Sexual health interventions delivered to participants by mobile technology: a systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Background

The use of mobile technologies to prevent sexually transmitted infections (STIs) is recognized as a promising approach worldwide, however evidence has been inconclusive and the field has developed rapidly. With about 1 million new STIs a day globally, up-to-date evidence is urgently needed.

Objective

To assess the effectiveness of mobile health interventions delivered to participants for preventing STIs and promoting preventive behaviour.

Methods

We searched seven databases and reference lists of 49 related reviews (January 1990-February 2020) and contacted experts in the field. We included randomised controlled trials of mobile interventions delivered to adolescents and adults to prevent sexual transmission of STIs. We conducted meta-analyses and assessed risk of bias and certainty of evidence following Cochrane guidance.

Results

After double screening 6682 records, we included 22 trials into the systematic review and 20 into meta-analyses; 18 trials used text messages, three used smartphone applications and one used Facebook messages as delivery modes. The certainty of evidence regarding intervention effects on STI/HIV occurrence and adverse events was low or very low. There was moderate certainty of evidence that in the short/medium-term text messaging interventions had little or no effect on condom use (SMD 0.02, 95% CI -0.09 to 0.14, 9 trials), but increased STI/HIV-testing (OR 1.83, 95% CI 1.41 to 2.36, 7 trials); although not if the standard-of-care control already contained an active text messaging component (OR 1.00, 95% CI 0.68 to 1.47, 2 trials). Smartphone application messages also increased STI/HIV-testing (RR 1.40, 95% CI 1.22 to

1.60, subgroup analysis, 2 trials). The effects on other outcomes or of social media or blended interventions is uncertain due to low or very low certainty evidence.

Conclusions

Text messaging interventions probably increase STI/HIV-testing, but not condom use in the short/medium-term. Ongoing trials will report the effects on biological and other outcomes.

[299 words]

INTRODUCTION

Background

Among the biggest challenges within the field of sexual health are continuing high rates of sexually transmitted infections (STIs). Recent estimates of incident cases of the most frequent curable STIs (chlamydia, gonorrhoea, trichomoniasis and syphilis) amounted to a global total of 376 million infections in 2016, which translates to an average of approximately 1 million new infections each day[1]. Globally, sexual transmission is also the main transmission route of the human immunodeficiency virus (HIV). Although HIV incidence has recently declined compared to previous years, there were still 1.7 million new infections recorded globally in 2019[2].

Given the high burden of STIs in both high-income countries (HIC) and low- and middle-income countries (LMIC), researchers and governments in both settings have increasingly turned to mobile wireless technologies in search of new and cost-effective approaches for STI prevention[3] [4]. Mobile technologies used in public health and health service settings ('mHealth')[5] are appreciated for their "ease of use, broad reach and wide acceptance"[6].

Almost the entire world population (97%) lives within reach of a mobile cellular signal, and even in least developed countries (LDC) mobile cellular subscriptions have increased

drastically (2005-2019, from 5 to 75 per 100 inhabitants). There has also been an increase of active mobile broadband subscriptions per 100 inhabitants (2010-2019, from 12 to 83 worldwide, and 0 to 33 in LDC)[7].

The rapid adoption of mobile technology globally offers unique and varied opportunities within the field of global health in general, and sexual health in particular. In general, supplying technology for mobile communication is often less expensive than providing in-person services[4 5]. Sexual health service users, in particular, also often prefer the anonymity and privacy of mobile solutions. As mobile phones are often carried by individuals wherever they go, they can act as reminders and allow for quick and easy access to stored information that can be listened to or read at an individual's own time and pace and can be shared with others to facilitate communication about sensitive topics, such as sexual health[8].

Mobile phone delivered interventions employ a variety of different modes of delivery to improve different aspects of sexual health. This review focuses on mobile interventions with a 'push' component, with information 'delivered to participants' (e.g. via video, voice or text messages) rather than being retrieved by them, as this has been described as a convenient, low-commitment way to receive and share information and gain support relating to sexual health[8 9]. After a number of pilot mHealth initiatives in various contexts, however, the WHO and others have called for increased rigour in the evaluation of mHealth interventions and also in the assessment of potential adverse effects[4 10].

Previous systematic reviews evaluating the effect of mHealth interventions on STI prevention have reported promising, but inconclusive results[3 11 12]. The most recently published meta-analyses reported that interventions may increase knowledge, STI testing and service use and

may not increase condom use, but the evidence was low certainty and the effects of interventions on partner notification, curable STI treatment adherence and STI/ HIV incidence is not known[13 14]. The mHealth literature has grown rapidly and further studies have been published since the most recent searches for these reviews were completed in 2017. To our knowledge, no up-to-date meta-analyses have been published that respond directly to our research question[10 15-17]: Are sexual health interventions delivered to participants by mobile technology effective in preventing STIs or promoting preventive behaviour among adolescents and adults if compared with an inactive control intervention?

