Division of Biomedical Engineering

Department of Human Biology

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The impact of mHealth on adolescent global health outcomes:

a scoping review of mHealth initiatives

In partial fulfilment of the requirements for the degree:

MPhil in Health Innovation

Ramonde Patientia (PTNRAY001)

Supervisor: Dr Jill Fortuin

Co-supervisor: Professor Tania Douglas

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Finally, to my nieces and nephews-Nova, Njabulo, Ziyanda, Sage and Jasmine-this is really for you. May you joyfully grasp every opportunity that life presents.

Abstract

Negative health behaviour during the period of adolescence contributes to the global burden of mortality, chronic disease, and preventable disability from physical injury. It is therefore essential to encourage positive health behaviour such as on-time vaccination, safer sex practices, and early recognition of infectious conditions and mental illness, before complications arise from unprotected sexual debut or undetected illness.

Our project aims to determine the favourable aspects of global mHealth interventions as applied to adolescent health outcomes for knowledge transfer to adolescent infectious disease programmes in low and middle-income countries (LMIC's). mHealth refers to the integration of mobile or wireless technology for health delivery and promotion and may appeal to adolescents as it allows for interactive, personalized, two-way communication on various digital platforms. However, it remains unclear what specific interventions work best to target vulnerable adolescents in LMIC's, as most of the evidence for mHealth stems from studies in high-income countries, conducted on groups other than adolescents such as caregivers, health workers and adult patients.

This report is a scoping review examining the global evidence of mHealth efficacy for common adolescent conditions, in order to gain insight into the types of interventions that best target adolescents for biological and behavioural health outcomes. These insights will facilitate knowledge transfer for the implementation of adolescent mHealth infectious disease management, and identification of research gaps. We included published and unpublished studies between 31 January 1990 and 30 November 2017, with no language limitation. Primary studies included adolescents (defined as 10-19 years of age) of any gender, location, or ethnicity, with access to a mobile phone or wireless device used for a health-related outcome. Studies reported on health outcomes of HIV, TB, vaccine-preventable disease, depression, suicide, road traffic accidents and substances other than tobacco use. Purely qualitative study designs and voice-only calls were excluded.

Despite the potential appeal of mHealth among adolescents, there is unclear overall evidence for efficacy in this population. We had hoped that the adolescent period itself would allow generalisability of interventions. However, the variable reporting quality between studies, often without rich contextual descriptions, necessitate caution with interpretation of findings. This incomplete reporting also impacted on knowledge transfer at multiple levels, despite the use of study-specific guidelines. Our recommendations for future researchers would be to undertake adequately-powered studies among clearly defined age groups, and examine biological health outcomes for longer periods of follow-up. We also encourage researchers to use mHealth-specific guidelines such as the CONSORT-EHEALTH and mERA checklists to enable effective knowledge transfer and scaling of interventions.

Abbreviations

ART	Antiretroviral Treatment
CDC	Centres of Disease Control
CENTRAL	Cochrane Central Register of Controlled Trials
CONSORT	Consolidated Standards of Reporting Trials
EQUATOR	Enhancing the quality and Transparency Of health Research
HPV	Human papillomavirus
ICT	Information Communication Technology
PsycINFO	Psychological Information Database
MeSH	Medical Subject Heading
mHealth	Mobile Health
mERA	mHealth Evidence Reporting and Assessment
NCBI	National Centre for Biotechnology Information
NIH	National Institutes of Health
NLM	National Library of Medicine
OR	Odds Ratio
PID	Pelvic Inflammatory Disease
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
SIM	Subscriber Identity Module
SRH	Sexual and reproductive health
STI	Sexually Transmitted Infection
TB	Tuberculosis
UN	United Nations
UNDESA	United Nations Department of Economic and Social Affairs
USA	United States of America
VPD	vaccine-preventable disease
WHO	World Health Organisation

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Chapter 1: Introduction

1.1 Background

For decades, the focus of global public health initiatives has been on the health of infants, children and pregnant women that has led to an "epidemiological transition" of reduced all-cause mortality in younger children and pregnant women (Sawyer, 2016). At the same time, adolescent health has been overlooked due to the assumption that this is the healthiest period of life (Blum, 2004; (Viner et al., 2011). However, many undiagnosed mental conditions and negative health behaviours (such as drunk-driving, substance use and unprotected sex), emerge during adolescence (Patton et al., 2012; Sawyer, 2016). These underpin later chronic disease or disability and limit full socio-economic independence in multiple ways (Das Gupta, 2014; WHO, 2013). Those adolescents with undiagnosed mental conditions are more at risk of being expelled or suspended from school, early pregnancy before completing their education, engaging in criminal behaviour, and illicit drug use (WHO, 2014a; Gore et al., 2011). Almost all adult smokers started using tobacco regularly in adolescence. These risks and behaviours may also negatively impact the health and early childhood development of their potential children (Laski, 2015; Patton et al., 2012).

Adolescents living in LMIC's are most vulnerable, where high prevalence of infectious diseases such as HIV, tuberculosis (TB) and malaria consume limited health staff and budget resources (Uppada, 2016; Oosthuizen, 2008). Newer, promising infectious disease vaccines for HIV and TB target the period of adolescence rather than childhood (Harris et al., 2016; da Costa, 2015). Many experts believe that this period may offer the greatest public health benefit through primary prevention, as it is a highly social age that potentiates infectious disease transmission. Critically, it also corresponds with period of waning immunity from childhood vaccines and missed boosters (Wiysonge, 2012; Stockwell, 2013). Although some of these vaccines are close to clinical registration, health systems may yet face implementation challenges as they begin to target immunisation and infectious disease control among this neglected demographic (Ginsberg, Ann M. et al., 2016).

Adolescents pose unique health communication challenges due to their stage of neuro-cognitive development (Viner et al., 2011). The limbic system, linked to emotion and reward, matures ahead of the pre-frontal cortex, which is linked to planning and logic (Casey, 2008). This results in a protracted period of vulnerable decision-making in which health promotion messages that emphasise rational content and future health benefit may appeal less than the immediacy of peer- or reward-driven messages (Patton, 2012; Sawyer, 2016). Information is therefore urgently needed on how best to engage adolescents in primary prevention efforts (Patton, 2016).

1.2 Problem identification

"mHealth" refers to the integration of wireless technology into health systems for improved health outcomes and has become recognised for its positive impact on health education, communication and behaviour change (Gurman et al., 2012). With the fastest-growing use of mobile phones globally being amongst youth[1], mHealth may be especially suited to adolescents for communication of positive health-related information (Agarwal, 2015). However, adolescents have been neglected as mHealth beneficiaries; the evidence base for improved mHealth outcomes comes from target groups such as caregivers, health professionals, and adult patients, mostly in high-income countries (Free C, 2013). Moreover, the same type of intervention may not have the same outcome when applied to another condition or setting.

Public health experts have identified adolescent immunisation as potentially the most promising target age-group for elimination of infectious disease. Current focus is on immunisation coverage among this age-group with vaccines already available, requiring boosters, such as pertussis, influenza, meningitis, diphtheria and tetanus. However, identifying what has worked previously for improving health-seeking behaviour for common adolescent conditions will be vital when the long-awaited vaccines against TB, HIV and malaria become available to the public. This knowledge will be needed for effective implementation, and immunisation coverage among the adolescent demographic. Given the recent proliferation of mHealth initiatives targeted at adolescents, it would be useful to examine intervention successes and failures in order to understand what has worked, and why. These insights are expected to aid the design and implementation of adolescent mHealth infectious disease management frameworks in low and middle-income countries.

1.3 Aim and research questions

This study examined the global evidence for adolescent mHealth across selected conditions, by identifying the common features of effective interventions, in order to facilitate transfer of this knowledge to low and middle-income countries.

