadherent to their ARV regimen in the past week. For persons living with HIV, medication management and ART adherence are critical aspects of daily functioning and positive health outcomes. Low adherence to ART can be a rate limiting step in the successful reduction of viral load to undetectable levels and can lead to AIDS-related comorbidities and an increased risk for mortality (Finitsis et al., 2016; Sherr et al., 2010; Bangsberg et al., 2001).

At the moment, little is known about the association between health-related INS and medication management in persons with HIV, but there is early evidence that these two factors may be related. At the practical level, brick-and-mortar pharmacy refills are sometimes used as manifest measures of medication adherence (Grossberg & Gross, 2007). As noted above, Woods et al. (2016) reported that TOPS accuracy was correlated with MMT-R performance ($r = 0.3$) and viremia ($r = -0.47$; a biomarker of non-adherence) in 36 persons with HIV; however, the MMT-R only measures one aspect of capacity for medication adherence and viremia can occur for many reasons other than non-adherence (e.g., ART resistance). In fact, there is no gold standard for measuring medication adherence in HIV disease. Rather it is recommended that adherence be measured in a multi-modal fashion, including self-report, capacity-based measures (e.g., MMR-R), behavioral monitoring, and manifest measures (e.g., pharmacy refills, viremia). In this way, online pharmacy INS tasks like the TOPS might be viewed as type of capacity measure of medication management, which would therefore relate to other ways of measuring medication adherence (e.g., self-report, MMT-R). Further, this effect may be amplified in HIV+ individuals with low health literacy, partially due to the fact that they are more likely to misunderstand medication instructions and miss doses or even overdose (Wolf et al., 2007). Indeed, previous studies have consistently shown a robust relationship between lower reading ability, numeral literacy and poor ART adherence (Kalichman et al., 2008b; Osborn et al., 2010; Waite et al., 2008; Waldrop- Valverde et al., 2010). Other consistent predictors of ART adherence include HIV symptoms, shame and stigma (e.g., Konkle-Parker et al., 2008), depression (Springer et al., 2012), social support (Sandelowski et al., 2009), alcohol and substance use (e.g., Azar et al., 2010), diet and exercise habits (Pellowski & Kalichman, 2016).

Reflecting upon this literature review, the current study aims to examine whether health literacy modulates the effects of HIV on pharmacy INS speed and accuracy. Based on the results of studies mentioned above, I hypothesize that the effects of HIV on pharmacy INS speed and accuracy will be larger among persons with lower health literacy. Additionally, this study sought to evaluate whether health literacy also modulates the relationship between pharmacy INS speed and accuracy and medication management among HIV+ individuals. I hypothesize that lower accuracy, higher errors, and slower speed on a measure of pharmacy INS will be associated with lower scores on performance-based medication management tasks, lower self-efficacy for managing medications in daily life, and poorer self-reported adherence in HIV+ individuals, independent of demographics, psychiatric factors, medical history, and neurocognitive performance. Further, this relationship between pharmacy INS performance and medication management will be larger among HIV+ persons with lower health literacy.

Method

Participants

This study used retrospective data from 217 participants enrolled in an NIH-funded study on memory in older adults with HIV disease as originally reported in Woods et al. (2020). Participants aged 50 and older who were recruited via flyers, word-of-mouth, and informational talks from greater San Diego county, including community-based organizations, infectious disease clinics, the general community, and cohort studies at the University of California San Diego (UCSD) HIV Neurobehavioral Research Program (HNRP). Adults 50 and older were the focus of the parent study, which examined the benefits of supporting various memory processes. The older age range is nevertheless highly relevant to the current study because HIV+ online pharmacy users tend to be older (Guthrie et al., 2010, Marzolini et al., 2011) and have more difficulty using online resources (Bastida et al., 2017), which may make them more vulnerable to difficulties with performance on online pharmacy tasks.

Participants received a small monetary incentive for their participation of the 3-4-hour test battery. Recruitment and procedures were reviewed and approved by the UCSD Institutional Review Board as well as the Institutional Review Board at University of Houston. HIV serostatus was confirmed with Medmira rapid tests. Exclusion criteria included a prior diagnosis of any of the following: (1) severe psychiatric disorder (e.g., schizophrenia); (2) neuromedical condition involving an active central nervous system opportunistic infection; (3) seizure disorder; (4) head injury with loss of consciousness for more than 30 minutes (n=2) ; (5) stroke with neurological sequelae; or (6) presence of a non-HAD neurodegenerative disorder. Individuals were also excluded if they had estimated verbal IQ scores < 70 (n=2), current substance dependence or tested positive on a breathalyzer or urine toxicology screen for illicit drugs (except marijuana) on the day of testing (n=2). Seventy-seven of the 211 otherwise eligible participants (36%) were excluded from these analyses, including 7 participants who did not attend the second study visit at which the task was given, 42 participants who did not complete the task due to time limitations, technical administration errors, or task refusal, 23 participants who had already participated in the task previously and 5 participants who did not have cognitive variables available. Thus, the final analyzable sample was 134 participants, which included 98 HIV+ persons and 36 HIV- persons whose demographic, psychiatric, neurocognitive, and medical characteristics are shown in Table 1. Of note, excluded participants did not differ on any demographic, disease, cognitive, or psychiatric characteristic from the analyzable sample (ps > .10), except for having a slightly lower rate of lifetime substance use disorders (p=.027). In the final sample, the HIV+ group included a higher proportion of men and persons with lifetime histories of depression and anxiety (ps<.05). The HIV+ and HIV- study groups did not differ from one another on any other variable listed in Table 1 (ps>.05).

Materials and Procedure

All participants provided written, informed consent prior to completing an IRB-approved medical, psychiatric, and neuropsychological research evaluation for which they received nominal financial compensation. The assessments were conducted in a quiet, private room at the HNRP.

eHealth Pharmacy Internet Navigation Skills (INS)

Participants completed the Test of Online Pharmacy Skills (TOPS; Woods et al., 2016), which is an experimenter-controlled, web-based task developed in PHP and Javascript. In this task, participants are asked to manage mock medication prescriptions in a manner modeled after various commercial institutions (CVS, Rite Aid, etc.). Specifically, the TOPS website included five main sections (including login) and six sub-pages. Participants were asked to log-in using a mock identity provided by the experimenter (contained in a wallet that included a mock driver's license, credit cards, and insurance information) at the start of the assessment. Once the participant successfully logged in, they saw five different tabs in the navigation bar (i.e., Welcome, Prescription Management, Resources, Drug Information Center, and Logout). Participants were instructed to complete the following specific tasks in any order on the pharmacy website: (i) Submit a request to refill their prescription for the medication, Celetra, which was part of the MMT-R administered just prior to TOPS (see below); (ii) Make a request to fill a new prescription for a new medication, Parlenol. In doing so, they were asked to enter all necessary primary insurance information (from the insurance card in their mock wallet) in order to process the medication for in-store pick-up; (iii) Activate a reminder that would alert them via text message to a smartphone (an iPhone provided by the experimenter) when the new Parlenol prescription was available for pick-up; (iv) Enter the confirmation code received via text on the smartphone on the TOPS pharmacy website to complete the activation process; and (v) Check for possible drug interactions for their new Parlenol prescription. Participants were instructed to pay close attention to these possible drug interactions, because they might be asked to recall them after completion of the task. The task instructions were in front of participants at all times.