METHODS

We conducted a systematic review and meta-analysis following Cochrane and PRISMA guidelines[18 19] (Suppl.1) after registering our protocol[20].

Eligibility criteria

We included randomised controlled trials (RCT) conducted worldwide among (potential) sexual health service users aged ≥10 years to evaluate mHealth interventions with a 'push' component focused on the sexual transmission of STIs, including HIV. (We define a 'push' component as intervention content that users receive without active request or engagement, beyond having signed up to receive the intervention initially.) To limit the scope of this review, we excluded studies that focused on voice calls alone (e.g. phone counselling sessions instead of face-to-face sessions that could also have been done via landlines), as well as emails, or websites alone, and did not necessarily require mobile devices and/or did not contain a 'push' component. We also excluded studies with interventions that are relevant for HIV prevention only, and only included trials with an 'inactive' control intervention, i.e. no intervention, standard-of-care (SOC), placebo, or waiting list control. We pre-specified the following most

important outcomes for our review (to be included in the summary of findings table): Biological outcomes, including long term (at ≥12 months) STI/HIV occurrence (objectively confirmed), short/medium term (<12 months) STI/HIV occurrence (objectively confirmed and subjective/self-reported); adverse effects, including experience of violence; behavioural outcomes, including condom use, compliance with treatment instructions for curable STIs, STI (self-)testing, and partner notification. Other review outcomes included costs and cognitive outcomes, such as STI-related knowledge or self-efficacy (Suppl.2).

Search strategy

We searched seven electronic bibliographic databases/trial registers (MEDLINE, Embase, PsychINFO, Global Health, CENTRAL, ClinicalTrials.gov, WHO ICTRP) without language restrictions to identify relevant published, unpublished, completed or ongoing trials. We developed a comprehensive search around two key concepts (STIs and mobile technology) and adapted an RCT filter (Suppl.3). We restricted the time period to 1 January 2010-19 February 2020, but also searched lists of studies included in our previous systematic review[3] covering January 1990-September 2010, and in other related reviews (n=48, Suppl.3), and contacted experts (n=11/15 responded).

Study selection

After deduplication in EndnoteX9, and pilot-testing of inclusion/exclusion criteria, two reviewers (sexual health experts masked to each other's decisions) independently screened all titles/abstracts and potentially relevant full-text articles for eligibility. Discrepancies were resolved by discussion and by consulting a third reviewer if necessary.

Data extraction and study appraisal

We developed a data extraction tool in excel for extracting various study data recommended by Cochrane[21]; we used the Cochrane risk of bias (ROB) assessment tool[22] to assess ROB of individual studies and GRADEpro|GDT software to assess certainty of evidence (CoE) across studies (considering ROB in individual studies, inconsistency of results between studies, indirectness of evidence, imprecision and publication bias) [23 24].

After piloting data extraction and ROB assessment, one reviewer extracted data and assessed ROB, with a second reviewer independently cross-checking after reading the whole article(s). Similarly, all CoE assessments were cross-checked. Disagreements were resolved by discussion and by consulting a third reviewer when necessary. We contacted 13 authors (maximum of three email attempts) for additional information/data.

Data synthesis and analysis

After summarizing studies according to type of intervention, comparison, and outcomes, we conducted meta-analyses, where sufficient data were available for at least two similar studies. We used Review Manager 5.3[25] for computing effect sizes and meta-analyses following Cochrane guidance[18].

First, we calculated risk ratios (RR) or odds ratios (OR) with 95% confidence intervals (CI) for dichotomous data, and converted dichotomous and continuous summary measures into standardized mean differences (SMD) where necessary to make them comparable across different studies and outcome measures (ensuring scales pointed in the same direction prior to standardization)[18 26]. We interpreted SMD values of 0.5 as important difference[19].

We then conducted meta-analyses using random-effects models, due to the anticipated variability of included studies. If a study reported more than one relevant comparison group or reported outcomes separately for different subgroups, we combined them if possible, or chose one most comparable to other studies. We pooled results separately for outcomes assessed after short/medium-term (<12 months) versus long-term (≥12 months) follow-ups[20]. For studies reporting results for multiple time points, we chose one closest to the mode of time points of all pooled studies. Where substantial heterogeneity ($I^2 \geq 50\%$)[18] was present and where possible (one instance only), we conducted a pre-specified subgroup analysis[20] and presented results in the main text. (Where heterogeneity was not substantial, we conducted additional subgroup analyses to better visualize results for pre-specified criteria, and displayed them in Supplementary file 10 only).

RESULTS

Study selection

From a total of 6683 identified unique articles, we included 41 articles reporting on 22 trials (Figure 1, Suppl.4). Among these, 20 trials with a total of 19,551 participants were included in meta-analyses. We also identified 12 ongoing trials.

