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Meta-Analysis on the Effect of Text Message Reminders for HIV-Related Compliance

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Abstract

For the treatment of HIV, compliance in regard to appointment attendance and medication usage is critical. Various methods have been attempted to increased HIV care compliance, and a method that has inspired many published studies is text message reminders. We conducted a meta-analysis of the literature from inception through May 2016 using the following databases: Pubmed, Embase, CINAHL, Web of Science, and Cochrane. Examples of terms used in the search included exploded versions of “HIV, “AIDS”, “cell phone”, “SMS”, “text message”, “reminder”. After abstract and manuscript review, articles were discussed with co-author and included based on consensus. We excluded qualitative analyses, observational studies without an intervention, and studies without a control or pre-intervention group. We used random-effects models to calculate odds ratios (OR) and standardized mean differences (SMD) for the text message intervention. Thirty-four unique studies were found and included in the meta-analysis. For the 7 articles relating to non-attendance, text message reminders significantly reduced the rates of non-attendance (OR, 0.66; 95% CI, 0.48–0.92; P= .01; I^2=52%). For the 20 articles on drug adherence, text message reminders significantly increased adherence (SMD, 0.87; 95% CI, 0.06–1.68; P=.04; I^2=99%). For the 11 articles with physiologic measures (CD4 count or viral load), text message reminders led to significant improvement (SMD, 1.53; 95% CI, 0.52–2.55; P=.003; I^2=99%). This meta-analysis reveals that text message reminders are a promising intervention that can be used to increase HIV care compliance when logistically feasible. Further study should focus on which populations benefit the most from this intervention, and successful implementers could create an established technological infrastructure for other clinics to adopt when seeking to boost compliance.

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Keywords

HIV; AIDS; compliance; text message; cell phones

INTRODUCTION

In the treatment of HIV infections, appointment attendance and medication adherence is critical to good control of this disease. Various methods have been attempted to increase compliance, including the use of text message reminders, which has had a number of published studies to evaluate its usefulness. Studies in urban HIV clinics in the U.S. have found that the vast majority of patients own mobile phones and would use them to enhance medication adherence (Miller & Himelhoch, 2013). Patients and providers both have noted some of the benefits of text message reminders, such as their ease of use and the ability to personalize messages and their timing (Baranoski et al., 2014).

In impoverished areas of the world, achieving HIV-related compliance can be even more difficult. At an established HIV program in Kibera, Nairobi, one of Africa's largest informal urban settlements, more than one third of patients were non-adherent to their treatment regimen (Unge et al., 2010). Therefore, looking to improve adherence rates, researchers have done research on text message reminders in resource-constrained settings. In studies in Peru (Curioso & Kurth, 2007; Menacho, Blas, Alva, & Roberto Orellana, 2013) and Botswana (Reid et al., 2014), patients viewed HIV-related health promotion via communication technology positively. Furthermore, in a 2010 study of an antiretroviral therapy clinic in Durban, South Africa, 81% of patients owned a cell phone, and 96% of respondents were willing to be contacted by the clinic via text messaging (Crankshaw et al., 2010). A survey of secondary school students in Mbarara, Uganda found that 61% of those who owned a cell phone said they would access a text messaging-based HIV prevention program if it were available (Mitchell, Bull, Kiwanuka, & Ybarra, 2011). In Asia, studies have found similar results. Across multiple HIV clinics in Vietnam, 85% of patients used mobile phones, 79% found cell phone reminders an effective adherence aid, and 64 % expressed willingness-to-use the service with an average willingness-to-pay of $2.50 per month (Tran & Houston, 2012). In a cross-sectional survey of 801 Chinese people living with HIV, 88% of the participants owned mobile phones and 80% felt daily text reminders to take medication would be helpful (Xiao et al., 2014).

Text message reminders have been effective in a number of fields unrelated to HIV care: antenatal and postnatal care (Watterson, Walsh, & Madeka, 2015), contraception (Halpern, Lopez, Grimes, Stockton, & Gallo, 2013), immunizations (Odone et al., 2015), breast cancer screening (Kerrison, Shukla, Cunningham, Oyebode, & Friedman, 2015), smoking cessation (Vodopivec-Jamsek, de Jongh, Gurol-Urganci, Atun, & Car, 2012), sunscreen use (Armstrong et al., 2009), and some asthma and diabetes outcomes (de Jongh, Gurol-Urganci, Vodopivec-Jamsek, Car, & Atun, 2012). For HIV care, a number of studies have accumulated that seek to quantify the benefit of text message reminders. Our current paper seeks to identify and amalgamate all HIV compliance-related text messaging studies – spanning a range of study types – into an up-to-date and comprehensive set of meta-

analyses. Our hypothesis was that text message reminders would improve compliance in all aspects of HIV care.