Raw data on participant actions (i.e., page loads and what triggered them) were stored in a MySQL database and later analyzed via a scoring script. Variables of interest included a total accuracy score, total errors, and total time to complete the task. The total score was generated from seven action steps from the 5 tasks mentioned above (Task ii was split into three action steps for scoring purposes including: (1) Fill prescription, (2) provide primary insurance information and (3) provide correct pick up location). Scores ranged from 2 to -1 (e.g. a score of 2 means action step was performed and *no* mistakes were made; a score of 1 means action step was performed but mistakes were made; a score of 0 means action step was *not* performed and *no* mistakes were made; a score of -1 means action step was *not* performed and mistakes were made). A seven-item total score was generated which ranged from -7 to 14. A total accuracy score was generated as well, which ranged from 0 to 8 (i.e. did they complete each of the 7 steps without errors and logged in without errors). A total error score was generated from summing up the following types of errors: (1) log-in errors; (2) errors in refill request (e.g. requesting "fill" instead or refilling the wrong medication); (3) errors in fill request (e.g. filling the wrong medication); (4) insurance information errors (e.g. not entering insurance); (5) pick up location errors (e.g. selecting pick up location as "home" instead of "store"; (6) errors in setting up reminder (e.g. activating reminder for wrong medication); (7) errors in confirmation code (e.g. confirmation code for wrong medication); (8) interaction errors (e.g. looking up interactions for wrong medication) and (9) extra errors (e.g. participant makes one of the errors mentioned above multiple times). Thus, a total error score ranged from 0 to 41. Total time was calculated as from the moment the participant sees the log in screen to the moment the participant notifies the examiner that they are finished.

Internet Use and Anxiety

Participants completed a brief self-report questionnaire regarding their Internet use habits, including whether they own (or have regular access to) a personal computer, how often and for what purposes they use the Internet (e.g., health activities), that was adapted from Woods et al. (2016). Participants were asked about the frequency and severity of any difficulties they experience using online pharmacy sites and completing health related tasks online. Participants also completed items from the Computer Anxiety Scale (CAS), which asks about general anxiety related to using computers and the Internet. For the purposes of this study, 3 CAS items (i.e. "How difficult is it for you to do basic computer functions?", "How anxious (or nervous) do you typically feel when using a computer?" and "How anxious did you feel using a computer to complete some of the tasks today?") were used with scores that ranged from 1 (not anxious/difficult) to 5 (extremely anxious/difficult). Additionally, participants completed the Health-Related Information Access and Trust (HRIAT) self-report questionnaire. This measure has 10 items on Internet use for health-related information (e.g. "I have used the Internet to find medical and health-related information"; responses were scored as "yes=1" or "no=0") (Benotsch, Kalichman & Weinhardt, 2004). A total raw score will be used for the purposes of this study which ranges from 0 to 10.

Health Literacy

Participants completed a brief battery of well-validated health literacy measures, including: (1) ***The Rapid Estimate of Adult Literacy in Medicine (REALM)***, which is a 66-item instrument used to assess an individual's capacity to recognize and pronounce health-related words (e.g., "pill" and "anemia") (Murphy et al., 1993). Scores range from 0 (no words read correctly) to 66 (all words read correctly), with scores 60 and below commonly used to indicate limited health literacy.; (2) The ***Newest Vital Sign (NVS)*** is a 6-item performance-based measure of health literacy (Weiss et al., 2005). The total score is derived by summing the correct answers about information contained on a nutrition label for ice cream, with a possible score range from 0 to 6. Sample items are "If you eat the entire container, how many calories will you eat?" and "Pretend you are allergic to the following substances: penicillin, peanuts, latex gloves, and bee stings. Is it safe for you to eat this ice cream?" Consistent with prior research in HIV (e.g., Kordovski et al., 2017), scores below 4 are considered as indicative of limited health literacy; (3) The ***3-BRIEF*** is a 3 item self-report measure used to detect inadequate health literacy (Chew et al., 2008). The three items are, "How often do you have someone (like a family member, friend, hospital/ clinic worker or caregiver) help you read hospital materials?", "How often do you have problems learning about your medical condition because of difficulty understanding written information?", and "How confident are you filling out forms by yourself?". Responses were scored on a scale from 0 (none of the time) to 4 (all of the time) for the first two items and from 0 (extremely) to 4 (not at all) for the third item. A score of the three items that was greater than or equal to 1 would be considered as indicative of limited health literacy (Kordovski et al., 2017). A continuous composite factor score will be developed by performing a principal component (PCA) data analytic tool in SPSS (version 25) software (Refer to *Data Analyses* section for further explanation of the use of this method for the purposes of this study).

Medication Management

The HIV+ participants completed four well-validated measures of medication management including: (1) The Medication Management Test-Revised (MMT-R; Heaton et al. 2004), which is a performance-based measure in which participants dispense medications and answer questions about a mock prescription regimen. The main component of the task is pill dispensing, whereby participants are given a prescription for several medications and asked to dispense the appropriate amount of pills for 1 day in a pill organizer. It is scored on a scale of 0 to 13, and higher scores indicate better performance. Due to a ceiling effect in our sample (median score = 13), continuous scores were transformed into a dichotomous pass/fail variable (i.e. score of 13 = pass, scores of <13 = fail); (2) the 24-item Memory for Medications scale from the Beliefs Related to Medications (BERMA) questionnaire (Mcdonald-Miszczak et al., 2004), which is a self-report measure that assesses one's perceptions of their ability to remember and follow a medication regimen. Sample items include: "I am good at remembering to take my medications" and "If I am put on the spot to remember why I am taking my medications, I know I will have difficulty doing it." All subscale items are rated on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), with several items being reversed so that higher sores indicate stronger self-efficacy for medication management. The possible range of scores ranges from 24 to 120. For purposes of this study, the total score was converted to a pass/fail variable (i.e. if score is ≥ 1 SD below the normative mean = fail, otherwise pass); (3) The visual analogue scale (VAS) is a type of rating system in which the respondent is presented with a line that visually represents a range of possible ratings or responses to a question (Wewers & Lowe, 1990). The respondent is instructed to place a mark at a point on the line that represents their rating or response. In HIV, the VAS is presented as a numerical scale of doses taken, anchored by 0% and 100% on either end of the line. Respondents are then asked to mark the line representing their medication adherence to for the past 30 days (Finitsis et al., 2016). A total raw score ranging from 0 to 100 was converted to a dichotomous pass/fail variable for the purposes of this study (i.e. score of ≥ 95 = pass, scores of < 95 = fail); and (4) AIDS Clinical Trials Group (ACTG) Adherence to Anti-HIV Medications (Chesney et al., 2000) is a self-report questionnaire in which participants provide the total number of pills they are prescribed and the number of doses that they missed in the past 4 days. Scores will be converted into an average adherence percentage (e.g. 100% indicating perfect adherence). Due to a ceiling effect in our sample (median score = 100), continuous scores were transformed into a dichotomous pass/fail variable (i.e. score of 100 = pass, scores of <100 = fail).