The following research questions were addressed using published evidence, grey literature, as well as consultation with relevant health practitioners:

1. What is the evidence for improved adolescent health outcomes using mHealth?

[1]The ages between 15-24 years.
http://www.unesco.org/new/en/social-and-human-sciences/themes/youth/youth-definition

2. How do the interventions differ in terms of:

    a) Demographics
    b) Modalities
    c) Biological/clinical outcomes
    d) Behavioural outcomes?

3. What are the implications of research question one and two for designing and implementing mHealth interventions for adolescents in LMIC's?

1.4 Rationale for a scoping review

A scoping review is a relatively new and specific style of literature review. It was first referred to in 2001 by Mays and Poppay, although largely attributed to Arksey and O'Malley in a 2005 International Journal of Social Research Methodology publication (Mays and Poppay, 2001; Arksey and O'Malley, 2005). Scoping reviews, although without exact definition or method, are done to "rapidly and systematically map key concepts underscoring a research area as well as the types and main sources of evidence" (Arksey and O'Malley, 2005). It is a method of knowledge synthesis that "examines the extent, range and nature" of existing research, so that the "findings may be summarised and disseminated". Further, they may be done to "identify research gaps in the existing literature" (Arksey and O'Malley, 2005).

Figure 1 depicts the framework for conducting scoping reviews as described in the literature (Arksey and O'Malley, 2005; Levac, 2010; Armstrong 2011). Mandatory steps taken in this review are: refining the research question (Stage 1), literature review and selection (Stages 2 and 3), data extraction (Stage 4) and concise reporting of results (Stage 5). The last stage of consultation (Stage 6), although often skipped, is vital if the review is undertaken to inform health or economic policy (Khalil, 2016).

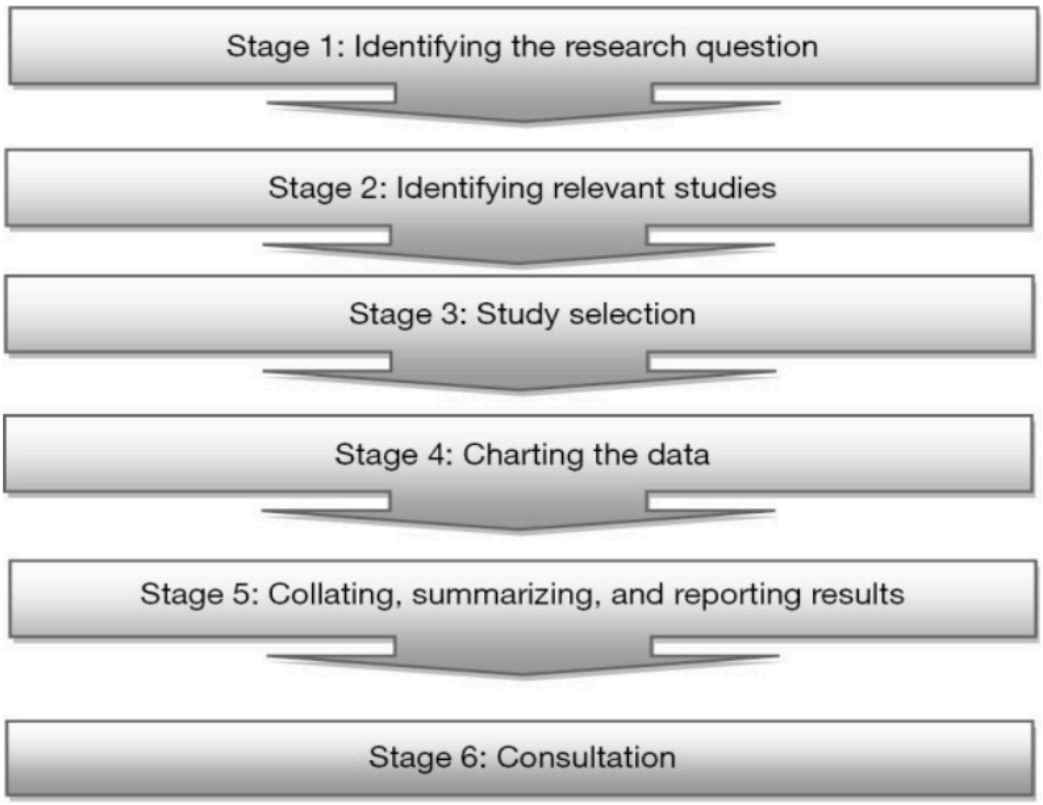


Figure 1 Scoping Review Framework

Arksey and O'Malley invited researchers using the scoping process to publish on their experiences in order to advance the methodology. Multiple researchers since then have done so, commenting on their experiences as a multi-disciplinary team, the time it took for the review, and whether quality assessment was done, among others (Levac, 2010; Daudt, 2013; Armstrong, 2011; Colquhoun, 2014; Peters et al., 2015a). The recent publications, which include a scoping review of more than 500 scoping reviews, are currently being used by the EQUATOR network to formalise scoping reporting guidelines which will be known as PRISMA-ScR[2].

Scoping reviews have been shown to be particularly useful when a research area is broad or variable, and has not yet been fully reviewed (Colquhoun, 2014; Peters et al., 2015b). They have therefore been done both to determine the feasibility of a full systematic review and in their own right to map the key concepts and evidence in a defined area or field (Levac, Colquhoun & O'Brien, 2010). A systematic review is accepted as the most rigorous form of knowledge synthesis in healthcare, as it uses "systematic and explicit methods to identify, select, critically appraise and analyse data from studies included in the review". However, systematic reviews require a certain amount of published studies (preferably randomised controlled trials) of similar quality and study setting, in order to use the statistical method of

[2]http://www.equator-network.org/reporting-guidelines/prisma/

meta-analysis to analyse and summarise the results (Guyatt et al., 2008). Cochrane-like systematic reviews may also not be the best approach for knowledge translation (Gough, Thomas & Oliver, 2012). This is especially so when examining complex and multi-disciplinary knowledge synthesis questions, and attempting to explain the framework for intervention success. Our method of choice was therefore a scoping study, as we were uncertain of the amount of published literature available to answer relatively complex research questions.

1.5 Overview of dissertation

Chapter two defines key terms, and consists of the literature review addressing adolescent development, health promotion for adolescent global health, and mHealth technology. Chapter three describes the methods used to find and select primary studies, and how data was extracted and analysed in the review. Chapter four gives the results of the included studies using the PICO framework, with reference to the participants, setting, study design and target conditions. It discusses and analyses the findings of the research, as well as the limitations thereof. The dissertation concludes with chapter five, which consists of recommendations, implications for future research and a conclusion.

Chapter 2: Literature Review

This chapter gives an overview of relevant literature related to adolescent development and mHealth, with definitions of commonly used terms. It also examines the state of adolescent global health, and concerns specific to low and middle-income countries.

2.1 The digital divide

The digital divide refers to the unequal access to technology between those of older age living in rural, less affluent communities and those who are younger, more urban, socially connected and relatively affluent (Ahmed et al., 2014, Dorsey & Topol, 2016). This often means that those who stand to benefit most from disruptive technologies, are least likely to use the technology. There remains, in the first instance, a digital divide between advanced economies and developing economies where the world is divided in terms of access to internet technology (Mechael, 2010). This is largely dependent on relative costs of data, infrastructure and ease of access. In 2017, the International Telecommunication Union (ITU), a branch of the UN dedicated to tracking access and usage of ICT globally, reported inequitable home internet access that decreased from 84% in advanced economies to 43% in developing economies. Least developed economies lagged furthest behind with only 15% home ICT access (ITU, 2017). This means that the vast majority of people in developing and least developed economies are reliant on access at work, schools or public spaces.