METHODS

No human participants were involved in this study and only previously published literature was included, thus the project was exempt from requirements for human subjects research review.

Search Strategy

We conducted a meta-analysis of the literature using the following databases from inception thru May 2016: PubMed (MEDLINE), EMBASE, CINAHL, Web of Science, and Cochrane. Studies in any language that investigated text message reminders for HIV care were available for inclusion. Terms used in the search included exploded versions of “HIV, “AIDS”, “cell phone”, “SMS”, “text message”, “reminder”. For example for PubMed, the search algorithm was “(HIV Infections[MeSH] OR HIV[MeSH] OR hiv[tiab] OR hiv-1[tiab] OR hiv-2*[tiab] OR hiv1[tiab] OR hiv2[tiab] OR hiv infect*[tiab] OR human immunodeficiency virus[tiab] OR human immune deficiency virus[tiab] OR human immunodeficiency virus[tiab] OR human immune-deficiency virus[tiab] OR (human immun*) OR (deficiency virus[tiab])) OR acquired immunodeficiency syndromes[tiab] OR acquired immune deficiency syndrome[tiab] OR acquired immunodeficiency syndrome[tiab] OR acquired immune-deficiency syndrome[tiab] OR (acquired immun*) OR (deficiency syndrome[tiab]) OR HIV[tiab] OR HIV/AIDS[tiab] OR HIV-infected[tiab] OR HIV[title] OR HIV/AIDS[title] OR HIV-infected[title]) AND (”Cellular Phone“[Mesh] OR telephone[tiab] OR phone[tiab] OR mobile[tiab] OR cellphone[tiab] OR ”cell phone"[tiab] OR sms[tiab] OR text*[ti] OR messag*[ti] OR remind*[ti]).” In order to capture any missed studies, we hand-searched the references from the discovered studies and reviews.

Study Selection

In our search for studies on text message reminders for HIV-related compliance, we excluded studies centered on qualitative measures; observations without an intervention; support groups or use of SMS messaging to connect with other patients or a physician; analyses without a control group or pre-intervention group; educational text messages; programmable medication reminder devices; texting for test result delivery; phone call interventions not in conjunction with text messaging. Prior to data analysis, we chose to include articles on text messaging via a pager because the intervention still consisted of a text reminder via a portable device. After abstract and manuscript review, all articles for potential inclusion were discussed amongst the co-authors and included based on consensus. Figure 1 summarizes the selection of articles used in this study.

Data Extraction

For each study, we extracted outcome data to calculate a standardized mean difference or odds ratio. When possible, we used intention-to-treat data. We classified the study focus into four categories: Appointment Non-Attendance, Medication Adherence, Physiologic Measures, and HIV Prevention (which was then divided into Appointment Non-Attendance

and Avoiding High-Risk Sexual Behavior). Points specific to the extraction of data from each study is included as a Supplemental Table.

Statistical Analyses

We generated meta-analytic estimates of intervention effect using random-effects models. Effect sizes were calculated as standardized mean difference (SMD) or odds ratios (OR). Analyses were performed using Review Manager (RevMan) version 5.2 software (Cochrane Collaboration). We measured heterogeneity for each outcome across studies using the I^2 test. When the data required to calculate a standard deviation (SD) were not included in an article, we requested it from the study's authors, and when information was not forthcoming, imputation of the mean SD of the group for that particular variable was utilized. Imputation of more than 2 SDs was not required for any analysis. When a study produced binary data (e.g. number who attended vs did not attend), the data was converted to a continuous percentage and the SD was estimated assuming a binomial distribution. An aggregate effect size was calculated for each group of articles. No subgroup analyses were planned a priori.