Neuropsychiatric evaluation

Neurocognition

All participants were administered a comprehensive neuropsychological test battery by certified research assistants. Eighty-one participants received the CogState (www.cogstate.com; Woods et al. 2017), 51 received the NIH toolbox (Casaletto et al. 2015) and 2 participants were missing neurocognitive data. Due to the fact that different test batteries were used, the data were summarized with z-scores based on the best available age-adjusted normative data and collapsed across studies. Further, participants who received the CogState did not differ from participants who received the NIH toolbox in any factor listed in Table 1.

Mood Disorders

Current (i.e., within the last 30 days) and lifetime diagnoses of major depressive and generalized anxiety disorders were determined using the Composite International Diagnostic Interview (CIDI version 2.128; World Health Organization, 1998). The CIDI is a semi-structured interview that was administered by certified research assistants and yields lifetime diagnoses of substance abuse and dependence according to the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 1994). For primary analyses, current and lifetime diagnoses of major depressive and generalized anxiety disorders were combined into a single "affective disorders" variable to help limit the number of highly related covariates in the statistical models. Participants also completed the Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1981) to assess current level of affective stress. The POMS is a 65-item, self-report measure of current mood states in which participants rate various adjectives (e.g., "unhappy") on a five-point Likert-type scale ranging from 0 ("*not at all*") to 4 ("*extremely*"). The Total Mood Disturbance Score, which ranges from 0 to 200, was used for this study, wherein higher values indicated greater affective distress.

Personality Traits

Personality traits were measured with the BFI-44 (John, Donahue & Kentle, 1991). The BFI-44 has suitable validity and psychometric properties (Soto & John, 2009), as well as high convergent validity with the NEO-FFI (John & Srivastava, 1999). The BFI consists of 44 items designed to measure the Big Five dimensions of personality: Agreeableness (e.g., *I see myself as someone who is considerate and kind to almost everyone*), Neuroticism (e.g., *I see myself as someone who is emotionally stable, not easily upset, reverse scored*), Conscientiousness (e.g., *I see myself as someone who is a reliable worker*), Extraversion (e.g., *I see myself as someone who is outgoing, sociable*), and Openness (e.g., *I see myself as someone who is curious about many different things*). Participants were asked to rate how well each of the characteristics applied to them on a 5-point scale ranging from 1 (*Disagree strongly*) to 5 (*Agree strongly*). Responses were averaged across 8-10 items corresponding to dimensions of each Big Five personality trait, to form the five scale scores.

Substance Use Disorders

Current (i.e., within the last 30 days) and lifetime diagnoses of substance use disorders were determined using the Composite International Diagnostic Interview (CIDI version 2.128; World Health Organization, 1998).

Medical evaluation

Participants underwent a brief medical evaluation led by a research nurse, which included a review of systems (nadir CD4 cells/μL), medications (e.g. ART), comorbidities (e.g., Hepatitis C virus [HCV] co-infection, urine toxicology, and a blood draw from which current CD4 cells/μL and HIV RNA were assessed.

Data Analytic Strategy

Prior to conducting the analyses, visual inspection and screening of the data was used to ensure accuracy and to identify outliers as well as any missing data (Van den Broeck, Cunningham, Eeckels & Herbst, 2005). Missing value, correlation, moderation and regression analyses were conducted using SPSS (version 25.0). Little's test failed to reject the null hypothesis ($\chi^2 = 0.197$, $p = .657$), which indicates that all data was missing completely at random (MCAR) (Little, 1988). Basic group demographic and clinical characteristics are displayed in Table 1.

The primary aim of the study is to examine the main and interactive effects of HIV status and health literacy in terms of performance on the TOPS (accuracy and speed).

A1H1: HIV status is significantly related to performance on eHealth pharmacy Internet navigation skill (TOPS task) speed and accuracy, such that HIV+ individuals will perform significantly worse on TOPS than HIV- individuals.

A1H2: The effects of HIV on eHealth pharmacy Internet navigation skill speed and accuracy will be larger among persons with lower health literacy.

Principal component (PCA) data analytic tool in SPSS (version 25) software was used in order to develop a health literacy composite score for subsequent moderation analyses. PCA is an exploratory data analytic approach, which captures a set of principle components that account for most variance across the different questionnaire items, thereby allowing for a potential reduction in the number of variables that need to be analyzed. Otherwise stated, PCA is a data reduction technique which can make the metrics measured more meaningful and help uncover the underlying structure of original variables by analyzing common/shared variance across variables (Osborne & Costello, 2005; Gorsuch, 1988). Factor loadings ≥ 0.40 will be considered significant for individual items (Floyd & Widaman, 1995) and eigenvalues ≥ 1.0 will be considered significant for a factor (Kaiser, 1960). In order to help determine the best number of components, the scree plot and parallel analysis were used to compare the components to simulated chance values (O'Connor, 2000; Glorfeld, 1995). Data were inspected prior to the analysis to ensure that the following assumptions are met: (1) univariate normality within the data must be observed; (2) each factor should at least be comprised of 3 variables; (3) the ratio of respondents to variables should be at a minimum 5:1; (4) the correlation (r) between the variables should be 0.30 or greater; (5) if data are missing, it should be in a random pattern; and (6) there should be an absence of multicollinearity and singularity (Yong & Pearce, 2013; Field, Miles & Field, 2012).

Next, to evaluate main and interactive effects of HIV status (independent variable) and the health literacy composite (proposed moderator), two hierarchical regression analyses were conducted; one for TOPS accuracy and one for TOPS speed (dependent variables). I tested the following assumptions of each model: causality, linearity, homogeneity of variance and measurement error. Overall, significance of the predictors was interpreted at $p < .05$. Covariates were entered in the first step of each model and were selected from the variables in Table 1 and Table 2 using a data-driven approach. I included all potential covariates that are associated with any two of the three variables in the model (i.e., HIV status, health literacy composite, and TOPS accuracy in the first model (or TOPS speed in the second model) at a critical alpha of 0.05. A power analysis conducted using the program *G*Power* (version 3.1.9.3; Faul, Erdfelder, Lang, & Buchner, 2009) revealed that the power was acceptable (0.95) to detect a medium effect size ($f_2 = 0.15$; Cohen, 1977) using a critical alpha of .05 with a sample size of at least 89 and up to 8 predictors. HIV status and the health literacy composite were then simultaneously entered in the second step of each model. Finally, the interaction of HIV status and the health literacy composite was added in the third step. Planned post-hoc simple slope analyses were conducted using the PROCESS module for SPSS (Hayes, 2013) to examine moderating effects of the health literacy composite on the association between HIV status and TOPS accuracy (or TOPS speed in the second model).

The secondary aim of the study is to examine the main and interactive effects of TOPS performance (accuracy and speed) and health literacy in terms of medication management in individuals with HIV. *A2H1: Lower accuracy and slower speed on a measure of eHealth pharmacy Internet navigation (TOPS task) is significantly related to lower performance on medication management tasks, self-efficacy for managing medications in daily life, and self-reported adherence in HIV.*

A2H2: The association between lower accuracy and slower speed on a measure of eHealth pharmacy Internet navigation and performance-based medication management tasks, self-efficacy for managing medications in daily life, and self-reported adherence in HIV+ individuals, will be larger among persons with lower health literacy.