Study characteristics

Among the 22 included trials, 15 were published between January 2015 and February 2020, 19 were parallel-group and three were cluster RCTs, 19 had two trial arms, and seven were pilot trials (Table 1, Suppl.6). Twelve trials had been conducted in HIC (US: n=6; Europe: n=3; Australia: n=3), and ten in LMIC (Africa: n=7; China: n=2; India: n=1); eleven focused on HIV, and ten targeted key populations, including men having sex with men (MSM, n=6), sex workers (n=3), truckers (n=2), and/or people with alcohol use disorder (n=1). Total sample

sizes ranged from N=52-7606. Thirteen trials were informed by behavioural theory and 12 involved users during intervention development.

Intervention aim, content, mode of delivery and duration varied, ranging from single re-testing reminder text messages to complex interventions delivered via different modes over months (1-6 months: 64%; >6 months:14%) targeting various behaviours.

Seven trials targeted diagnosis-related behaviour only (HIC: n=1, LMIC: n=6) mostly sending unidirectional text messages over short time-periods (<4 weeks) to remind people to (re-)test for HIV/STIs or in one case to notify partners. One stepped-wedge (4x3 months) cluster RCT educated and encouraged participants to test for HIV via a multi-component, smartphone application-based intervention.

Six trials targeted preventive behaviour only, and nine targeted both preventive, and STI/HIV-testing behaviour; fifteen educated and reminded participants about condom use, and seven also taught condom use (negotiation) skills; a few interventions also discussed contraception, illegal drug use, and/or delay of first sex/abstinence. Only two trials included treatment-related messages to educate and remind people about taking STI medications and abstaining from sex until treatment-completion.

Overall, thirteen trials included only unidirectional messages; eleven included both unidirectional and bidirectional messages, for example, where participants could respond to quiz questions, or had the option to text a number back to hear more; Six interventions also involved direct interaction with peers or health providers (as part and/or on top of the mHealth intervention), and five directed participants to external online or telephone services, such as free helplines. Eight trials employed some form of tailoring (details in Suppl.6).

Comparisons included different types of mobile interventions and control arms (Table 1). The majority (82%) of trials included mobile phone text messaging/short message services (SMS) as mode of delivery; most of these compared SMS interventions to inactive control groups not containing any active SMS component. In two trials though, control group participants obtained SOC that already contained sexual health-related SMS (in lower dosage). Two other trials compared SMS interventions 'blended' with in-person interventions to inactive controls. Only four (18%) of the eligible trials evaluated mHealth interventions with a 'push' component other than SMS, including person-delivered Facebook messages (n=1 trial) and messages sent via smartphone applications (app, n=2 via 'WeChat' and n=1 via another app).

Outcomes included mostly behavioural outcomes with 68% of trials assessing condom use and 64% assessing STI/HIV-(self)testing; only three trials assessed biological outcomes, and only one trial assessed adverse events. Most trials (82%) assessed outcomes after short/moderate-term follow-ups.

Among the 12 ongoing trials all target key/specific populations, seven use behavioural theory, five assess biological outcomes, and one adverse events (Suppl.5).

Risk of bias and certainty of evidence

ROB regarding random sequence generation and allocation concealment was low in 86% and 50% of trials respectively and unclear in the remaining trials. ROB for other domains varied (details in Suppl.7).

The certainty of evidence (CoE) was very low or low for adverse events, all biological and most behavioural outcomes; CoE was moderate for short/medium-term condom use and STI/HIV-testing outcomes in two comparisons (Table 2, details in Suppl.8).