On a deeper level, the digital divide describes how access to information is unequally distributed as regards demographics of age, location, affluence and social standing (Ashraf, 2008; Wu, 2012). Those who are of older age living in rural, less affluent communities are 'information-poor' compared to their younger, more urban, socially-connected and relatively affluent counterparts (Ahmed et al., 2014, Dorsey & Topol, 2016). The unequal flow of information is critical when one considers that much of the available information on education, health and employment is increasingly digitally distributed. As a result, those who stand to benefit most from disruptive technology may be least likely to use it. As far back as 1997, the former UN secretary General summed this up by stating (Annan, quoted in UN, 1997):

> "The new information and communication technologies are among the driving forces of globalisation. They are bringing people together, and bringing decision makers unprecedented new tools for development. At the same time, however, the gap between information "haves" and "have-nots" is widening, and there is a real danger that the world's poor will be excluded from the emerging knowledge-based global economy."

However, as mobile phone ownership grows globally, a new digital divide is emerging in the discrepancy between mobile phone and smartphone ownership, with adults more likely to own smartphones than youth (Lenhart, 2018). Smartphones, of all the wireless technologies, may be best suited to mHealth interventions as they are capable of supporting interactive websites, video, and mobile applications, while being compact and portable. In a recent global survey of adult smartphone ownership, none of the emerging and developing economies from the Africa region had ownership above 40% (ITU, 2017). Japan was the only one of eleven advanced economies with less than 40% smartphone ownership among adults (Lenhart, 2015). While 70% of the world's youth are online globally, it remains that 9 out of 10 adolescents without any internet access live in Asia, Africa or the Pacific region (ITU, 2017).

2.2 mHealth

Information and communication technology (ICT) through mobile phones, the internet, social networking sites and instant messaging have provided means to an expanded social environment (Black, 2011; Buhi, 2013). ICT disrupts the need for transport, access and proximity for communication or entertainment. Its potential in reaching vulnerable populations has led to rapid integration in health care delivery, especially in LMIC's where mobile phone ownership has grown the most in the last decade (Wu & Raghupathi, 2012).

This integration of mobile or wireless technology into healthcare and health systems for improved delivery, health promotion and outcomes is also known as mHealth (Curioso & Mechael, 2010). mHealth may include health information systems; clinical decision-making tools such as software applications or 'apps'; reminder services; short message services (SMS) and telephone calls or any other wireless communication for the purpose of improving health implementation and outcomes (Aranda-Jan, Mohutsiwa-Dibe & Loukanova, 2014; Fortuin et al., 2016). Smartphones, of all the wireless technologies, may be best suited to mHealth interventions as they are capable of supporting interactive websites, video, and mobile applications, while being compact and portable.

mHealth has been shown to be effective for a range of improved health outcomes that include disease surveillance, health information for patients, supply chain management, vaccine implementation and provider decision aids (Devi et al., 2015; Free C, 2013; Kalan et al., 2014; Oyo-Ita et al., 2016; Wiysonge et al., 2012). It has also been shown to be effective for adult HIV and TB disease management through improved adherence, visit reminders, education, communication of results, data collection and follow-up care (Devi et al., 2015). Adherence rates required to yield viral suppression and reduce drug resistance in conditions such as HIV and TB are 95% and 90% respectively. This poses immense challenges in

resource-limited settings, but may be viable due to the growing access to mobile phones globally and the cost- and time-saving benefits that have been shown with mHealth (Dempsey & Zimet, 2015). Owing to its low cost, ease of use, growing mobile phone ownership, and ability to deliver health messages directly to the target patient, the mHealth platform of engagement may be uniquely placed to impact adolescent health attitudes, behaviour and outcomes, even in rural areas (Buhi, 2013).

Despite widespread acceptance of mHealth's positive impact, it remains unclear what determines success in one country or disease setting, and failure in another. For example, the success of two-way SMS messaging for improved adherence to antiretroviral treatment reported in the WelTelKenya trial (Lester et al., 2010), has been replicated in a Canadian setting (King et al., 2017). Yet a similar, well-conducted randomised trial found no evidence for SMS messaging for drug-sensitive tuberculosis treatment adherence (Nglazi et al., 2013). This mHealth evidence base is similarly inconsistent for adolescents. For example, a US study of brief telephone counselling for adolescent girls aged 14-19 years showed sustained reductions in STI's up to 36 months after the intervention (DiClemente, 2014). Yet a similar telephone intervention for contraception adherence showed no effect (Trent, 2015). mHealth also remains under-utilised and is rarely scaled to capacity in low and middle-income countries (Brinkel et al., 2014; Falzon et al., 2016; Hall et al., 2014).

2.3 Adolescent development, communication and mHealth

The World Health Organisation (WHO) defines "adolescents" as those aged 10–19 years, and "youth" as those aged 15-24 years (United Nations Department of Economic and Social Affairs, 2013), definitions to which this report will adhere. The transition from adolescence into healthy, productive adulthood requires access to health education, quality appropriate health services, and supportive home and community environments (Laski, 2015). However, negative attitudes towards exercise, nutrition and risk behaviour may persist into later life, adding to the global burden of chronic disease and disability, instead. In addition, undetected health conditions such as STI's, depression, substance and tobacco use directly affect their health and the early childhood development of their potential children (Laski, 2015; Patton et al., 2012). Addressing their wellbeing becomes vital as this enables independence, completion of schooling with better employment options, and healthy relationships (Gore et al., 2011, Sawyer et al., 2012). Furthermore, encouraging positive adolescent health behaviour (such as on-time vaccination, safer sex practice, early recognition of infectious and mental illness) before complications arise is therefore essential.

Adolescents pose health systems challenges in terms of engagement and positive health knowledge (Viner, 2011). In addition, they contribute unique communication challenges due

to their stage of neuro-cognitive development (Viner et al., 2011; Patton, 2012). The limbic system, linked to emotion and reward, matures ahead of the pre-frontal cortex, which is linked to planning and logic (Casey, 2008). This coincides with wide variations in peak levels of Dopamine, a regulatory neurotransmitter which balances activity between the various areas of the brain (Casey, 2008). Multiple social cognitive and functional brain imaging studies have shown that adolescents make clearer decisions when situations are hypothetical (Steyn, 2005 quoted in Casey, 2008). In contrast, when making decisions that involve conditions of stress, emotion or personal relevance, adolescents are more likely to respond according to their feelings (Steinberg, 2005 quoted in Casey, 2008). There is thus a difference in how adolescents perceive information which is "personal" to that which is "general or rational". This difference in perception and processing is consistent with the adolescents' relatively mature and dominant limbic system, yet still-developing prefrontal cortex. They may therefore make "poor decisions", even when "knowing better", in emotionally-charged situations. Eventual maturity of the pre-frontal cortex may be anywhere up to 25-30 years of age, with an interim protracted period of vulnerable decision-making and potential risk-taking behaviour (Casey, 2008). This highlights the importance of perceived stigma and peer group acceptance in this period of emotionally-reactive decision-making until the prefrontal cortex matures (Patton, 2015).

From a health promotion and delivery perspective, this means that rational content of communication may appeal less than peer- or reward-driven messages of personal benefit. The wireless, portable capabilities of mobile phones and smartphones allow for individualization, all of which have been attributed to the growing evidence for mHealth success. These capabilities may include targeting of messages (i.e. specific content sent to specific groups), tailoring (i.e. content relevant only to pre-specified goals or behaviours), personalization (i.e. sending information or content aligned to how one self-identifies by use of personal details, culture or group membership) as well as scheduling of message delivery and content to suit individuals (Reback et al., 2012). All of these features work to increase the personal relevance and appeal of health messages; it is postulated that when messages are perceived as personally relevant, they may be effective at persuading positive health behaviours. Smartphones are especially capable of supporting tailored mHealth interventions by accommodating web browsing, video features, chat functions and application software that older mobile phones cannot.

As adolescents globally (regardless of country per-capita income or location) are the group with growing access to wireless technologies, these are theoretically well-suited for communication with them. Wireless technologies include WAP-enabled mobile phones, smartphones, tablets and laptops (Amacizia, 2013; Agarwal et al., 2015). Furthermore,

mHealth interventions transcend the need for in-person clinic attendance and may be especially suited to adolescents due to their convenience, confidentiality and potential personalisation in relaying health information. These aspects of mHealth may be especially beneficial in reaching males, younger adolescents before sexual debut, and those in LMIC's i.e. those whose high burden of disease has been least impacted by global public health initiatives (Viner, 2011; WHO 2011).