A continuous medication management composite score (range 0-4) was developed from the sum of four dichotomous pass/fail variables created for each of the medication management measures: MMT-R, BERMA Memory for Medications, (ACTG) Adherence to Anti-HIV Medications and VAS. Refer to the *Methods* section for further explanation of the analyses involved in creating the pass/fail variables for each of the four measures for the purposes of this study.

Next, two hierarchical regression analyses were conducted within the HIV+ subset of sample to evaluate main and interactive effects of TOPS performance (independent variable; TOPS accuracy in model 1 and TOPS speed in model 2) and the health literacy composite (moderator), on the medication management composite (the dependent variable). I tested the following assumptions of each model: causality, linearity, homogeneity of variance and measurement error. Overall, significance of the predictors was interpreted at $p < 0.05$. Covariates were entered in the first step of each model and were selected from the variables in

Table 1 and Table 2 using a data-driven approach. I included all potential covariates that are associated with any two of the three variables in the model (i.e., TOPS accuracy in the first model (TOPS speed in the second model), health literacy composite and medication management composite at a critical alpha of 0.05. A power analysis conducted using the program *G*Power* (version 3.1.9.3; Faul, Erdfelder, Lang, & Buchner, 2009) revealed that the power was acceptable (0.95) to detect a medium effect size (f_2 = 0.15; Cohen, 1977) using a critical alpha of .05 with a sample size of at least 89 and up to 7 predictors. TOPS accuracy (TOPS speed in the second model) and the health literacy composite were then simultaneously entered in the second step of the model. Finally, the interaction of TOPS accuracy (TOPS speed in the second model) and the health literacy composite was added in the third step. Planned post-hoc simple slope analyses were conducted using the PROCESS module for SPSS (Hayes, 2013) to examine interaction effects of the health literacy composite on the association between TOPS performance and medication management in individuals with HIV.

Results

Factor Structure of the Health Literacy Composite

Examination of the data suggested that most assumptions were met. Data were verified for normality (Assumption 1) and all components (i.e., items within each measure) were comprised of comprised of at least 3 variables (Assumption 2). Data were analyzed on a total of 3 total scores; our sample of 134 individuals satisfies the recommended minimum 5:1 ratio of respondents to variables (Assumption 3). Correlations between response items were 0.30 and higher (Assumption 4). It was noted that missing data (Assumption 5) were missing completely at random (MCAR), as tested by Little's MCAR Test, p = .584. Multicollinearity and singularity (Assumption 6) were assessed using the Variance Inflation Factor (VIF) for each measure; VIF values greater than 4 are considered of concern while values greater than 10 are considered unacceptable (Menard, 1995). VIF values ranged from 1.09 to 2.21 suggesting acceptable collinearity between items within a single measure. Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was 0.597, suggesting slightly adequate sampling and utility of the PCA, but still acceptable for the purposes of the analysis (Kaiser, 1974). Bartlett's test of sphericity was significant, approximate X_2 (3) = 34.7, $p<0.001$, suggesting sufficient relation between variables to detect an underlying component structure (Snedecor & Cochran, 1989). All three total scores loaded on to a single component in the PCA analysis, which accounted for 53.3% of the total variance. The oblique (non-orthogonal) rotation allowed for best interpretation of item loadings. Thus, the factor scores from this single component were used for further analyses.

TOPS Accuracy Moderation Model

All variables listed in Tables 1 and 2 were examined as possible covariates for both hierarchical regression analyses in the entire sample (n= 134).

Covariates for TOPS Accuracy Moderation Analysis.

Among the variables listed in Table 1, HIV status was significantly related to sex ($\chi_2[1]=7.70$, $p=.006$), computer anxiety ($\chi_2[1]=4.26$, $p=.039$), Big 5 Extraversion ($\chi_2[1]=4.71$, $p=.030$), and lifetime diagnosis of MDD ($\chi_2[1]=19.46$, $p<.001$), HCV ($\chi_2[1]=4.04$, $p=.045$), and GAD ($\chi_2[1]=4.67$, $p=.031$). Health literacy was significantly related to education (t=5.13, $p<.001$), ethnicity ($\chi_2[1]=13.4$, $p<.001$), computer anxiety ($\chi_2[1]=16.1$, $p<.001$), Big 5

Openness (t=2.71, p=.008), daily online use (χ^2[1]=28.0, p<.001), pharmacy use (χ^2[1]=5.60, p=.018) and neurocognition (t=3.58, p<.001). Finally, TOPS accuracy was significantly related to education (t= 3.66, p<.001), ethnicity (χ^2[1]=5.90, p=.015), neurocognition (t=3.07, p=.003), computer anxiety (χ^2[1]=14.4, p<.001), daily online use (χ^2[1]=14.8, p<.001), and online pharmacy use (χ^2[1]=17.3, p<.001). Thus, the following six potential covariates were related to at least two of the three primary variables and were included in the TOPS accuracy moderation model: education, ethnicity, computer anxiety, neurocognition, daily online use and pharmacy use.

TOPS Accuracy Moderation Analysis.

In the TOPS Accuracy model (see Table 3), the six covariates entered in the first step accounted for a significant amount of variance (R^2 Adjusted= 0.244, F(6,117) = 7.617, p<.001). Among those covariates, online pharmacy use (p=.004), computer anxiety (p=.024) and education (p=.064) were the only significant contributors. The entry of HIV and health literacy at step two did not account for more variance in the outcome (ΔR^2=.028, ΔF(2,115)=2.32, p=.103). Likewise, entry of the interaction term between HIV and health literacy at step three did not account for more variance in TOPS Accuracy (ΔR^2=.002, ΔF(1,114)=.287, p=.593).

TOPS Speed Moderation Model

Covariates for TOPS Speed Moderation Model

Among the variables listed in Table 1, TOPS speed was only associated with neurocognition (t=-3.63, p<. 001). Considering the covariate analyses reported above for HIV and health literacy, only neurocognition and computer anxiety met our a priori covariate inclusion criteria of being associated with two of the three variables in the model (all ps < .05). Thus, only these two variables were included in the TOPS speed model as covariates.

TOPS Speed Moderation Analysis

In the TOPS Speed model (see Table 4), the two covariates entered in the first step accounted for a significant amount of variance (R^2 Adjusted= 0.042, F(2,121)=3.725, p=.027) with neurocognition being the only significant contributor (p =.020). The entry of HIV and health literacy at step two accounted for significantly more variance in the outcome (ΔR^2=.064, ΔF(2,119)=4.35, p=.015), which was exclusively attributable to the contribution of health literacy (p=.004). Entry of the interaction term for HIV and health literacy at step three did not account for more variance in TOPS Speed (ΔR^2=.002, ΔF(1,118)=0.268, p=.606).

Medication Management Moderation Model (TOPS Accuracy)

All variables listed in Tables 1 and 2 were examined as possible covariates for both hierarchical regression analyses within the HIV+ subset of the sample (n=98).