Table 1 – Characteristics of included studies

Study	Design (name)	Participants & setting (total number)	Target behav.[]	Intervention(s) & comparator*	Outcome(s)* (assessment timepoint~)
de Tolly (2012)[27]	RCT, 5-arm	People listed in mobile phone database, South Africa (N=2553)	D	Four SMS intervention arms (3 or 10 motivational vs 3 or 10 informational SMSs) vs no intervention	[HIV testing, Costs (1m3w)] ^
Delamere (2006)[28]	RCT, 2-arm	Young persons clinic clients, Ireland (N=60)	P	Weekly SMS messages for 3 m vs no intervention	Condom use (3m)
Downing (2013)[29]	RCT, 3-arm	SH service clients, Australia (N=94)	D	One SMS reminder message at 10-12 weeks vs SOC	STI testing (3-4m)
Free (2016)[30]	Pilot RCT, 2-arm (Safetxt)	Young people attending SH services, UK (N=200)	P, D, T	SMS messages (initially up to 4 per day, gradually less, at the end 1 per month) over 12 m vs monthly SMSs checking contact details	STI occurrence (3, 12m), AE (12m), Condom use, STI testing (1, 12m), treatm. compl., PN (1m)
Gold (2011)[31]	Pilot RCT, 2-arm (S5 Proj.)	Mobile advertising service subscribers, Australia (N=7606)	P, D	Safer sex SMSs (fortnightly during summer plus 8 at annual events) vs sun safety SMS placebo control	Condom use, STI testing, SH knowledge (5-6m)
Govender (2019)[32]	RCT, 2-arm	Transient/resident populations near roadside clinics, SA, Zim-babwe, Mozambique (N=1783)	P, D	SMS messages (daily during the first week, then weekly) for 29 weeks (about 6 months) vs SOC	Condom use, HIV testing, self-efficacy, knowledge, & risk perception (6m)
Kelvin (2019a)[33]	RCT, 3-arm	Male truckers registered in EHRS, Kenya (N=2262)	D	Enhanced SOC (3 SMS reminders) vs SOC (1 SMS reminder)	HIV testing, SMS costs (2m)
Kelvin (2019b)[34]	RCT, 3-arm	Female sex workers registered in EHRS, Kenya (N=2196)	D	Enhanced SOC (3 SMS reminders) vs SOC (1 SMS reminder)	HIV testing, SMS costs (2m)
Lim (2012)[35]	RCT, 2-arm	Music festival attendees, Australia (N=994)	P, D	SMS messages (3-4 per w) and emails (less than monthly) over 12 m vs no intervention	Condom use, STI testing, STI knowledge (6, 12m)
Mimiaga (2017)[36]	Pilot RCT, 2-arm	MSM engaging in sex work, India (N=100)	P	Blended SMS intervention (phone and in-person sessions & daily SMS for 3 m) vs SOC	Condom use (3m)
Mugo (2016)[37]	RCT, 2-arm	Health facility/ pharmacy clients, Kenya (N=410)	D	SMS and phone call (or in-person) reminders vs SOC appointment card	HIV testing (2w)

Nielsen (2019)[38]	RCT, 2-arm (MOSEXY)	Youth Health Clinic attendees, Sweden (N=433)	P, D	Interactive smartphone app, incl. info sent over 6 months vs 'dummy' app with questionnaires	STI occurrence, Condom use, STI testing (6m)
Parkes-Ratanshi (2018)[39]	RCT, 3-arm (STOP)	Pregnant women with positive syphilis test, Uganda (N=442)	D	Weekly SMS reminders for up to 8 weeks vs SOC partner notification slips	PN/ Partner attendance (median 20 days)
Reback (2019a)[40]	RCT, 3-arm (Project Tech Support 2)	MSM who use methamphetamine, US (N=286)	P	SMS conversation with PHE, automated SMS and self-monitoring assessment (SMA) vs automated SMS and SMA vs SMA only	Condom use (9 m), costs
Rinehart (2019)[41]	Pilot RCT, 2-arm (t4she)	Community health centre patients, US (N=244)	P	Automated SMS messages over 12 weeks vs SOC	Condom use, STI knowledge, condom use self-efficacy (3, 6m)
Rokicki (2017)[42]	C-RCT, 3-arm	Students at 38 secondary schools, Ghana (N=756)	P	Interactive quiz SMS vs unidirectional SMS intervention vs placebo control (malaria info)	Condom use, age at sexual debut (15 m), knowledge (3, 15m)
Suffoletto (2013)[43]	Pilot RCT, 2-arm	Female emergency department patients, US (N=52)	P	SMS intervention over 12 w vs SMS announcing time of final survey completion	Condom use, abstinence (3m)
Tang (2018)[44]	Stepped wedge C-RCT	MSM using social networking mobile app, China (N=1381)	D	Biweekly WeChat images/texts over 3 m and HIV self-testing platform vs wait list control	HIV testing, self-efficacy, stigma, social norms (3, 6, 9, 12m)
Trent (2019)[45]	RCT, 2-arm (TECH-N)	Patients with pelvic inflam. disease, US (N=292)	P, D, T	Blended SMS intervention (daily SMS for 2 w, then weekly for 1 m plus 1 nurse visit) vs SOC	STI occurrence, condom use (3 m) treatment compliance, PN (2 w)
Ybarra 2017[46]	Pilot RCT, 2-arm (G2G)	Men identifying as gay, bisexual and/or queer, US (N=302)	P, D	SMS messages for 5 w (5-10 per day) plus booster vs SMS placebo control (general health info)	Condom use, abstinence, HIV testing, knowledge, perceived condom use skills (5w, 4m1w)
Young (2013)[47]	Pilot C-RCT, 2-arm (HOPE)	Mostly African American and Latino MSM, US (N=122)	P, D	Peer-delivered Facebook intervention for 12 weeks vs placebo control (general health info)	HIV testing (3 m)
Zhu (2019)[48]	Pilot RCT, 2-arm (WeTest)	MSM, China (N=100)	P, D	Smartphone App-based info and weekly messages plus HIVST kits vs HIVST kits only	Condom use, HIV testing (6 m)