2.4 The state of adolescent global health

In much the same way as countries have neglected the future economic potential of their adolescents over the past 50 years (Das Gupta et al., 2014), adolescents have been overlooked in global health initiatives due to the assumption that it is the healthiest period of their life (Blum, 2004). For example, half of all mental health disorders in adulthood start by age 14, but most cases are undetected, and therefore remain untreated. Those adolescents with undiagnosed mental conditions are more at risk of being expelled or suspended from school, falling pregnant before completing their education, and engaging in criminal behaviour and illicit drug use (WHO, 2014c; Gore et al., 2011). Despite the belief that they are 'healthy', adolescents face daily health risks from potentially unprotected sexual debut, social groupings potentiating infectious disease transmission, missed mental health diagnoses, and exposure to maladaptive coping strategies such as substance and alcohol use.

Around 1.2 million adolescents died in 2015, more than 3000 per day. Most of these deaths were preventable or treatable (Mokdad et al., 2016; WHO, 2017). African and South-East Asian LMIC's together constitute half of the global adolescent population, and also carry abouttwo thirds of all adolescent lives lost to death and disability in 2015 (WHO, 2017). Rates of adolescent mortality ranged from 243 deaths per 100 000 in African LMICs, to 24 per 100 000 in high-income countries. Road traffic accidents caused the most adolescent deaths globally in 2015. Violence was the leading cause of death among older adolescent males, whereas older girls died from pregnancy-related complications. Depression ranked third as a cause of illness and disability among adolescents overall, and suicide was ranked third as a cause of death in older adolescents aged 15-19 years.

More than 2 million adolescents are HIV-positive, and contrary to the decline in adult infections, adolescent HIV and STI infections are rising (WHO, 2017). US sexual health statistics show that adolescents account for 50% of all new STI's diagnosed (Cornelius et al., 2013). Most HIV-infected adolescents live in Sub-Saharan Africa, yet only 10-15% of them are aware of their HIV status. Minority Black, Hispanic and male adolescents constituted 50% of all new HIV infections in the US ten years ago, and this has not reduced (Besoain,

2015; Gold, 2011). A 2008 Centres of Disease Control publication reported that younger men-who-have-sex-with-men (MSM) had a much higher false assumption of their own untested HIV status (Oluoch et al., 2015). Seventy-five percent of eighteen to nineteen year-old MSM who believed themselves to be HIV negative, tested HIV positive. STI and HIV prevention curricula delivered in face-to-face sessions have been implemented effectively to reach adolescents in small groups and schools (Barry, 2016). However, the reach of this information needs to be extended outside of middle-school settings (Champion, 2017; Barry, 2016). Target groups also need to include younger adolescent age groups; up to 70% of sexual debut among females occurs due to coercion, and under the age of fifteen years (Mustanski et al., 2014).

The WHO's Regional Strategic Plan for Africa (WHO/AFRO) and the Global Alliance for Vaccines and Immunisation (GAVI) have prioritised immunisation coverage, new vaccine development and health innovation in African countries (Bangure et al., 2015). Immunisation coverage refers to the ratio of vaccinated to unvaccinated individuals. By reducing the number of currently infectious people through reduced transmission, it indirectly protects even those with immature immune systems (elderly, infants, pregnant and immuno-suppressed). Unfortunately, average coverage for various countries remains below most vaccine-preventable disease programme targets of 85-90%. Furthermore, decades have passed with the focus of global health bodies on immunisation coverage on infants and children.

Adolescents were included in the WHO Global Strategy Report for the first time as recently as 2016 (Kuruvilla, 2016). This growing global commitment has been underpinned by the realisation that adolescents constitute the largest global demographic, about 1.2 billion people (WHO, 2017). As such, an effective adolescent immunisation programme would return huge dividends in reduced transmission of infectious disease. Adolescent health promotion efforts may reduce the growing burden of non-communicable disease and disability (Patton et al., 2016). When viewing the period of adolescence as a tipping point for chronic disease and disability later in life, its importance for public health is clear as regards early substance use, risky sexual activity and STI's.

Little attempt has been made to facilitate knowledge transfer from the mHealth interventions undertaken in high-income countries focused predominantly on lifestyle and mental health concerns to pressing LMIC needs such as infectious disease control. As regards infectious diseases, systematic reviews have addressed HIV and TB medication adherence among adults (Kalan et al., 2014; Smillie et al., 2014) or immunisation among children and infants. One recent review (Grist et al, 2017), addressing mHealth for adolescent mental health

found insufficient evidence for efficacy, given the limited sample sizes in 24 studies with variable reporting quality. Conversely, a growing number of recent systematic reviews have addressed adolescent lifestyle factors, diet and physical activity as modifiable risk factors for later chronic disease. Here, the evidence base is largely positive, is from well-reported studies although reporting periods could be extended (Rose, Barker et al 2017; McIntosh, 2017). More pertinently, for the adolescent HIV, TB and malaria vaccines pending registration, no such published evidence exists outside of ongoing clinical trials. This gap in the evidence base may delay roll-out once such vaccines are registered, as health systems may find it challenging to target adolescents directly.

A recent review conducted in Kenya has focused on knowledge transfer from HIV to chronic disease (Mbuagbaw, 2015). The commonalities between the disease conditions, setting and health infrastructure served as a basis for knowledge transfer from the extensive HIV evidence base to chronic disease, which is less well-researched in LMIC's. By combining this element of commonality between the adolescent conditions, and the scoping ability to rapidly map the literature, we hope to derive meaningful insights for knowledge transfer to implement the adolescent vaccines pending registration in low and middle-income countries.

Enabling positive adolescent health behaviour could have significant impact on such varied health outcomes as mental and reproductive health, infectious disease transmission, substance use and self-harm. Understanding and promoting health behaviour among adolescents is therefore essential because this group constitutes the future health and economic potential of especially low and middle-income countries (UNICEF, 2002; Wiysonge, 2012).

Chapter 3: Methods

Conventional systematic reviews risk excluding large bodies of evidence due to stringent inclusion and exclusion criteria (Leon, Schneider & Daviaud, 2012). Our approach was therefore a scoping review, in order to include a broad range of relevant evidence for policy makers, disease control planners and health practitioners to understand and effectively implement adolescent mHealth interventions in their particular context.

3.1 Criteria for considering studies for this review

Our initial search included all studies targeting adolescents directly for a biological or behavioural health outcome, where the primary component being evaluated was an mHealth intervention. Behavioural outcomes described measures such as self-efficacy, therapeutic alliance with health providers, adherence to medication and change in risk behaviour; these were subjective and largely self-reported. Biological outcomes referred to clinical tests for diagnosis or monitoring of conditions, clinical cure or relapse rates, change in prevalence of the condition, on-time appointments and other findings that may be measured objectively.

We examined mHealth interventions targeting the most common adolescent conditions, stated as being the four most common causes of disability and death in male and female adolescents according to the 2015 Global Burden of Disease Study (Mokdad et al., 2016). Target conditions covered the three broad categories of (i) reproductive health, (ii) mental health and injury, and (iii) infectious disease. The final target conditions differ from those stated in the protocol, as they were amended based on results of the initial title-abstract screening. Certain keywords returned high numbers of studies on participants outside of our defined age range without any studies being eligible on title-abstract screen. Examples of such keywords are ‘anaemia’, ‘smoking’, ‘malaria’, ‘PTSD’, ‘bipolar disorder’ and ‘anxiety’. These keywords were thus omitted in later search iterations. Table 1 summarises the changes through iterations, acceptable in the scoping process (but less desirable in systematic reviews). The first column contains keywords as originally stated in the study protocol and the last column shows those terms omitted during the search iterations. The central column contains the final search strategy target conditions. Studies with additional non-mHealth measures (such as health visits or counselling) that differed between the control and intervention groups, or used non-portable devices, were also excluded in later iterations. The initial and final search strategy may be found in Appendix 1.