RESULTS

The results of the search strategy are shown in Figure 1 and all studies are characterized in Table 1. The search identified a total of 5,718 articles from all databases. Articles were systematically excluded: 1,338 duplicates, 4,196 articles with irrelevant titles, 150 off-topic articles based on review of the abstract or manuscript. This left 34 unique studies to be included in the meta-analysis. Seven articles contained data on "Appointment Non-Attendance," 20 articles on "Medication Adherence," 11 articles on "Physiologic Measures", 7 articles on "HIV Prevention" (5 with "Did Not Attend Rates" and 2 on "Avoidance of High-Risk Sexual Behavior"). Some studies contained data on multiple outcome measures and thus fit into two of the above categories for meta-analysis.

For the 7 articles relating to "Appointment Non-Attendance," 5 were RCTs and 2 were pre-post studies. Altogether, there were 1,608 experimental subjects and 1,607 control subjects (Figure 2). Overall, text message reminders significantly reduced the rates of non-attendance (OR, 0.66; 95% CI, 0.48–0.92; P= .01; I^2=52%; Figure 2). For the 20 articles on "Medication Adherence," 14 were RCTs and 6 were pre-post studies. Altogether, there were 1,844 experimental subjects and 1,731 control subjects (Figure 3). Overall, text message reminders significantly increased medication adherence (SMD, 0.87; 95% CI, 0.06–1.68; P=.04; I^2=99%; Figure 3). For the 11 articles with "Physiologic Measures," 7 were RCTs and 4 were pre-post studies. Altogether, there were 1,154 experimental subjects and 1,139 control subjects (Figure 4). Overall, text message reminders led to improvement in the physiologic measures (SMD, 1.53; 95% CI, 0.52–2.55; P=.003; I^2=99%; Figure 4). For the 5 articles relating to "HIV Prevention – Appointment Non-Attendance," 2 were RCTs and 3 were pre-post studies. Altogether, there were 3,129 experimental subjects and 3,095 control subjects. Overall, text message reminders significantly reduced the rates of non-attendance (OR, 0.63; 95% CI, 0.47–0.84; P= .002; I^2=83%; Figure 5). For the 2 articles relating to "HIV Prevention – Avoidance of Certain High-Risk Sexual Behavior," 1 was an RCT and 1 was a pre-post study. Altogether, there were 539 experimental subjects and 545 control

subjects. Overall, text message reminders did not significantly reduce the rates of high-risk sexual acts (OR, 0.66; 95% CI, 0.19–2.35; P= .52; I^2=86%; Figure 6).

DISCUSSION

This meta-analysis reveals that text message reminders are a valuable tool to increase HIV-related compliance. We found significant benefits in regard to non-attendance, medication adherence, and physiologic measures. For both of the HIV primary prevention meta-analyses, decreases in non-attendance and high-risk sexual behaviors were present (however, only the former was statistically significant).

Our findings regarding the effectiveness of text message reminders are consistent with the meta-analyses discussed in the Introduction showing increased compliance with text message reminders used in other healthcare settings. Our meta-analysis focused on all aspects of HIV care that have been studied in relation to text messaging, which includes studies beyond RCTs. Moreover, it has been updated with studies through mid-2016. One advantage we see in this study is that previous systematic reviews, while comprehensive in scope, did not involve statistical synthesis of the data and instead drew more subjective conclusions. For example, a 2013 systematic review on the use of mobile phone messaging for HIV infection prevention, treatment, and care and concluded that there was “limited evidence on the effectiveness of mobile phone messaging for HIV care” (van Velthoven, Brusamento, Majeed, & Car, 2013). With the inclusion of more recent published reports in this meta-analysis, it appears that there is sufficient evidence on the effectiveness of text messaging for HIV care.

One of the limitations of this meta-analysis is the high rates of heterogeneity within each analysis. This is likely secondary to the multiple types of studies included, the various different study populations, and the slightly different interventions (e.g. timing of text messages). To reduce the chance of type 1 error from multiple comparisons, we did not do further meta-analyses within subgroups. With the addition of more studies going forward, future analyses may limit their *a priori* hypotheses to specific populations or types of studies, and this would likely lower the high heterogeneity levels we found. Another limitation of this analysis is that it gave the same weight to an RCT as a non-RCT. We considered this as acceptable since we believed that it was outweighed by greater inclusivity and increasing the number of data points for analysis. In addition, the RCT studies tended to be more robust with larger sample sizes, so they naturally received more weight than a smaller non-RCT.