Covariates for Medication Management Moderation Model (TOPS Accuracy)

Among the variables listed in Table 1, TOPS accuracy was significantly related to years of education (*t*=2.38, *p*=.019), ethnicity (χ^2[1]=7.76, *p*=.005), computer anxiety (χ^2[1]=7.06, *p*=.007), neurocognition (t=2.38, *p*=.020), daily online use (χ^2[1]=10.8, *p*=.001) and pharmacy use (χ^2[1]=13.6, *p*<.001) in the HIV+ subsample. Health literacy was significantly related to years of education (*t*=3.68, *p*<.001), ethnicity (χ^2[1]=10.0, *p*=.002), computer anxiety (χ^2[1]=12.6, *p*<.001), neurocognition (t=2.56, *p*=.012) and daily online use (χ^2[1]=22.4, *p*<.001). Lastly, medication management was related to computer anxiety (χ^2[1]=3.96, *p*=.047), neurocognition (t=2.58, *p*=.012) and daily online use (χ^2[1]=5.09, *p*=.024). Thus, the following five potential covariates were related to at least two of the three primary variables and were included in the moderation model using TOPS accuracy as the predictor variable: years of education, ethnicity, computer anxiety, daily online use and neurocognition.

Medication Management Moderation Analysis (TOPS Accuracy)

In the medication management model with TOPS accuracy as a predictor (see Table 5), the 5 covariates entered in the first step did not account for a significant amount of variance (R^2 Adjusted=.040, F (5,87)=1.76, *p*=.129). The entry of TOPS accuracy and health literacy in step two accounted for significantly more variance in the outcome (ΔR^2=.065, ΔF(2,85) =3.26, *p*=.043), which was primarily attributable to health literacy (*p*=.042). Entry of the interaction term between TOPS accuracy and health literacy at step three did not account for more variance in medication management (ΔR^2=.012, ΔF(1,84) =1.25, *p*=.267).

Medication Management Moderation Model (TOPS Speed)

Covariates for Medication Management Moderation Model (TOPS Speed)

Among the variables listed in Table 1, TOPS speed was only associated with neurocognition in the HIV+ subsample (t=-3.10, p=.003). Considering the covariate analyses reported above for medication management and health literacy, only computer anxiety, online daily use and neurocognition met our a priori covariate inclusion criteria of being associated with two of the three variables in the model (all ps <.05). Thus, only these two variables were included as covariates in the moderation model using TOPS speed as the predictor variable.

Medication Management Moderation Analysis (TOPS Speed)

In the medication management model with TOPS speed as a predictor (see Table 6), the 3 covariates entered in the first step accounted for a significant amount of variance (R^2 Adjusted=.057, F(3,89)=2.86, p=.041), which was primarily attributable to a trend level contribution of neurocognition (p=.052). The entry of TOPS speed and health literacy in step two did not account for more variance in the outcome (ΔR^2 = .050, $\Delta F(2, 87)$ = 2.54, p=.085), but there was a significant individual contribution of health literacy (p = .027). Entry of the interaction term between TOPS speed and health literacy at step three did not account for more variance in medication management (ΔR^2 = .000, $\Delta F(1, 86)$ = 0.02, p=.882).

Discussion

The literature suggested that INS might be an important component of successful online pharmacy use in persons living with HIV disease, which prior research showed may be affected by a multitude of factors, including education, cognition, Internet use frequency, and health literacy (Woods et al., 2016). Contrary to my prediction, HIV status was not related to speed or accuracy performance on the pharmacy INS task used in this study (i.e., TOPS) . Of note, these null results were produced in a relatively small sample (n=134) using a hierarchical regression analysis that included covariates (i.e. race/ethnicity, education, computer anxiety, daily internet use, online pharmacy use and neurocognition) and were accompanied by small effect sizes. These null results are only partially in line with research from Woods et al. (2016), which is the only other study available to date that examined effects of HIV disease on pharmacy INS performance. Commensurate with the results from the current study, their three study groups (HIV-, HAND-, HAND+) did not differ in TOPS error rates or time to completion, and the accompanying effect sizes for those analyses were also small. However, contrasting the null findings from the current study, the HAND+ group (n=19) from the Woods et al. (2016) study demonstrated significant, large effect size differences in TOPS accuracy relative to the other two study groups.

There are several possible reasons why the results of this study diverged from those of Woods et al. (2016). First, it is possible that the original finding was unstable and could not be replicated (Open Science Collaboration, 2015) in this slightly larger sample, which used the same TOPS measure. One argument against that interpretation is that Woods et al used a 3-group designed to specifically examine HAND, which was diagnosed with a well-validated clinical battery, whereas the current study collapsed all HIV participants and used a mixed, computerized screening battery that may have decreased the signal-to-noise ratio of this study by omitting critical domains of interest (e.g., executive functions). Of note, the current study did find a small but notable effect of HAND (d=.31, post-hoc) on TOPS accuracy, which supports the idea that the current study may not have been optimally designed or powered to detect HAND effects.

Another potential important interpretive difference is that the current study was focused on older adults (mean age=57.6 yrs), whereas Woods et al. (2016) included participants across the lifespan who had lower mean age (47.3 yrs). Older age has been shown to be a robust predictor of worse performance (e.g. speed, accuracy) on performance-based Internet search tasks (Chevalier et al., 2015; Laberge & Scialfa, 2005; Czaja, Sharit, Ownby, Roth, & Nair, 2001; Woods et al., 2019). Nevertheless, there is also evidence of a significant survival bias that has led to considerable heterogeneity in older HIV+ adults (Centers for Disease Control and Prevention [CDC], 2010). Thus, although neither study found effects of age, the lack of a younger control group is a limitation of this study and thus I cannot rule out that age may be a contributing factor, which may also account for the null results of HAND in this study. Indeed, older adults may have particular difficulties navigating online health tasks (Czaja et al., 2001; Woods et al., 2019), which may dampen the ability to detect disease effects in older samples. Future studies may look at possible interactive effects of HIV and age on health-related INS.

It was also plausible that health literacy might modulate the effects of HIV on TOPS performance (e.g., Woods & Sullivan, 2019). However, results from the current study showed that health literacy did not moderate the relationship between HIV and TOPS accuracy or speed. This finding provides evidence against the hypothesis that HIV and health literacy have a synergistic relationship in affecting INS performance. Instead these data suggest that low health literacy may play an independent role in health-related INS, such as TOPS performance (Agree et al., 2015; Neter & Brainin, 2017; Woods et al., 2016). In fact, results from hierarchical regression models show that health literacy was an independent predictor of TOPS speed. The relationship between health literacy and TOPS accuracy fell at a trend level, which may indicate that this study was limited in power to detect the association between online pharmacy accuracy and health literacy. Notably, univariable analyses between health literacy and TOPS accuracy yielded a slightly larger effect size (medium effect size; r=.40, p= <.001) than the univariable analyses between health literacy and TOPS speed (medium effect size; r=-.36, p= <.001). One possible explanation for this pattern of results is that the TOPS accuracy model included more covariates than the TOPS speed model, which as a result limit the power of detecting a main effect of health literacy on TOPS accuracy.