Table 1 Summary of the process of refinement of target conditions

All initial target conditions by category	Target conditions included in final search strategy	Target conditions omitted in the final search strategy
<u>Infectious Disease:</u> HIV TB Malaria Vaccine-preventable disease (VPD): influenza VPD: Human papilloma virus(HPV)	HIV TB VPD: Influenza VPD: HPV	Malaria
<u>Reproductive health</u> Curable STI's Contraception adherence Safer sex practice		
<u>Mental Health and Injury:</u> Depression Suicide Anxiety Bipolar Disorder Substances other than tobacco Smoking (tobacco) Road traffic accidents	Depression Suicide Road traffic accidents Substances other than tobacco	Anxiety Bipolar disorder PTSD Smoking (tobacco)
<u>Other Conditions</u> Anaemia		Anaemia

3.1.1 Types of Studies

Primary studies included were experimental (RCT's, quasi-experimental), mixed-methods surveys or observational (descriptive or analytical) study designs. Purely qualitative studies were excluded to facilitate potential meta-analysis. Systematic reviews were excluded (as this was not a review of reviews), but their references were checked to ensure that no relevant primary studies were missed. No primary study population was included twice, but all eligible studies were read in conjunction with qualitative publications on the same study population. This was vital for understanding features such as participant demographics,

setting, message frequency and intervention technology; aspects sometimes not fully reported, but essential for knowledge transfer.

3.1.2 Types of participants

Primary studies included adolescents of any gender, location, or ethnicity with access to a mobile phone or wireless device used for a health-related outcome. The intervention had to target adolescents themselves; not schoolteachers, caregivers or other health providers. Included studies were required to report clearly on the mHealth modality used, and state the study objectives a priori.

3.1.3 Types of interventions

mHealth modalities included were applications, social networking sites, interactive websites, text messages, web-based interviews and counselling, compared to standard of care or another mHealth intervention. Although our initial intention was to include all wireless communication for the purpose of improving health implementation and outcomes, iterations through the scoping stages led us to exclude telephone calls, as they were not explicitly wireless technology and it proved difficult to objectively assess the features of a telephone call as an intervention.

3.1.4 Review outcomes

The outcome of this review is an assessment of whether mHealth improves management of the most common global adolescent conditions. This knowledge will inform how mHealth may be implemented for infectious disease management in low and middle-income countries. Secondary outcomes include identifying further research needs, and identifying opportunities for scaling up mHealth interventions in LMIC's.

3.2 Search Strategy

Primary studies published in peer-reviewed journals with no language limitation, were extracted from the following electronic databases: PubMed (NLM), Scopus, CINAHL, EBSCO Host, Africa-Wide, PsychINFO, Web of Science (Thomson Reuters), Cochrane Library (including Cochrane Central Register of Controlled Trials (CENTRAL), Academic Search Premier, Communication and Mass Media Complete, Computer and Applied Sciences Complete and NHS Health Technology Assessment Database. Our search period was January 1990 to 30 November 2017.The initial search date was 27 May 2017; the final search for updates was run on 10 December 2017.

The studies were selected using predefined search terms comprising both free text word and medical subject heading (MeSH) for PubMed, and adapted appropriately for other

databases. The search terms described mHealth, the adolescent population, and the amended target conditions. The search strategy was developed in consultation with a health sciences information specialist, and updated before the final search. The reference lists of identified systematic reviews were hand searched for relevant articles; NCBI citation index was used to identify relevant articles until no new citations for the search period were found. Unpublished sources were evaluated in the form of the WHO institutional website, as well as conference proceedings and abstracts.

Criteria for study inclusion at the level of full-text review were:

i) the intervention must target a "health outcome" which may be biological, subjective, or a health behaviour for at least one of the pre-defined conditions;
ii) adolescents must be targeted directly, not through parents/caregivers/healthcare workers;
iii) at least 50% of the sample must be between the age of 10-19 years; if a mean outside of this age range was reported the study authors were contacted to get age-disaggregated data;
iv) experimental, mixed-methods or observational study designs; and
v) conference abstracts and posters may be included if sufficient information about sample and findings are reported;

An eligibility prompt tool was developed by the author based on earlier iterative searches, after noting incomplete reporting of sample ages, effect sizes and intervention features (Appendix 2).

3.3 Study selection

All articles identified in the search were screened by title and abstract and the full-text was drawn if relevant, or more information was needed. Endnote software manager was used to remove all duplicate material. The author and a second reviewer met for abstract and text review, and any disagreements were carried forward to the next round of screening. Disagreements were adjudicated by a third reviewer.

3.4 Data extraction and management

A data extraction form (Appendix 3) was piloted and refined on four primary studies across the various disciplines. The descriptive and outcome data were extracted by the author and checked by her primary supervisor, with any studies not meeting full consensus moved ahead to full-text review. The data extracted were: author, title, year of publication; number and type of included participants and subgroups as reported; target condition and countries

in which the primary studies were done; mHealth modality and wireless technology targeted; reporting quality regarding allocation concealment, blinding of outcome assessors, loss to follow-up, and other sources of bias.

The author entered the final data into statistical software package (Cochrane Collaboration Review Manager Version 5.3). All data entries were then crosschecked independently by the information specialist before analysis.

3.4.1 Dealing with missing data

Authors of ten primary studies were contacted by email for clarification of age-disaggregated data, methods and details on how the intervention was accessed. Six studies were excluded due to non-response despite multiple attempts.

3.4.2 Assessing methodological quality

The quality assessment forms were piloted on four selected studies. The author and the information specialist independently assessed quality using an amended Cochrane Risk of Bias tool (Higgins, 2011). Blinding of interventions for outcome assessors was omitted from the standard Cochrane Risk of Bias tool, as it was not possible to assess allocation bias for most of the mHealth interventions.

3.5 Data Analysis

Meta-analysis, the statistical process of pooling comparable results to determine effect size, was undertaken. Pooling of data was conducted only on studies with low heterogeneity, as defined by an I-squared value of less than 50%. Heterogeneity refers to the degree of clinical and methodological variability between studies. It may be assessed as absent (below 25%), low (25-50%), medium (50-75%) or high (Alonso-Coello et al., 2016). Where studies show high heterogeneity once pooled, possible reasons for this are discussed. As the effect sizes reported between studies varied greatly, we grouped the effect measures by outcome variable. For dichotomous outcomes, we expressed the outcomes as risk ratios (RR) with a 95% confidence interval. Continuous outcomes proved most challenging in analysis as they were reported in various ways. Where possible, where the same scale was used and post-intervention means and standard deviations were reported, the mean difference (MD) and 95% confidence interval was calculated using RevMan calculator. Where different scales were used to report effect sizes for the same outcomes, the standardised mean difference (SMD), was calculated. To check the results, the data was entered separately into statistical software programme, Comprehensive Meta-Analysis version 3.1 (Borenstein et al., 2009).

The measures of effect per intervention are shown as a forest plot with 95% confidence intervals, where a p value of below 0.05 denotes statistical significance. Analyses were conducted using the random effects model unless specified otherwise, as it was unlikely that conditions were exactly the same across the various studies. Subgroup analyses were conducted by gender, sexual activity, target condition and modality of intervention.

Chapter 4: Results

This section gives an overview of the studies included in the review, and highlights selected target conditions and subgroups (based on age, gender, and time points), before summarising the evidence with reference to the original research questions. A detailed narrative account of each individual mHealth intervention is beyond the scope of this thesis.

4.1 Study flow

We obtained 3498 studies in the initial search, which led to the iterative changes described previously in Section 3.1.

A total of 452 studies were identified in the revised search. Four hundred and forty-two were published studies, and six studies were found through conference databases and grey literature. Four further studies were identified by hand-searching reference lists and systematic reviews. Two-hundred and forty-eight studies were screened by title-abstract, after removal of duplicates.