* Interventions, comparators and outcomes relevant to this review only; | P, preventive-, D, diagnosis-, T, treatment-related behaviour; ~ post baseline; ^data unextractable due to figures not adding up and failed attempts to obtain response from authors; AE, adverse events; App, application; (C-)RCT, (Cluster-) randomized controlled trial; HIVST, HIV self-testing; MSM, men having sex with men; EHRS, electronic health record system; PHE, peer health educators; PN, partner notification; SA, South Africa; SH, sexual health; SMS, short message service; SOC, standard of care; treatm. compl., compliance with STI treatment instructions (drug adherence and abstinence till infection has cleared); behav., behaviour; m, month(s), w, week(s); vs, versus

Results of meta-analyses by comparison, outcome and certainty of evidence

Below and in table 2, we report results separately for different comparisons and outcomes (details in Suppl.9). Figure 2 includes forest plots for most important outcomes (predefined in protocol) of moderate CoE only (for others and subgroup analysis see Suppl.10).

SMS intervention versus inactive control

Biological outcomes: Meta-analyses of biological outcomes were not possible, as only one pilot trial[30] examined long-term STI/HIV-occurrence (cumulative chlamydia incidence), and short/medium-term STI/HIV-occurrence with low CoE due to imprecision (table 2).

Adverse events: Similarly, only one pilot trial[30] reported on adverse events with very low CoE.

Behavioural outcomes: The CoE for intervention effects on behavioural outcomes ranged from very low to moderate, and meta-analyses were only possible for five outcomes: Long-term condom use was examined by three trials[30 35 42], but CoE was low; nine trials[28 30-32 35 40 41 43 46] did not show an effect on short/medium-term condom use (SMD 0.02, CI -0.09-0.14, moderate CoE, Figure 2). CoE was very low for long-term STI/HIV-testing (2 trials[30 35]), but was moderate for short/medium-term STI/HIV-testing (7 trials[29-32 35 37 46]); here, a benefit was detected (OR 1.83, CI 1.41-2.36, Figure 2). Two trials[30 39] targeted partner notification, but CoE was very low.

Other review outcomes: Four trials[31 35 41 46] revealed a small effect on STI/HIV-knowledge (SMD 0.22, CI 0.09-0.36) with moderate CoE, and two trials[41 46] failed to show a statistically significant effect on condom use self-efficacy (SMD 0.24, CI -0.01-0.48), but CoE was low. Data on costs and other outcomes were limited (Suppl.9).

SMS intervention versus SOC control containing active SMS component

Behavioural outcomes: Two trials[33 34] conducted in the same setting failed to show an effect on STI/HIV-testing (OR 1.00, CI 0.68-1.47, moderate CoE, Figure 2).

SMS intervention blended with in-person contact versus inactive control

Behavioural outcomes: Only one trial[45] examined short/medium-term STI/HIV-occurrence, with very low CoE. CoE for all behavioural outcomes was low, including short/medium-term condom use (2 trials[36 45]), STI treatment-related abstinence, drug adherence and partner notification (1 trial[45]).

Facebook intervention versus inactive control

No meta-analysis was possible and CoE for the only reported outcome was very low (1 trial[47]).

Smartphone App intervention versus inactive control

Behavioural outcomes: A single trial[38] assessed short/medium-term STI/HIV-occurrence, and CoE was low. It was also low for short/medium-term condom use (2 trials[38 48]). CoE for self-reported short/medium-term STI/HIV-testing was low when three trials[38 44 48] were pooled (partly due to heterogeneity), but was moderate in a subgroup analysis with two trials[44 48] that displayed an important benefit (RR 1.40, CI 1.22-1.60). One trial[48] also reported objectively confirmed STI/HIV-testing results, but CoE was low.

Table 2 – Summary of Findings (for predefined review outcomes)