These findings partially map onto those from Woods et al. (2016), who used the same TOPS measure as the current study and found a significant relationship, with medium to large effect sizes, between TOPS accuracy and health literacy. The other two studies published to date on the relationship between health literacy and INS also show a significant relationship between the online navigation task accuracy and health literacy (Agree et al., 2015; Neter & Brainin, 2017). However, none of the previous studies reported on the relationship between INS task speed and health literacy. Thus, this study extends previous findings with preliminary evidence of the association between health literacy and TOPS speed performance. Interestingly, it may also be the case that there was a time/accuracy trade-off in the studies published to date (see Woods et al., 2019 for review), such that slower time to completion may be contributing to the relationship between online navigation task performance and health literacy. For example, Neter & Brainin (2017) included a time limit for their tasks, such that participants were offered assistance once the time limit for task completion elapsed. The researchers evaluated the amount of assistance given, which contributed to the medium sized relationship they reported between perceived electronic health literacy and performance on search tasks that were designed to measure different components of electronic health literacy. Likewise, Agree et al (2015) reported that the search time for their online search task was limited to 15 minutes and the authors concluded that that participants may have been more successful in their online health seeking if they were given more time to search online. Based on the current data, it is possible that low health literacy may adversely impact an individual's ability to quickly and efficiently navigate online platforms over and above the minimal effects of HIV infection. Future work should further explore this association to help delineate the impact of low health literacy on successful TOPS performance in the context of both speed and accuracy. For example, future studies may consider using an accuracy residual score in order to delineate the effect of accuracy performance from speed. In addition, a diffusion model analysis may be used to calculate the boundary separation (*a*; how "sure" a person needs to be before committing to a response, or their speed–accuracy trade-off setting) (see Voss & Voss, 2007).

Despite the null primary findings in the full sample, there are several notable covariates worth briefly discussing since so little is known about the correlates of pharmacy INS. Expectedly, education and computer-based anxiety were independently associated with TOPS accuracy, which is consistent with extant literature showing medium effect sizes for the association between INS accuracy and more years of education in clinical populations (e.g., Woods et al., 2016; Goverover et al., 2016), as well as INS task accuracy being related to both state and trait computer-related anxiety (Woods et al., 2016, 2017). Of note, these findings became null once health literacy was entered into the model suggesting that these associations may actually be a function of low health literacy. Future prospective studies would be needed to more carefully examine this question and might include a broader, multidimensional assessment of health literacy.

Intriguingly, the frequency of online pharmacy use was also associated with TOPS accuracy performance in the model, but daily internet use was not. In fact, online pharmacy use was the only covariate entered into the model that remained significant after the health literacy variable was added in. This is surprising considering that prior work (Agree et al., 2015; Woods et al., 2016) shows associations between increases in daily Internet use and better Internet search performance, as well as higher accuracy scores on TOPS and medical records tasks. In the current study, frequency of internet use was independently associated with TOPS accuracy performance at the univariate level, but this association became null as soon as both covariates were entered into the model. This finding suggests that the relationship between online pharmacy use and accuracy performance on TOPS washed out the effect of general daily internet use. Future work may consider looking at the potential mediating role of online pharmacy use on the relationship between other factors (e.g. frequency of internet use) and TOPS performance. Moreover, it would be interesting to examine this construct at a deeper level to gauge how much experience with online pharmacy use is enough to make a difference in performance on online pharmacy tasks.

In Aim 2, this study sought to evaluate whether TOPS performance is related to medication management in persons living with HIV disease, and whether health literacy would moderate this relationship. The only study published on the topic to date showed that TOPS accuracy was significantly correlated with MMT-R performance and viremia (a biomarker of non-adherence) in persons with HIV (Woods et al., 2016). However, both of these measures are very limited in their capacity for measuring medication adherence and do not control for confounds (e.g., ART resistance). To my knowledge, this study is the first to date to use an online pharmacy INS task (i.e. TOPS) as a type of capacity measure of medication management and examine its association with a composite score comprised of four well-validated measures of medication management in HIV. Yet the results show that neither TOPS accuracy, nor speed, performance was associated with medication management among HIV+ participants, and health literacy did not moderate this relation in either model.

One possible reason for these null findings is that TOPS performance may not be an effective predictor of medication adherence in HIV. Some arguments against that interpretation are that there was limited variance in medication management to be explained, as only 2% of the sample had detectable HIV RNA (as compared to 15% of the sample from Woods et al., 2016) and many of the measures used here had major ceiling effects. It is plausible that the medication management measures used in this study (i.e. MMT-R, BERMA Memory for Medications, (ACTG) Adherence to Anti-HIV Medications and VAS) did not fully capture the complete picture medication management capacity, as this construct is multifaceted and complex and there is no gold standard for measurement. At the conceptual level, results from the current study show that TOPS performance is not related to medication management in persons living with HIV disease. However, univariable analyses provide evidence against this interpretation and further support the notion that the medication management composite used in this study failed to capture this capacity accurately. Specifically, TOPS accuracy was related to MMT-R (medium effect size; r=.33), which is comparable to the findings from Woods et al. (2016) who reported a similar medium effect size (r=.29) Thus, it would be advantageous for future work to measure medication adherence using pharmacy refills, behavioral monitoring, and directly observed therapy when examining the association between health-related INS and medication management in persons with HIV. Such work would provide a nuanced understanding for the role of online pharmacy INS tasks as a type of capacity measure of medication management.

Further, analyses showed that health literacy was independently associated with medication management in both models (i.e. moderation model with TOPS accuracy as the predictor and moderation model with TOPS speed as the predictor). These findings provide support towards a robust body of literature reporting a significant relationship between lower reading ability, numeral literacy and poor ART adherence (Wolf et al., 2007; Kalichman et al., 2008b; Osborn et al., 2010; Waite et al., 2008; Waldrop-Valverde et al., 2010). Among HIV+ individuals, suboptimal health literacy is common (Kalichman & Rompa, 2000) and is consistently associated with lower disease prevention and treatment knowledge, higher rates of non-adherence, and lower perceived self-efficacy for medication management and health behaviors (see Reynolds, Smoller, Allen & Nicolas, 2019 for review). The overarching results from this study show that poor health literacy adversely affects an individual's ability to successfully and efficiently navigate online pharmacy tasks and has downstream effects on medication management in individuals with HIV.