Given the improvements in compliance seen in this meta-analysis, the use of text messaging reminders should be pursued when feasible in HIV clinics. The populations in the analyzed studies varied significantly, and the future studies should delve deeper into who benefits the most and least from text message interventions within one population. Until further characterization is possible, it seems likely that any clinic with high rates of noncompliance with HIV care would benefit from text message reminders. With the near-ubiquity of mobile phones worldwide and now smartphones in the developed world, implementation of text message interventions is a natural next step in using technology for health maintenance, especially with younger patients, who typically feel the most comfortable with new

technology. In the near future, with the increasing prevalence of wearable devices, reminders via these devices may become alternatives to cell phone reminders.

Text message intervention studies have reported varying costs, on the scale of hundreds to thousands of dollars for initial set-up of a reminder system (van Velthoven et al., 2013). A 2014 study in South India determined the cost of implementing a text reminder system to be $1.27-$1.57 per patient per year (Rodrigues, Bogg, Shet, Kumar, & De Costa, 2014). However, once the texting system was instituted, maintenance costs could be as low as $0.005 per text message (Kunutsor et al., 2010). If systems are established on a large scale in a country, perhaps by a central health agency, costs for a new clinic to implement text message reminders would be minimal. Moreover, multiple websites advertise free services for setting up individual or group text reminders. However, concerns regarding HIPAA, confidentiality and other privacy concerns would need to be strongly considered before such services could be used, especially with sensitive information such as HIV status.

Conclusion

It appears that text message reminders are a promising intervention that should be used to increase HIV care compliance when feasible. Further study should focus on which populations benefit the most from this intervention, and adoption of this intervention would benefit from a central infrastructure created by an organization such as the government or other public health organization, thus enabling easier adoption of text message reminders in clinics with poor compliance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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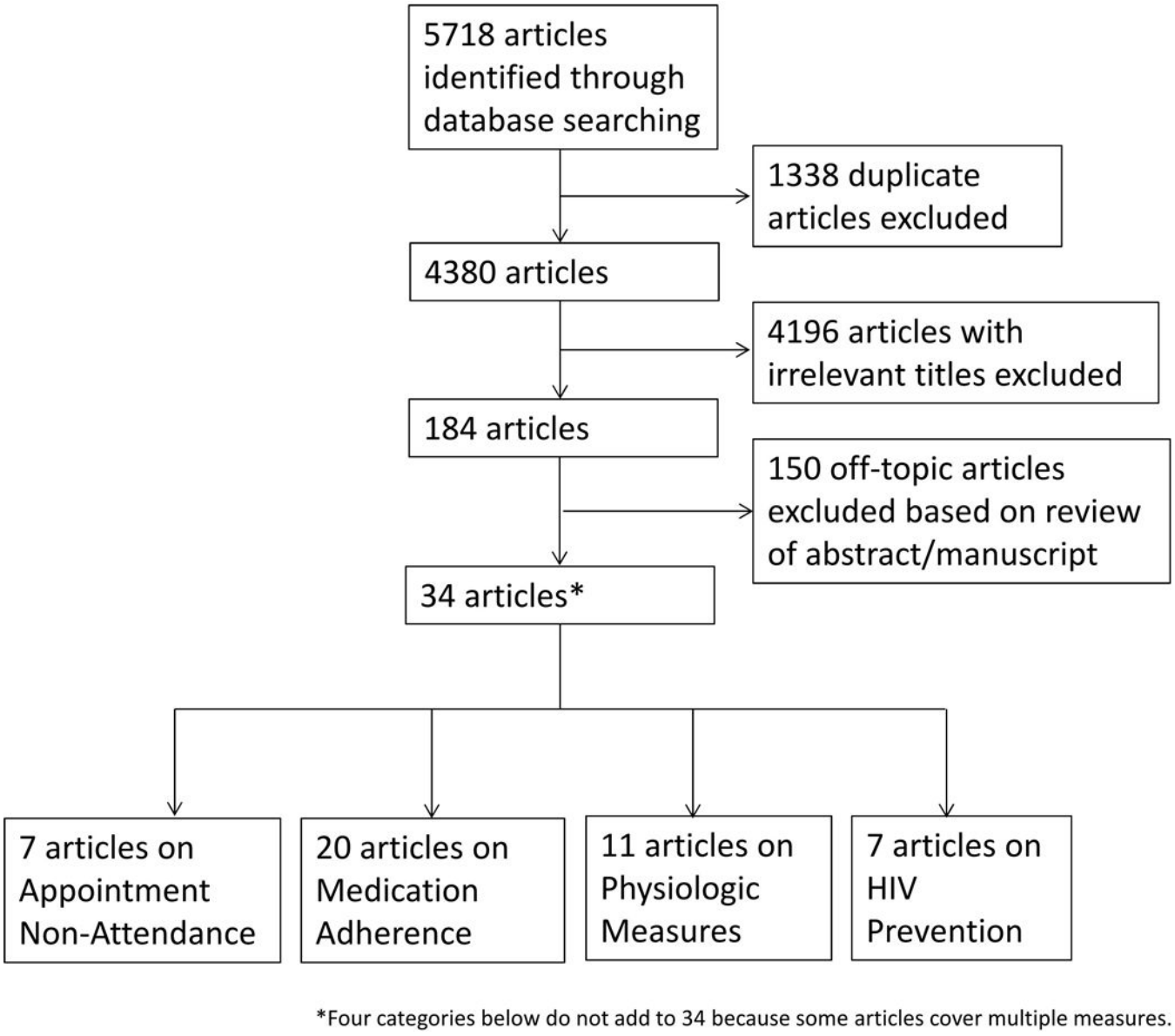