Outcome[#]	Effect		Certainty*	Description^
№ of participants (studies)	Relative (CI)	Absolute˜(CI)		
SMS interventions vs inactive controls				
STI/HIV occurrence, obj. at ≥12 m; N=200 (1 RCT)[30]	RR 0.61 (0.28 to 1.34)	58 fewer per 1000 (107 fewer to 49 more)	⊕⊕◯◯ LOW	SMS interventions may result in little to no difference in STI/HIV occurrence at ≥12 m.
STI/HIV occurrence, obj. at <12 m; N=171 (1 RCT)[30]	RR 2.17 (0.56 to 8.40)	39 more per 1,000 (15 fewer to 249 more)	⊕⊕◯◯ LOW	SMS interventions may result in little to no difference in STI occurrence at <12 m.
Adverse events - car accident where partic. was driver, at ≥12m; N=157 (1 RCT)[30]	RR 2.08 (0.19 to 22.45)	14 more per 1,000 (10 fewer to 268 more)	⊕◯◯◯ VERY LOW	The evidence is very uncertain about the effect of SMS interventions on adverse events.
Condom use, subj. at ≥12 m); N=667 (3 RCTs)[30 35 42]	OR 1.10 (0.77 to 1.56)	-˜	⊕⊕◯◯ LOW	SMS interventions may not change condom use at ≥12 m.
Condom use, subj. at <12 m) N=2307 (9 RCTs)[28 30-32 35 40 41 43 46]	SMD 0.02 (-0.09 to 0.14)	-˜	⊕⊕⊕◯ MODERATE	SMS interventions probably do not increase condom use at <12 m.
STI/HIV testing, obj. or subj. at ≥12 m; N=492 (2 RCTs)[30 35]	OR 0.86 (0.25 to 2.95)	23 fewer per 1,000 (138 fewer to 222 more)	⊕◯◯◯ VERY LOW	The evidence is very uncertain about the effect of SMS interv. on STI/HIV testing at ≥12 m.
STI/HIV testing, obj. or subj. at <12 m); N=2151 (7 RCTs)[29-32 35 37 46]	OR 1.83 (1.41 to 2.36)	150 more per 1,000 (85 more to 211 more)	⊕⊕⊕◯ MODERATE	SMS interventions probably lead to increased STI/HIV testing at <12 m.
Compliance - took treatment for curable STI; N=38 (1 RCT)[30]	RR 0.95 (0.82 to 1.09)	50 fewer per 1,000 (180 fewer to 90 more)	⊕◯◯◯ VERY LOW	The evidence is very uncertain about the effect of SMS interv. on treatment adherence.
Compliance - abstinence during treatment of curable STI; N=37 (1 RCT)[30]	RR 1.12 (0.90 to 1.40)	101 more per 1,000 (84 fewer to 337 more)	⊕◯◯◯ VERY LOW	The evidence is very uncertain about the effect of SMS interv. on treatment-related abstinence.
Partner notification; N=336 (2 RCTs)[30 39]	OR 1.04 (0.31 to 3.48)	7 more per 1,000 (152 fewer to 285 more)	⊕◯◯◯ VERY LOW	The evidence is very uncertain about the effect of SMS interventions on partner notification.
SMS interventions vs SOC with active SMS				
STI/HIV testing, obj. or subj., at <12 m; N=2956 (2 RCTs)[33 34]	OR 1.00 (0.68 to 1.47)	0 fewer per 1,000 (11 fewer to 16 more)	⊕⊕⊕◯ MODERATE	SMS interv. probably don't change STI/HIV testing if compared to active SMS controls
Blended SMS interventions vs inactive control				
STI/HIV occurrence, obj., at <12 m); N=260 (1 RCT)[45]	OR 0.40 (0.15 to 1.09)	60 fewer per 1,000 (87 fewer to 8 more)	⊕◯◯◯ VERY LOW	The evidence is very uncertain about the effect of blended SMS interv. on STI/HIV occ.

Condom use, at < 12 m N=360 (2 RCTs)[36 45]	SMD 0.25 (0.02, 0.48)	-~	⊕⊕◯◯ LOW	Blended SMS interventions may increase condom use slightly.
Compliance - took treatment for curable STI; N=260 (1 RCT)[45]	OR 0.64 (0.39 to 1.05)	109 fewer per 1,000 (217 fewer to 12 more)	⊕⊕◯◯ LOW	Blended SMS interv. may result in little to no difference in STI treatment adherence.
Compliance -abstinence during treatment of curable STI; N=260 (1 RCT)[45]	OR 0.73 (0.39 to 1.37)	49 fewer per 1,000 (175 fewer to 40 more)	⊕⊕◯◯ LOW	Blended SMS interv. may result in little to no difference in treatment-related abstinence.
Partner notification; N=260 (1 RCT)[45]	OR 0.84 (0.36 to 2.00)	14 fewer per 1,000 (116 fewer to 39 more)	⊕⊕◯◯ LOW	Blended SMS interventions may result in little to no difference in partner notification.
Facebook interventions vs inactive control				
STI/HIV testing, obj., at <12 m; N=122 (1 RCT)[47]	MD, 24 pp (8 to 41 pp)	-~	⊕◯◯◯ VERY LOW	The evidence is very uncertain about the effect of Facebook interv. on STI/HIV testing
Smartphone App interventions vs inactive control				
STI/HIV occurrence, subj. at <12 m; N=433 (1 RCT)[38]	OR 1.03 (0.69 to 1.55)	6 more per 1,000 (74 fewer to 101 more)	⊕⊕◯◯ LOW	App interv. may result in little to no difference in self-reported STI/HIV occurrence
Condom use at < 12 m; N=485 (2 RCTs)[38 48]	OR 0.85 (0.53 to 1.37)	25 fewer per 1,000 (84 fewer to 55 more)	⊕⊕◯◯ LOW	App interventions may result in little to no difference in condom use.
STI/HIV testing, obj.| at <12 m; N=100 (1 RCT)[48|]	RR 4.56 (2.49 to 8.35)	641 more per 1,000 (268 to 1,000 more)	⊕⊕◯◯ LOW	App interventions may result in a large increase in STI/HIV testing.
STI/HIV testing, subj.| at <12m; N=2971 (3 RCTs)[38 44 48]	RR 1.27 (1.05 to 1.52)	-~	⊕⊕◯◯ LOW	App interventions may result in a slight increase in STI/HIV testing.
Subgroup analysis: STI/HIV testing, subj., at <12 m) - MSM, LMIC; N=2538 (2 RCTs)[44 48]	RR 1.40 (1.22 to 1.60)	-~	⊕⊕⊕◯ MODERATE	App interv. probably increase STI/HIV testing slightly among MSM in LMIC
Subgroup analysis: STI/HIV testing, subj., at <12 m) - general population, HIC; N=433 (1 RCT)[38]	RR 1.1 (1.0 to 1.2)	77 more per 1,000 (0 fewer to 153 more)	⊕⊕◯◯ LOW	App interv. may result in little to no difference in STI/HIV testing among general populations in HIC.