There are multiple limitations of the current study that are important to consider. First, the present study utilized a cross-sectional design and therefore causal inferences cannot be isolated. It is possible that suboptimal health literacy contributes to poor TOPS performance and leads to worse medication management among individuals with HIV. Future research is needed using a prospective research design to clarify the complex systems that dictate the interplay between HAND status, health literacy and functional outcomes such as TOPS performance and medication management in this vulnerable population. Second, the current sample was largely comprised of older, white, fairly well-educated men from an urban setting. Thus, the external validity and generalizability of findings to other aspects of online health behaviors and persons with different sociodemographic characteristics (e.g., HIV+ women, as well as younger, more diverse HIV+ adults with less years of education) remains to be determined. Future studied should examine the role of health literacy on other online tasks of everyday functioning including measures of online health care (e.g., provider and insurance searches), communication (e.g., email and social networking), transportation (e.g., planning a trip on a mass transit system), and household activities (e.g., shopping and banking) in persons living with HIV. Additionally, the restricted age range limited my ability to explore an effect of age, which would require a lifespan sample. Third, the self-report measures used in the health literacy composite were short, which may restrict the range of responses that a participant can give. Future studies should consider including a more extensive, well validated self-report measure of health literacy (e.g. The European health literacy survey (HLS-EU); Sorensen et al., 2015). Fourth, despite being powered to detect medium sized effects, this study was limited by several methodological factors. One such factor is the use of a mixed, computerized screening battery may have limited power to detect HAND effects and thus limited interpretations on the association between HIV status and TOPS performance. Another factor was the number of covariates included in the TOPS model, which limited the power of detecting a main effect of health literacy on TOPS accuracy, despite yielding a medium effect size in univariable comparisons. Finally, a few of the medication management tasks had ceiling effects, which may have limited the sensitivity of the medication management composite and did not accurately capture the complete picture medication management capacity in individuals with HIV.

Overall, the current work uniquely extends past research by evaluating the interaction between HIV and health literacy on functional outcomes, such as TOPS accuracy and speed. Further, this study evaluated the interaction between TOPS performance and health literacy on medication management in individuals with HIV. Results suggest that health literacy plays a major role in predicting both functional outcomes; online pharmacy use performance and medication management.

Table 1
Demographic and Clinical Information For HIV- and HIV+ Adults

Variable	HIV+ (n = 98)	HIV- (n = 36)	*p*
Age (years)	57.6 (6.4) (50-75)	58.8 (7.1) (50-73)	0.126
Gender (% men)	81.6	58.3	0.006
Handedness (% right)	90.8	86.1	0.430
Education (years)	14.0 (2.6) (7-20)	14.2 (2.8) (9-21)	0.626
Race/Ethnicity (%)			0.698
Caucasian	60.2	63.9	
African American	20.4	13.9	
Hispanic	17.3	13.9	
Other	2.1	8.3	
Sexual Orientation (%)			<.001
Heterosexual	24.5	74.3	
LGB	75.5	25.7	
Major Depressive Disorder (%)			<.001
Current	14.3	2.8	
Lifetime	72.4	30.6	
Generalized Anxiety Disorder (%)			0.031
Current	4.1	0.0	
Lifetime	21.4	5.6	
Substance Use Disorder (%)	73.5	63.9	0.279
Neurocognition Z score	-0.31 (0.72) (-2.81-1.61)	-0.08 (0.63) (-1.49-1.07)	0.108
Medical			
Hepatitis C Infection (HCV,%)	24.5	8.6	0.045
Estimated duration of infection (years) [a]	24.2 (17.0, 28.4) (1.0, 38.0)	--	--
Plasma HIV RNA (rnlog10) [a]	1.6 (1.3, 1.6) (0, 4)	--	--
Current CD4 count (cells/µL) [a]	583 (400, 784) (210, 1487)	--	--
Nadir CD4 count (cells/µL) [a]	113 (30, 251) (0, 764)	--	--
AIDS (%)	72.4	--	--
Antiretroviral therapy (% prescribed)	94.8	--	--
Big Five Personality			
Openness (of 50)	36.5 (5.1) (27-48)	36.7 (5.9) (25-50)	0.817
Conscientiousness (of 45)	33.5 (4.9) (21-45)	34.5 (4.9) (25-45)	0.299
Extraversion (of 40)	25.7 (5.3) (14-39)	28.1 (5.6) (18-40)	0.030
Agreeableness (of 45)	35.2 (4.8) (22-45)	36 (4.5) (27-45)	0.364
Neuroticism (of 40)	22.7 (5.9) (10-35)	20.3 (6.9) (8-35)	0.059

Note. Data represent *M* (*SD*) (Range) or valid population % values. HIV = Human Immunodeficiency Virus. CD4 = cluster of differentiation.
[a] Based on median, interquartile range (IQR) and range scores

Table 2

Health literacy, medication management, and computer use data in the study sample

Variable	HIV+ (n = 98)	HIV- (n = 36)	*p*
Health Literacy			
PCA Composite [a]	0.17 (-0.51, 0.62) (-6.00, 1.02)	0.37 (-0.40, 0.69) (-2.63, 1.02)	0.597
Newest Vital Sign (of 6) [a]	4 (4, 6) (0, 6)	4 (3,6) (1, 6)	0.836
Rapid Estimate of Adult Literacy in Medicine (of 66)[a]	65 (63, 66) (11, 66)	66 (64, 66) (56, 66)	0.175
3-BRIEF (of 8) [a]	0 (0, 2) (0, 8)	0 (0,1) (0, 8)	0.771
Medication Management [b]			
Composite score (of 4)[a]	3 (2,4) (0, 4)	--	--
Medication Management Test–Revised (of 13)[a]	13 (12, 13) (0, 13)	--	--
% Pass	63.9		
BERMA Memory for Medications (of 120)	75.8 (11.3) (46-100)	--	--
% Pass	69.5		
Visual Analog Scale (of 100)[a]	100 (96,100) (76, 100)	--	--
% Pass	80.6		
ACTG for Adherence to Anti-HIV Medications (of 100)[a]	100 (100, 100) (50, 100)	--	--
% Pass	92.9		
CAS Any Computer Anxiety (% yes)	43.6	23.5	0.039
Internet Use Daily (% of sample)	69.4	83.3	0.107
Internet Use for Pharmacy (% yes)	38.0	38.2	0.858

Note. Data represent *M* (*SD*) (Range) or valid population % values. HIV = Human Immunodeficiency Virus; BERMA = Beliefs Related to Medication Adherence; 3-BRIEF is a 3 item self-report measure used to detect inadequate health literacy; ACTG = AIDS Clinical Trials Group; CAS = Computer Anxiety Scale.

[a] Based on median, interquartile range (IQR) and range scores

Table 3

Test of Pharmacy Skills (TOPS) Accuracy Regression Model in the Full Study Sample (N=134)

	β	95% CI [LL,UL]	*SE*	*t*	*p*	sr_2	R_2 Change
Step 1							.281***
Race/Ethnicity[a]	.120	[-0.18, 1.22]	.352	1.47	.014	.02	
Education	.156	[-0.01, 0.26]	.066	1.87	.064	.03	
Neurocognition	.043	[-0.39, 0.65]	.263	0.51	.612	.001	
CAS Any Computer Anxiety (% yes)	-.199	[-1.60, -0.12]	.375	-2.30	.024	.03	
Internet Use Daily (% of sample)	.124	[-0.25, 1.46]	.434	1.40	.166	.01	
Internet Use for Pharmacy (% yes)	.249	[0.39, 1.98]	.402	2.95	.004	.06	
Step 2							.028
HIV Status	-.102	[-1.27, 0.28]	.392	-1.27	.208	.009	
Health Literacy	.179	[-0.03, 0.79]	.207	1.84	.068	.02	
Step 3							.002
HIV Status*Health Literacy	.104	[-0.65, 1.14]	.452	.539	0.593	.001	

Note. *** $p < .001$, ** $p < .01$, * $p < .05$. Ethnicity: 0 = White, 1 = Non-White; CAS = Computer Anxiety Scale; β represents standardized regression weights; LL and UL indicate the lower and upper limits of a confidence interval, respectively.