Figure 1.
Search protocol flow chart
*Four categories below do not add to 34 because some articles cover multiple measures.

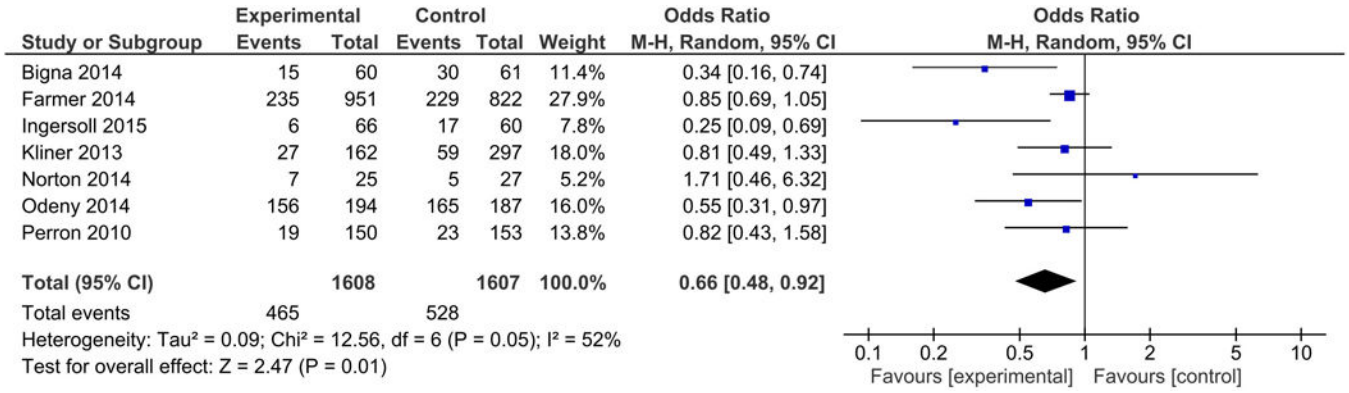

Figure 2.
Forest plot for the Appointment Non-Attendance Meta-Analysis