Sixty-eight full-text articles remained after screening and were assessed for final eligibility. Forty-seven articles were excluded for the following reasons: non-adolescent study population (n=23), insufficient detail reported on health outcomes (n=8), other target condition (n=5); use of non-wireless technology (n=6); and other study designs (n=5).The studies retrieved by hand-searching the reference lists of systematic reviews found in the search were excluded due to participant ages.

Twenty-two primary studies remained, which met all eligibility criteria. The majority of studies were experimental studies with small sample sizes consistent with pilot studies, predominantly in sexual and reproductive health. Twelve studies were RCT's; there were equal numbers of observational and quasi-experimental studies (n=4), and two mixed-methods surveys.

Figure 2 depicts the study flow of screening, study selection as well as the number of publications extracted and retained at each step of the search (Moher et al., 2015).

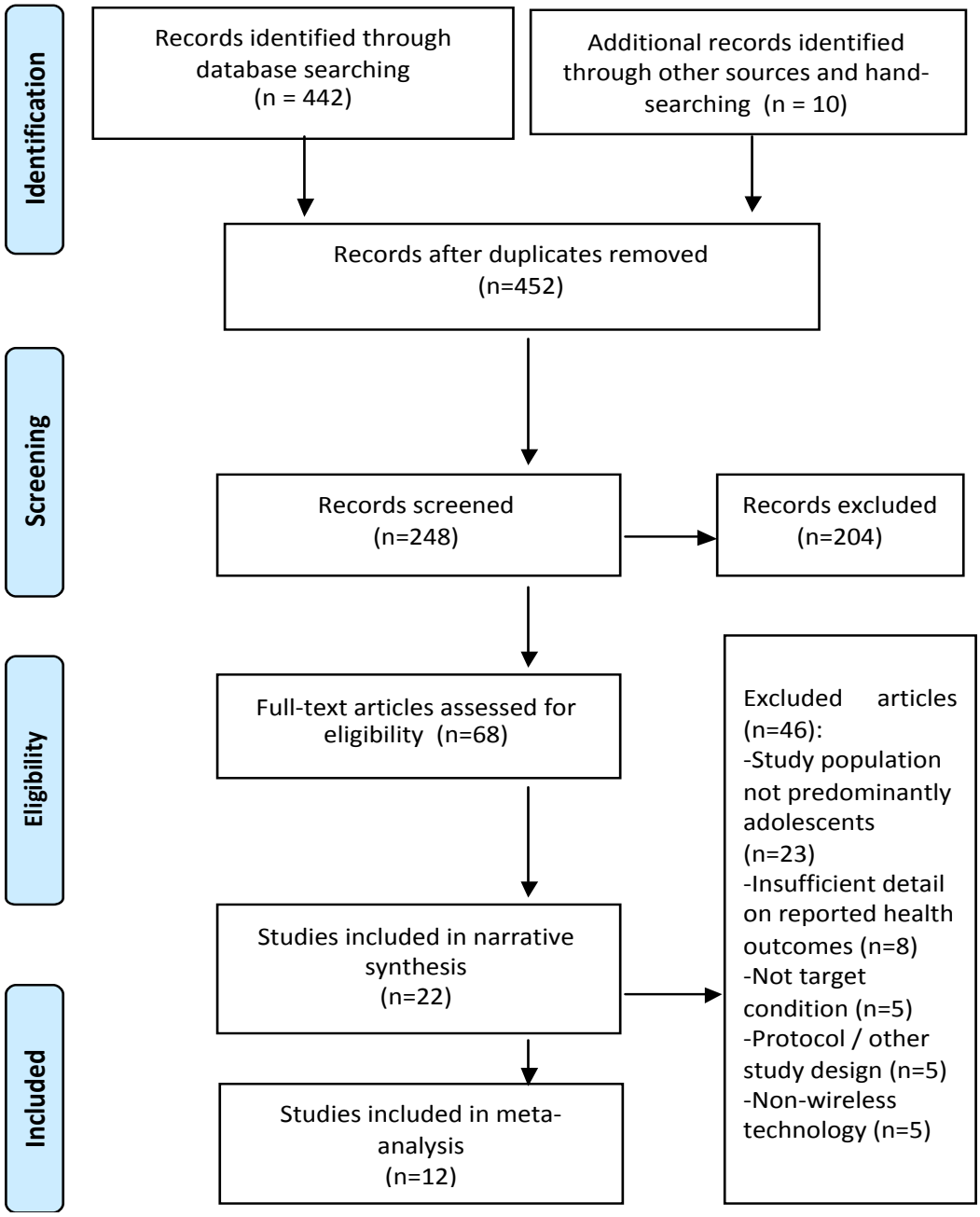


Figure 2 PRISMA Diagram (Moher et al., 2015)

Table 2 outlines the target conditions represented in the search results, and those amenable to narrative or statistical synthesis methods.

Table 2 Included studies: summary by target condition and type of evidence synthesis

Meta-analysis	Narrative synthesis	Conditions not represented in evidence synthesis
Reproductive health (n=6) Ybarraet al (2017) Lim et al(2012) Rokickiet al(2017) Scull et al (2017) Bull et al (2012) Trent et al(2015) Depression (n= 5) Ranney et al(2016) Manicavasagar et al(2014) Narring et al(2013) Branson et al (2013) Kobak(2015) Substances other than tobacco (n=1) Haug (2017)	Reproductive health (n=5): Cornelius et al (2013) Matheson et al (2014) Brayboy (2017) Fiellin et al (2017) Juzang et al (2011) Substances other than tobacco (n=5) Jeffries et al (2017) Weitzel et al(2007) Larimer (2009) Tahaney et al (2017) Montanaro et al (2015)	Infectious disease – TB Infectious disease – HIV * Suicide Road traffic accidents Vaccine-preventable disease: HPV Vaccine-preventable disease: Influenza

4.2 Details of included studies

Twenty-two studies were included. All were published in English between 2007 and 2017. These studies covered conditions such as: mental health, substance and alcohol use, and infectious disease. They reported on knowledge, behavioural, or biological outcomes, or combinations thereof. Knowledge of STI's and substance use was assessed by repeat questionnaire administered by primary study authors, with improvement reflected by an improved test score. Knowledge assessment studies totalled seven in number, and were excluded from the meta-analysis, due to published evidence suggesting that improvements in knowledge do not consistently lead to improved behavioural outcomes or medication adherence (Kim et al., 2015). Improvements in risk behaviour and testing, as well as compliance with scheduled appointments and medication, were grouped as behavioural outcomes of interest. Biological outcomes reported included pregnancy, blood alcohol levels, and change scores on validated depression and wellbeing scales.

Of the twenty-two eligible studies, the vast majority (n=11) were sexual and reproductive health publications. A total of twelve studies were pooled in the meta-analysis, as they reported clearly on behavioural and biological outcomes required for answering research question 2. Similarly, the majority of these were on sexual and reproductive health (n=6) and mental health (n=5) topics.

Table 3 shows the target conditions, intervention details, and key outcomes of all eligible studies selected for evidence synthesis (both narrative synthesis and meta-analysis, or statistical synthesis). The quality assessment based on the amended Cochrane tool is not reported in the evidence profile as allocation concealment was impossible due to the nature of the mHealth interventions. This did not detract from the scoping process as quality assessment is not mandatory, unlike for a systematic review. The majority of studies reported different methods of outcome aggregation and metrics, and thus these were not pooled.

The table follows the classification of mental health, substance use and reproductive health for knowledge, behavioural and biological outcomes, shown in bold text. Three studies reporting on knowledge exclusively (namely Juzang et al., 2011; Brayboy et al., 2017; Montanaro et al., 2015) have not been elaborated on beyond this table.

Table 3 Characteristics of included studies (* denotes studies on knowledge only that are not further considered).