[a] Variable was coded dichotomously.

Table 4

Test of Pharmacy Skills (TOPS) Speed Regression Model in the Full Sample (N=134)

	β	95% CI [LL,UL]	*SE*	*t*	*p*	sr_2	R_2 Change
Step 1							.058*
Neurocognition	-.210	[-4.11, -0.36]	.947	-2.36	.020	.02	
CAS Any Computer Anxiety (% yes)	.092	[-1.24, 3.94]	1.31	1.03	.304	.01	
Step 2							.064*
HIV Status	-.013	[-3.11, 2.68]	1.46	-.15	.884	.0007	
Health Literacy	-.279	[-3.38, -0.65]	.688	-2.93	.004	.08	
Step 3							.002
HIV Status*Health Literacy	-.108	[-4.14, 2.43]	1.66	-.52	.606	.00002	

Note. *** $p < .001$, ** $p < .01$, * $p < .05$. HIV Status: 0 = HIV-, 1 = HIV+; CAS = Computer Anxiety Scale; Neurocognition = summarized with the Global Deficit Score (GDS); β represents standardized regression weights; LL and UL indicate the lower and upper limits of a confidence interval, respectively.

Table 5

Medication Management Regression Model for TOPS Accuracy in HIV+ Participants (n=98)

	β	95% CI [LL,UL]	*SE*	*t*	*p*	sr^2	R^2 Change
Step 1							.092
Race/Ethnicity[a]	.033	[-0.31, 0.43]	.188	.316	.753	.005	
Education	-.061	[-0.09, 0.05]	.036	-.571	.569	.003	
Neurocognition	.198	[-0.02, 0.52]	.133	1.88	.064	.003	
CAS Any Computer Anxiety (% yes)	-.119	[-0.58, 0.16]	.186	-1.11	.270	.02	
Internet Use Daily (% of sample)	.126	[-0.19, 0.67]	.217	1.11	.270	.02	
Step 2							.065*
TOPS Accuracy	.126	[-0.04, 0.15]	.047	1.10	.275	.02	
Health Literacy	.260	[0.01, 0.43]	.105	2.06	.042	.05	
Step 3							.012
TOPS Accuracy *Health Literacy	.166	[-0.04, 0.13]	.042	1.12	0.267	.02	

Note. *** p < .001, ** p < .01, * p < .05. Ethnicity: 0 = White, 1 = Non-White; TOPS = Test of Pharmacy Skills; CAS = Computer Anxiety Scale; β represents standardized regression weights*;* LL and UL indicate the lower and upper limits of a confidence interval, respectively.
[a] Variable was coded dichotomously.

Table 6

Medication Management Regression Model for TOPS Speed in HIV+ Participants (n=98)

	β	95% CI [LL,UL]	*SE*	*t*	*p*	sr^2	R^2 Change
Step 1							.088*
CAS Any Computer Anxiety (% yes)	-.118	[-0.57, 0.16]	.184	-.1.11	.268	.01	
Internet Use Daily (% of sample)	.113	[-0.19, 0.62]	.205	1.06	.294	.01	
Neurocognition	.203	[-0.00, 0.52]	.131	1.97	.052	.01	
Step 2							.050
TOPS Speed	.088	[-0.02, 0.04]	.013	.809	.420	.005	
Health Literacy	.281	[0.03, 0.44]	.104	2.25	.027	.06	
Step 3							.000
TOPS Speed *Health Literacy	-.030	[-0.01, 0.01]	.005	-.149	.882	.001	

Note. *** p < .001, ** p < .01, * p < .05; TOPS = Test of Pharmacy Skills*;* Neurocognition = summarized with the Global Deficit Score (GDS)*;* CAS = Computer Anxiety Scale; β represents standardized regression weights; LL and UL indicate the lower and upper limits of a confidence interval, respectively.

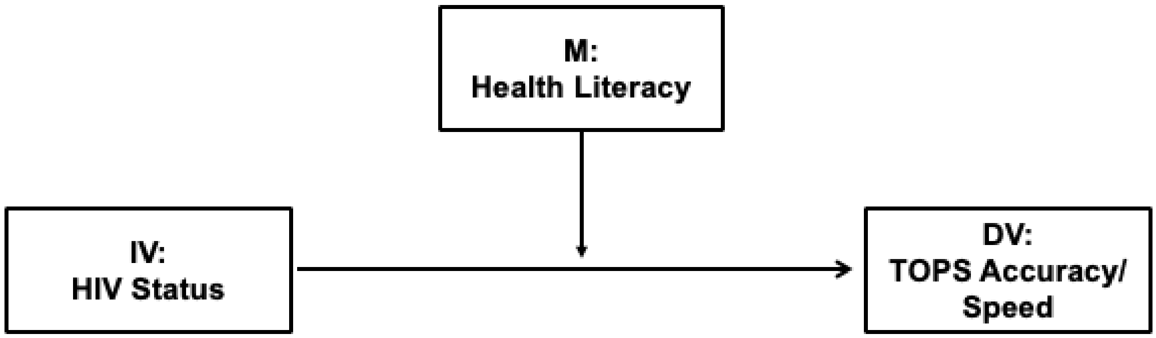

Figure 1. Conceptual Moderation Model showing the Interaction between HIV Status and Health Literacy on TOPS performance in the full sample.

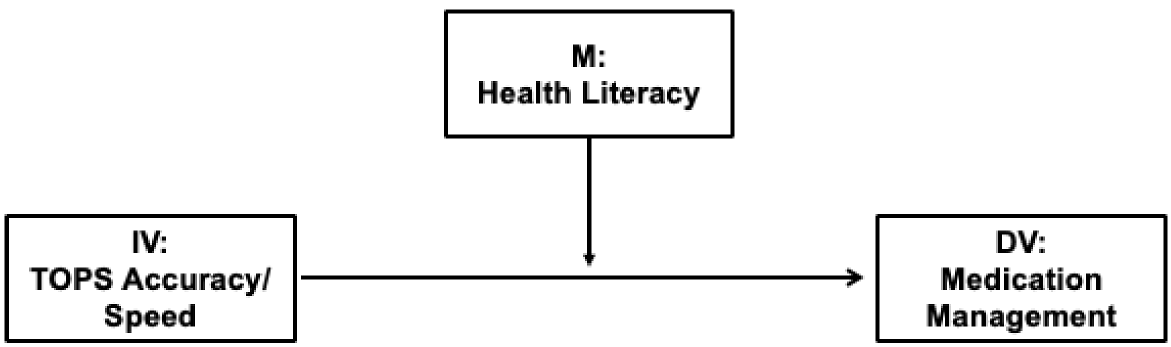

Figure 2. Conceptual Moderation Model showing the Interaction between TOPS performance and Health Literacy on Medication Management in HIV+ participants.

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