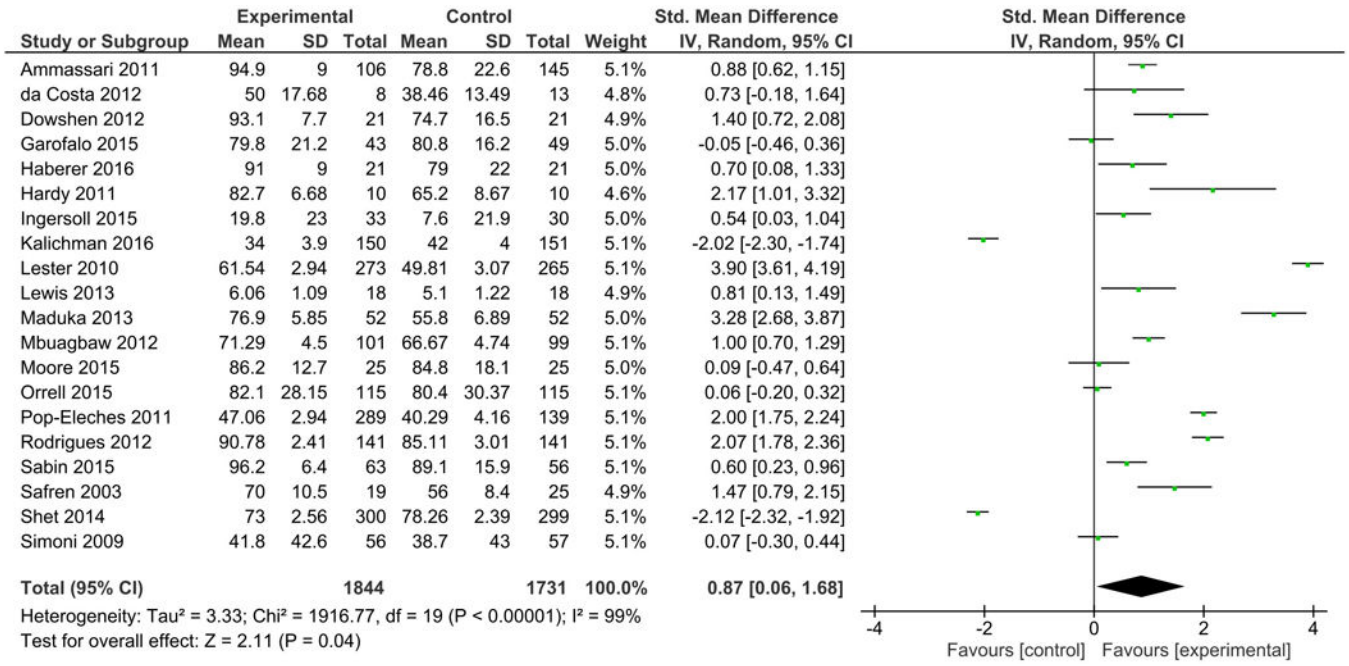

Figure 3.
Forest plot for the Medication Adherence Meta-Analysis

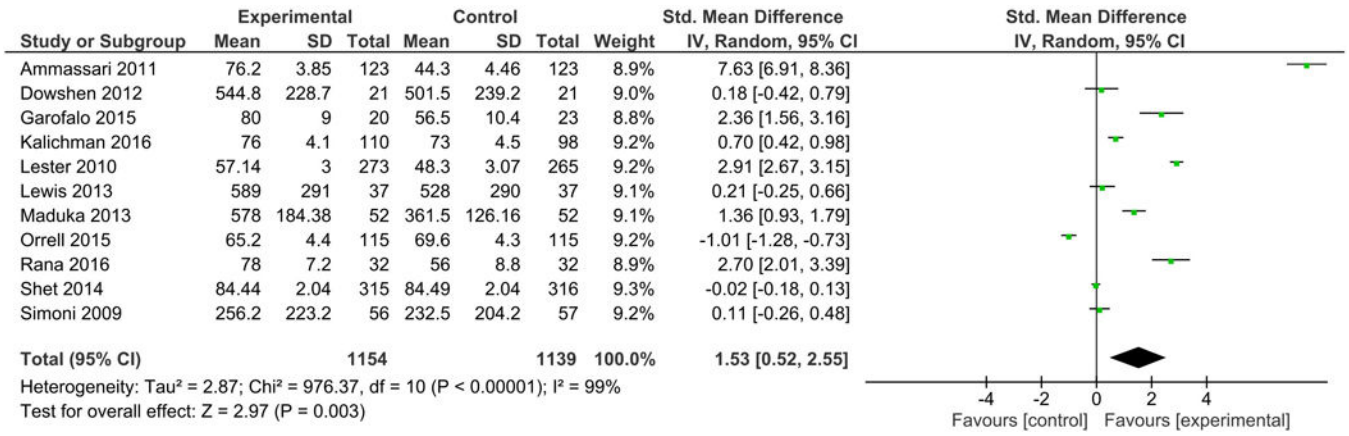

Figure 4.
Forest plot for the Physiologic Measures Meta-Analysis