CI, 95% confidence interval; MD, mean difference; MSM, men having sex with men; OR, odds ratio; pp, percentage points; RCT, randomized controlled trial; RR, risk ratio; SMD, standardized mean difference; SMS, short message service (mobile phone text messaging); SOC, standard of care; STI, sexually transmitted infection; m, month(s) – referring to the number of months from baseline until the outcome assessment time point; obj., objectively reported, e.g. confirmed by laboratory or clinic records; subj., subjective/self-reported, e.g. participants responding to survey question; # Outcomes relevant to this review, as pre-specified in protocol; ^ Here (and throughout the manuscript) we used standardized language[19 24]; ~ Absolute effects generated in GRADEpro|GDT[24] if sufficient data on baseline risks were available; | Obj. and subj. outcomes presented separately here, as one of the studies [48] reported both obj. and subj. outcomes; * Details on the certainty of evidence can be found in Suppl.8 (GRADE evidence profiles); Certainty definitions[24]: HIGH - Further research is very unlikely to change our confidence in the estimate of effect; MODERATE - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.; LOW - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. VERY LOW - Any estimate of effect is very uncertain.

DISCUSSION

This review pooled data from 22 RCTs with a total of 19,551 participants to explore effects of specific mHealth interventions on various predefined outcomes. For biological outcomes and adverse events, meta-analyses were not possible, as too few studies assessed these outcomes. Meta-analyses were possible, however, for some of the behavioural outcomes, and allow us to state the following with moderate certainty: in the short/medium-term, SMS interventions probably make little or no difference to condom use, but moderately increase STI/HIV-testing if compared to inactive controls that do not already contain an active SMS component. Similarly, smartphone applications with push content probably increase STI/HIV-testing if targeting MSM in LMIC. CoE ranged from very low to low for all other review outcomes and comparisons, apart from a small positive effect of SMS interventions on STI/HIV-knowledge, for which CoE was moderate.

Our results provide greater certainty evidence corroborating findings of a Cochrane review on targeted client communication via mobile devices (with literature search through Jul/2017)[14]. It had only partly overlapping comparisons and outcomes, and for those relevant to our current review pooled fewer trials and had lower CoE, but showed similar effects; findings suggested positive effects on short/medium-term STI-testing (low certainty), and no effect on condom use (very low CoE). CoE was also very low for STI-occurrence, and unintended consequences. Similarly, another recently published review[13] (with comprehensive search through Aug/2013, and Medline search till Mar/2017) identified fewer trials, but also exhibited no effect of SMS interventions on condom use (based on two trials only), and a positive effect on testing (based on four trials, but including CD4 and virological testing in infants).

Contrary to our findings, Xin and colleagues[16] yielded small positive effects on condom use among MSM when pooling various eHealth interventions; statistical heterogeneity was substantial though, and the review included also nonrandomised studies. Swanton and colleagues[49] previously showed that a positive effect of new-media interventions on condom use disappeared when only RCTs were included, but a positive effect on STI-testing remained. The inclusion of nonrandomised studies might also have influenced the slight positive effect of technology-based interventions on condom use for both STI prevention and/or contraception among youth in another review[50]; here, moderator analyses exhibited statistically significant effects only for follow-ups <6 months. The same review also reported increasing knowledge, but not self-efficacy, in line with our findings.

Our review has added evidence from newly published studies, which allowed us to include RCTs only and still be able to pool data and generate meaningful results for at least some of our outcomes. We have carried out the review and reported results following internationally recognized guidelines[18 19 22 23]. In a few instances, we had to exclude studies from meta-analyses, or include only part of the results, where additional information/data could not be obtained. Our eligibility criteria were broad regarding populations/settings, but relatively narrow regarding interventions. We restricted mHealth interventions to those that reported a 'push' component, as these might also reach people, who would not readily interact with apps or seek information on the internet anyway. This does not imply that other types of mHealth interventions are less important. To reduce the scope of our review, we also excluded HIV- and reproductive health-related studies not directly relevant to the sexual transmission of curable STIs; we recognize, however, that integrating related services[51] and linking various steps in the STI and HIV cascades of prevention and care[52] is crucial.