Study author, date, and setting	Age range and number of participants	Target condition category /details of intervention and control groups	Outcomes
Brayboy* 2017 USA	Mixed methods survey conducted on adolescent girls aged 12-17 years	Reproductive health: *GirlTalk* smartphone application with culturally sensitive avatar to teach sexual health education to adolescent girls	Modest improved **knowledge on STI**, anatomy, and relationships components only
Bull et al 2015 USA	Mixed methods study on adolescents between 16-25 years, mean age of 19 years	Reproductive health: Facebook page link to intervention website *JustUs* compared to an information-only popular culture website	Statistically significant **condom use** in intervention group which was not sustained at 2-month follow-up, also reported on reduced **risky sexual behaviour in terms of condom use.**
Juzang et al* 2011 USA	Quasi-experimental trial in Black sexually active adolescents between 16-20 years in Philadelphia, n=60, using their own phone. Intervention group mean age 19, control age 17 years	Reproductive health: Three texts per week for 12 weeks on **HIV risk behaviour** and **sexual health,** were sent to the intervention group. The control group received placebo text messages on nutrition.	Intervention group participants showed significantly greater **HIV knowledge** and a trend to monogamy at 3 months. No difference in protected sex acts and delayed sexual debut at 3 months.
Haug 2017 Switzerland	Parallel group RCT among 1041 high-school students, mean age of 16.9 years. 494 students in control; 547 in intervention group.	Alcohol use:*MobileCoach Alcohol* is an automated intervention of online feedback and individually tailored text messages addressing social norms, outcome expectations, motivation, self-efficacy, and planning processes. Only the alcohol-related integrated intervention outcomes were reviewed.	Reduced **risky single-occasion drinking (RSOD) prevalence** in the intervention group by 5.9%; control RSOD prevalence increased by 2.6% over 3 months. No difference was seen in volume of alcohol consumed or estimated peak blood alcohol levels.
Larimer 2009 USA/Sweden	Observational study with 2236 participants (852 in USA; 1384 in Sweden; 731 received PFI). 30% of USA sample and 52% Swedish sample classified as risky drinkers according to AUDIT-C.	Alcohol use: To evaluate a web-based personalised feedback intervention (PFI) in high school seniors 17-19 years old. Participants completed a survey 1 week after PFI, and at 6- and 12- months follow up. 6-month outcomes reported. No clear follow-up publication found for 12-month outcomes.	Those in PFI group drank **significantly less alcohol per occasion**, had **lower blood alcohol concentration** (typical and peak) and drank on fewer occasions than those who did not receive the PFI. Effect sizes ranged from d = 0.12 to d = 0.22. No significant interaction seen from country setting in sensitivity analysis.
Lim et al 2012 Australia	Observational study with 994 participants aged 16-29 years recruited at a music festival; 58% of sample16-19 years, with clear reporting of age disaggregates.	Reproductive health: Protected sex, **STI testing** and **knowledg**e, and change in **health provider relationship** measured at 6 and 12 months after intervention.The 12-month intervention included SMS (catchy sexually transmissible infections prevention slogans) and emails.	Outcomes measured were health-seeking behaviour, condom use, risky sexual behaviour, STI knowledge.At 12 months, intervention group STI knowledge was higher for both males and females; Women (but not men) in the intervention group were more likely to have had an STI test or discuss sexual health with a clinician.

Kobak et al 2015 USA	Quasi-experimental study with 65 adolescents aged 12-17 years. Refresher online CBT teaching for consulting therapists, who recruited participants with depression from their practice and assessed them 12 weeks after initiating treatment. Clinicians in the standard care arm also recruited patients initiating treatment for depression from their clinical practice, and treated them for 12 weeks using usual care.	Depression: Three components, each using technology; part 3 only is assessed, as an add-on to conventional treatment:(1) CBT online therapist training and (2) in-session tablet teaching CBT skills (both used by therapist);(3) SMS for between-session homework reminders and self-monitoring, directed at the adolescent. Two daily texts, with timing agreed upon beforehand: initial reminder text followed by one later to record results. Reports of all in- and outgoing texts sent to therapist before the next session. Individualized text messages were integrated into treatment as a between-session resource for participants.	Effective in improving **symptoms of depression** in adolescents. User satisfaction with the technology was high for both therapists and patients. The **therapeutic alliance** was stronger in the cohort receiving the technology-enhanced intervention. Effect sizes comparing clinical outcomes between CBT and TAU were small. Measures of symptomatic improvement were greater on all outcome measures for the CBT arm, but none reached statistical significance.
Manicavasagar et al 2014 Australia	RCT feasibility in 235 adolescents aged 12-18 years.	Depression: Intervention is online delivery of an interactive positive psychology program, called *BiteBack*. **Wellbeing** and change in **depression** score was measured at baseline and 6 months after using *BiteBack*.	Intervention participants had significantly improved depression and stress scores at 6 weeks post-intervention. None of these significant differences were found in the control condition from pre-assessment to post-assessment.
Ranney et al 2016 USA	Quasi-experimental study with 16 adolescents aged 13-17yrs with non-clinical depression.	Depression: Depression and violence self-report measured at baseline and 8 weeks. Intervention was cognitive behavioural therapy tool for depression prevention.	Improved **depression and wellbeing scores** after initial and 8 week follow-up, no change to **violence self-report**
Montanaro et al* 2015 USA	Ages 11-14 years, 333 participants in RCT. 166 in intervention, 167 in control. Analysed only 166 participants in intervention group.	Substances other than tobacco: Videogame *PlayForward* developed for risk reduction in substance use. Participants played the intervention game or a set of attention- and time-matched control games for a maximum of 16 hours over 6 weeks.	Mastery of the game rather than time spent using intervention was significantly correlated with **improved substance knowledge** at 3 and 6 months. Later publication (Fiellin et al, 2017) examined full study sample for sexual health behaviour after 1 year.
Rokicki et al 2017 Ghana, Africa	Cluster–randomized controlled trial among 756 female students aged 14 to 24 years in Accra, Ghana, in 2014.	Reproductive health: Unidirectional and bidirectional text messaging-based interventions for **sexual health**. The unidirectional intervention sent participants text messages with reproductive health information. The interactive intervention engaged adolescents in text messaging reproductive health quizzes. Control group participants received weekly placebo messages on malaria.	The unidirectional and the interactive programs significantly lowered the odds of **self-reported pregnancy** by 86% in the adjusted models (odds ratio [OR] = 0.14; 95% CI = 0.03, 0.71) and 85% (OR = 0.15; 95% CI = 0.03, 0.86), respectively. There were significant improvements in **knowledge** at 3 months that were sustained after 15 months for both uni- and bi-directional programmes. The bi-directional