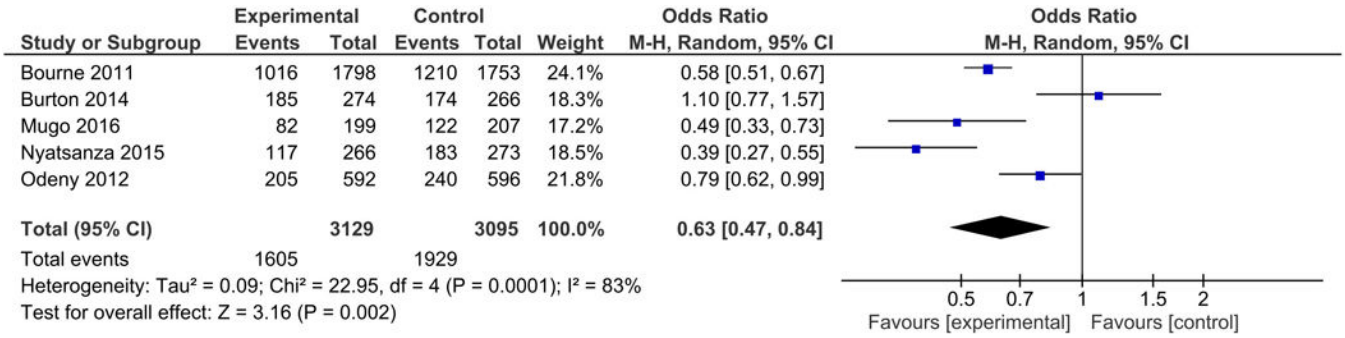

Figure 5.
Forest plot for the HIV Prevention – Appointment Non-Attendance

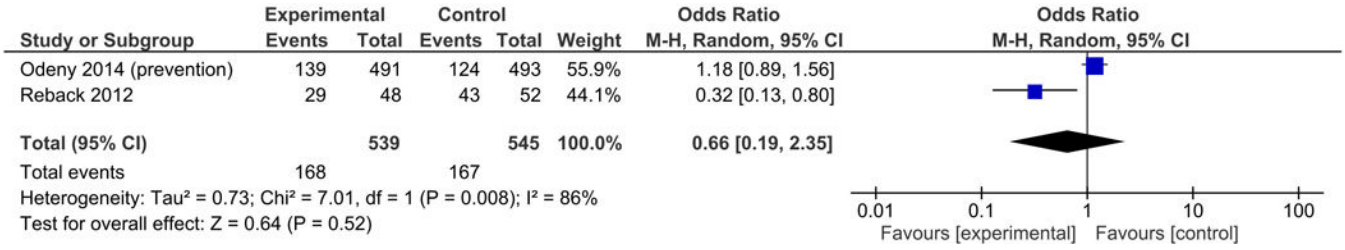

Figure 6.

Forest plot for the HIV Prevention – Avoidance of Certain High-Risk Sexual Behavior