It exceeded the scope of our review to explore various motivational and structural factors that might explain our results[53 54 55]; for example, even if behavioural interventions can influence through informing, reminding, teaching skills and supporting people by linking them to health services[56], this might not be sufficient to achieve condom use, where access to condoms is a problem or power imbalances between partners are too stark. On the other hand, it is possible that condom use might be increased by further improving the quality of behavioural mHealth interventions. To achieve this, experts have called for increased use of behavioural theory (reported by 59% of our included trials), user involvement (55% of trials) and tailoring (36% of trials)[12 57]. The trial reports did not always contain sufficient detail about intervention development and content, but generally, the content of mHealth interventions was less comprehensive than the content of effective condom promotion face-to-face interventions we reviewed previously[58].

Our positive findings regarding STI/HIV-testing, should encourage health care providers and policymakers to consider integrating mHealth interventions with other types of services, including eHealth platforms[59 60] that facilitate anonymous partner notification, and self-testing/self-sampling with remote result notification and postal treatment. This becomes particularly advantageous where access to sexual health services is restricted for socio-economic or other reasons, including during Covid-19-related lockdowns[61]. Further implementation research on such integration is needed. Researchers should also assess costs and explicitly measure adverse events/potential harm[62 63]. Ongoing trials[64 65] will report the effects of interventions on biological outcomes.

KEY MESSAGES

- In the short/medium-term, SMS interventions probably make little or no difference to condom use, but increase STI/HIV-testing if compared to controls without an active SMS component.
- In the short/medium-term, smartphone applications with content delivered to participants probably increase STI/HIV-testing among MSM in LMIC.
- Further evidence on the cost-effectiveness and effect of mHealth interventions on STI treatment-adherence, partner notification, biological and other outcomes with long-term follow-ups is needed.
- Future RCTs should explicitly measure and report adverse events/ unintended consequences of sexual health interventions delivered to participants by mobile technology.

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Competing Interests

CF, OM and MP are co-authors on one of the studies included in this review. Otherwise, the authors declare that they have nothing to disclose.

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Contributions of authors

SB and CF wrote the protocol with support from all authors; SB developed and implemented the search strategy with support from AG, MP, OM and CF; SB retrieved full papers with support from EW; All authors agreed on the eligibility criteria and selection process. AG, SB and EW screened titles/abstracts, and AG, SB and OM assessed full text articles for eligibility. SB designed the data extraction tool with support from CF, MP, OM and AG; SB extracted data, and completed ROB assessments and AG and OM cross-checked these; SB conducted the meta-analysis with support from CF and MP; SB completed GRADE assessments and AG cross-checked these. SB, AG and OM discussed conflicting or complex screening, ROB and GRADE assessment decisions with CF until reaching agreement; SB wrote the first draft of the manuscript; CF and OM contributed to the writing of the manuscript and all authors commented on revised versions, and approved the final manuscript.

Data sharing- Data for this systematic review can be obtained from the corresponding author upon reasonable request.

Figure legends

Figure 1 - Flow chart of the study selection process

Figure legend:

[#] Details and list of excluded articles with reasons in Suppl.4

* n=22 included studies reported in n=41 articles; n=12 ongoing studies reported in n=13 articles (Suppl.5)

Flow chart adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097.

Figure 2 – Forest plots of studies comparing interventions to inactive controls for outcomes of moderate certainty of evidence

Figure legend: HIC, high-income countries; LMIC, low- and middle- income countries; ICC, intra-cluster correlation coefficient; CI, confidence interval; AOR, adjusted odds ratio; RCT, randomised controlled trial; SE, standard error; SMD, standardised mean difference; SMS, short message service (mobile phone text messaging); STI, sexually transmitted infection; TXT, text messaging; f/m comb., female/male combined; m, month(s); w, week(s);

Note: Studies within forest plots are sorted by objectively confirmed versus self-reported outcome (where applicable) and by study weight

Risk of bias domains:

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Other bias (e.g. contamination bias)
(G) Selective recruitment of cluster participants (for cluster RCTs only)

Supplementary materials

Supplementary file 1 - PRISMA checklist
Supplementary file 2 – PICOS table of eligibility criteria
Supplementary file 3 – Full search strategy and list of relevant systematic reviews
Supplementary file 4 – List of excluded studies with reason
Supplementary file 5 – List of ongoing studies with main characteristics
Supplementary file 6 – Characteristics of included studies (summary and details)
Supplementary file 7 – Risk of bias assessments of all included studies
Supplementary file 8 – GRADE evidence profiles
Supplementary file 9 – Outcomes and results for all included studies by comparison type
Supplementary file 10 - Forest plots of all pooled studies by type of comparison and pre-specified outcomes

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