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Table 1

Author	Year	Study Type	Location	Study Population (HIV-positive)	Study Duration	Intervention	Experimental #	Control #
Non-Attendance								
Bigna et al	2014	RCT	Cameroon	Carers of children with or exposed to HIV	1 appt	Text message	60	61
Farmer et al	2014	Pre-Post	London	Clinic patients	1 year	Text message	951	822
Ingersoll et al	2015	RCT	USA: VA	People with drug use & recent ART nonadherence	12 weeks	Text message	33	30
Kliner et al	2013	Pre-Post	Swaziland	Newly-diagnosed and obtaining CD4 results	1 appt	Text message	162	297
Norton et al	2014	RCT	USA: NC	Clinic patients	1 appt	Text message	25	27
Odeny et al	2014	RCT	Kenya	Pregnant women	1 appt	Text message	194	187
Perron et al	2010	RCT	Switzerland	Clinic patients	1 appt	Call ± text	150	153
Medication Adherence								
Ammassari et al	2011	Pre-Post	Italy	Adults with suboptimal adherence	9 months	Text message	106	145
da Costa et al	2012	RCT	Brazil	Brazilian women	4 months	Text message	8	13
Dowshen et al	2012	Pre-Post	USA: PA	Youths on ART with poor adherence	24 weeks	Text message	21	21
Garofalo et al	2015	RCT	USA: IL	Youths and young adults with poor adherence	6 months	Text message	43	49
Haberer et al	2016	RCT	Uganda	Individuals initiating ART	9 months	Text message	21	21
Hardy et al	2011	Pre-Post	USA: MA	Adults receiving HIV primary care	6 weeks	Text message	10	10
Ingersoll et al	2015	RCT	USA: VA	People with drug use & recent ART nonadherence	12 weeks	Text message	33	30
Kalichman	2016	RCT	USA: GA	Adults with poor adherence	12 months	Text message	150	151
Lester et al	2010	RCT	Kenya	Patients initiating ART	12 months	Text message	273	265
Lewis et al	2012	Pre-Post	USA	MSM aged ≥ 25	3 months	Text message	18	18
Maduka et al	2012	RCT	Nigeria	Patients with a history of non-adherence	4 months	Text + counseling	52	52
Mbuabaw et al	2012	RCT	Cameroon	Adults aged ≥ 21 on ART	6 months	Text message	101	99
Moore et al	2014	RCT	USA: CA	Patients with co-occurring bipolar disorder	30 days	Text message	25	25
Orrell et al	2015	RCT	South Africa	ART-naïve patients	48 weeks	Text message	115	115
Pop-Eleches et al	2011	RCT	Kenya	Adults who had initiated ART within 3 months	48 weeks	Text message	289	139
Rodrigues et al	2012	Pre-Post	India	Patients on ART	6 months	Pictorial text + call	141	141
Sabin et al	2015	RCT	China	Adults on ART	6 months	Text message	63	56
Safren et al	2010	RCT	USA: MA	Patients with poor adherence	2 weeks	Pager text message	19	25
Shet et al	2014	RCT	India	Adult, ART naïve patients	2 years	Pictorial text + call	300	299
Simoni et al	2009	RCT	USA: WA	Patients at a public HIV clinic	3 months	Pager text message	56	57

Author	Year	Study Type	Location	Study Population (HIV-positive)	Study Duration	Intervention	Experimental #	Control #
Physiologic Measures								
Ammassari et al	2011	Pre-Post	Italy	Adults with suboptimal adherence	9 months	Text message	123	123
Dowshen et al	2012	Pre-Post	USA: PA	Youths on ART with documented poor adherence	24 weeks	Text message	21	21
Garofalo et al	2015	RCT	USA: IL	Youths and young adults with poor adherence	6 months	Text message	20	23
Kalichman et al	2016	RCT	USA: GA	Adults with poor adherence	12 months	Text message	110	98
Lester et al	2010	RCT	Kenya	Adults initiating ART	12 months	Text message	273	265
Lewis et al	2012	Pre-Post	USA	MSM aged ≥ 25	3 months	Text message	37	37
Maduka et al	2012	RCT	Nigeria	Patients with a history of non-adherence	4 months	Text message	52	52
Orrell et al	2015	RCT	South Africa	ART-naïve patients	48 weeks	Text message	115	115
Rana et al	2016	Pre-Post	USA: RI	Adults with higher risk of loss-to-follow-up	6 months	Text message	32	32
Shet et al	2014	RCT	India	Adult, ART naïve patients	2 years	Pictorial text + call	315	316
Simoni et al	2009	RCT	USA: WA	Patients at a public HIV clinic	3 months	Pager text message	56	57
Prevention - Non-attendance								
Bourne et al	2011	Pre-Post	Australia	HIV-negative MSM categorized as high-risk	1 testing appt	Text message	1798	1753
Burton et al	2013	Pre-Post	UK	HIV-negative patients categorized as high-risk	1 testing appt	Text message	274	266
Mugo et al	2016	RCT	Kenya	HIV-negative patients	1 testing appt	Text + call	199	207
Nyatsanza et al	2015	Pre-Post	UK	HIV-negative patients categorized as high-risk	1 testing appt	Personalized text	266	273
Odeny et al	2012	RCT	Kenya	HIV-positive males with recent circumcisions	1 testing appt	Text message	592	596
Prevention - Avoiding High-Risk Behaviors								
Odeny et al	2014	RCT	Kenya	HIV-positive males with recent circumcisions	6 weeks	Text message	491	493
Reback et al	2012	Pre-Post	USA: CA	HIV-negative methamphetamine-using MSM	2 weeks	Text message	48	52