			programme was significantly more effective than the one-way programme.
Scull et al 2017 USA	A cluster randomized controlled trial (RCT) design among 35 adolescents aged 18-19 years.	Reproductive health: Use of intervention *MediaAware*. **Knowledge of STI's** and change in **sexual risk behaviour** measured at intervention-end.	Compared to the control group, both men and women in the intervention group reported fewer instances of oral, vaginal, or anal sex with someone who has not been tested for STIs or whose STI status is unknown. At post-test, the intervention group participants scored significantly higher on knowledge scores than the control group.
Tahaney et al 2017 USA	College undergraduate students, with high-risk drinking behaviour as defined by authors, were recruited online (N = 113) and randomized to Assessment only (AO), web intervention (WI) or WI plus text messaging (WI plus TXT).	Alcohol use: Commercially-available web-based intervention (*eCHECKUP TO GO-alcohol*) that provides individualized feedback on drinking behavior, such as drinking norms, costs and consequences of use, alternative activities, and change strategies. WI + TXT condition received one text per day over the month between baseline and follow-up, delivered before anticipated weekend drinking episodes.	WI + TXT condition showed significantly less weekend drinking than those in the AO and WI group. The WI + TXT and WI only groups showed comparable, significantly **fewer heavy drinking episodes** compared to AO. No differences were observed on alcohol-related problems. No group sizes reported and only adjusted effect size. Plot digitizer used to impute values into RevMan.
Weitzel et al 2007 USA	Forty college students randomised to either intervention or control.	Alcohol use: Feasibility and short-term outcomes of tailored text messaging intervention. Intervention group additionally received text messages tailored to reported behaviour, self-efficacy and outcomes expected regarding alcohol-related consequences.	Intervention group participants reported significantly **less binge drinking**(p=0.02) than control on-study. Little detail on the text message frequency. Mean duration of receiving messages was only 14 days. Unable to contact author for raw data.
Ybarra et al 2017 USA	RCT on male 14 to 18 year- old gay or bisexual participants recruited via Facebook.	Reproductive health: Interactive website *Guy2Guy* (G2G) used together with text messaging for 5 weeks. Between 5-10 text messages delivered daily, with a 1-week booster was delivered after 6 weeks. Control group received an attention-matched “healthy lifestyle” (e.g. self- esteem) programme. **Protected sex** acts, **abstinence** and **HIV testing** measured at 3 months after intervention-end.	90 days post-intervention participants were significantly more likely to report getting an HIV test (adjusted odds ratio = 3.42, P = .001) and CSAs were significantly lower for those in the intervention versus control at intervention end (incident rate ratio = 0.39, P = 0.04).

Narring et al 2013 Switzerland	Participants were 12-24 years, with a mean age of 17 years in the setting of a primary care youth clinic. 462 adolescents were randomised to mHealth intervention, 529 in control group.	Reproductive and Mental health:'Easy Smart Care', a software product developed by EasyMed Services Inc. Phone numbers were entered into a secure web platform which automatically sent generic text-message reminders between 08:00 and 11:00 the day before the planned appointment, including on Sundays. The text, written in French, stated: 'You have an appointment on... (date) at ... (time) with Dr ... (name) Please answer NO if you do not intend to come'. Patients in the control group received no reminder.	Assessed clinic attendance at gynaecology and mental health youth outpatient clinic. The outcome was the proportion of unexplained missed appointments, without prior notification. The study is included in pooled analysis to show the mental health clinic attendance results only. The proportion of missed appointments was 16.4% (95% CI 13.1% to 19.8%) in the text-message group (N 462) and 20.0% (95% CI 16.6% to 23.4%) in the control group (N 529), showing no significant effect of the intervention (p=0.346).
Branson et al 2013 USA	Adolescents between 13-17 years of age, drawn from a convenience sample of an outpatient mental health clinic. Quasi-experimental study design with an historical control.	Mental health:The control treatment as usual group (TAU) did not receive any reminders, while the intervention text messaging (TM) group received additional reminders for each therapy session over a 3-month period. The intervention was static, with no option of replying to the reminder message.	Assessed Mental Health clinic attendance. Adolescents receiving TM reminders had significantly higher rates of clinic attendance (65%) than a historical control group (49%) (p = 0.05). The attendance rate for the TM group (Mean 64.9%, SD 22.3%) was significantly higher than control group (Mean 49.3%, SD 24.5%), F (1, 46) = 5.33, p 0 .026, d = 0.67.
Trent et al 2015 USA	Observational study among 100 adolescents and youth (ages16-25) with mean age of 19yrs.	Reproductive health: Follow-up for three 3-monthly cycles of Depo-Provera injectable contraceptive. Intervention (n=50) received daily bidirectional SMS reminders starting 72 hours before scheduled appointment. SOC (n=50) was automated reminder message to home telephone androutine call by nurse after missed appointment to return in on-time	Assessed the proportion of on-time injectable contraceptive administration (Depo Provera). Non-statistically significant on-time appointments for second and third cycle in Intervention group. No overall difference to on-time administration. Intervention may have potentially greater impact in settings without nurse call after missed appointments.
Cornelius et al 2013 USA	A single- group pre-post observational study with assessment of outcomes at three timepoints among 40 Black adolescents aged 13-18 years.	Reproductive health and substance use: BART (Becoming a Responsible Teen) is a 7-week community-based **HIV prevention** programme to develop **safer sex behaviour**. This project examined the add-on effect of bi-directional booster messages for 3 months after completion of the BART course. Daily booster messages (SMS, video, pictures) for 3months, sent at 3pm daily and participants were able to text their facilitators with related questions.	Participants in the intervention group showed no significant improvement in **HIV knowledge, reduced risky sex acts and reduced risk drug use** compared to control at 3 months. Age was a primary factor in change, with a trend to benefit among older participants (16–18 years of age).

Matheson et al 2014 USA	Adolescents between 11-22 years of age, with mean age of 19 from an urban paediatric clinic setting. 37 participants were randomised to intervention, 232 to control.	Reproductive health: Participants received text message reminders for the second and third dose of HPV vaccine over an 8-month study period. Each participant received three text message reminders per dose: one message 7 days prior to each HPV vaccine due date, one on the vaccine due date, and one 7 days after the due date.	Assessed **HPV completion and HPV doses on-time**for dose 2 and 3. 14% of participants in intervention group completed the vaccine series on-time 3% of control completed the vaccine series on-time
Fiellin et al 2017 USA	Randomised trial with 11-14 year olds, with mean age 12.9 years. 258 evaluable participants at 12 months; 129 in intervention, 129 in control	Reproductive health: Interactive videogame where the player avatar "travels" through life, facing challenges and making decisions in sexual risk and substance risk, unsafe driving scenarios. Control group played time and attention-matched games for the same 6-week period.	Outcomes assessed 1 year after intervention: No difference was found in **delay of sexual debut.**Boys and younger intervention participants showed improved sexual health attitudes overall compared to the control group at 12 months. This effect was not seen in girls, or older adolescents.
Jeffries et al 2017 USA	Poster presentation of a randomised pilot trial among 146 HIV-positive 15-24 year-olds.	Reproductive health, alcohol use: Intervention group received 12 texts per week. Control received standard of care.	Incompletely reported on outcomes of HIV viral load and risky single-occasion drinking. Viral load for intervention group was statistically significantly lower than control at 3 and 6 months follow-up. Those who were non-adherent or new to ART benefited most with lower viral loads and substance use knowledge.

Five studies addressed mental health conditions of depression, wellbeing and violence (Branson et al., 2013; Narring et al., 2013; Manicavasagar et al., 2014; Kobak et al., 2015 and Ranney et al., 2016).No studies reported on suicide, and only one study reflected violence by participant self-report.

Infectious disease categories were non-SRH (e.g. TB, influenza) and SRH. SRH was further sub-categorised into

i) curable STI's (chlamydia, gonorrhoea, syphilis, etc.)
ii) non-curable STI's (HIV) and
iii) vaccine-preventable STI's (HPV)

STI studies reported on condom use, risky sex behaviour and STI knowledge. One study reported on HPV immunisation adherence as both completed and on-time vaccination (Matheson et al., 2014).

No studies were found on adolescent non-sexual and reproductive health infectious disease, specifically TB and vaccine-preventable influenza. One conference poster (Jeffries et al., 2017) incompletely reported on HIV viral load and binge-drinking in adolescents with HIV, and was thus not included in the meta-analysis.

Biological outcome reporting was rare. Only one study reported on the incidence of pregnancy (Rokicki et al., 2017). A single poster presentation reported on biological HIV-related outcomes of viral load measurement (Jeffries et al., 2017).

4.3 Country settings and participant ages

Figure 3 depicts where adolescent mHealth research occurs. Most studies were conducted in advanced economy settings of the global North, specifically in the US (n=16) and Europe (n=3). Only three studies were conducted in global South settings, Africa and Australasia. The study that took place in Ghana, Africa, was conducted on14-19 year old adolescent girls for sexual health outcomes (Rokicki et al., 2017). The other two studies were on sexual and mental health outcomes in Australia (Lim et al., 2012; Manicavasagar et al., 2017).

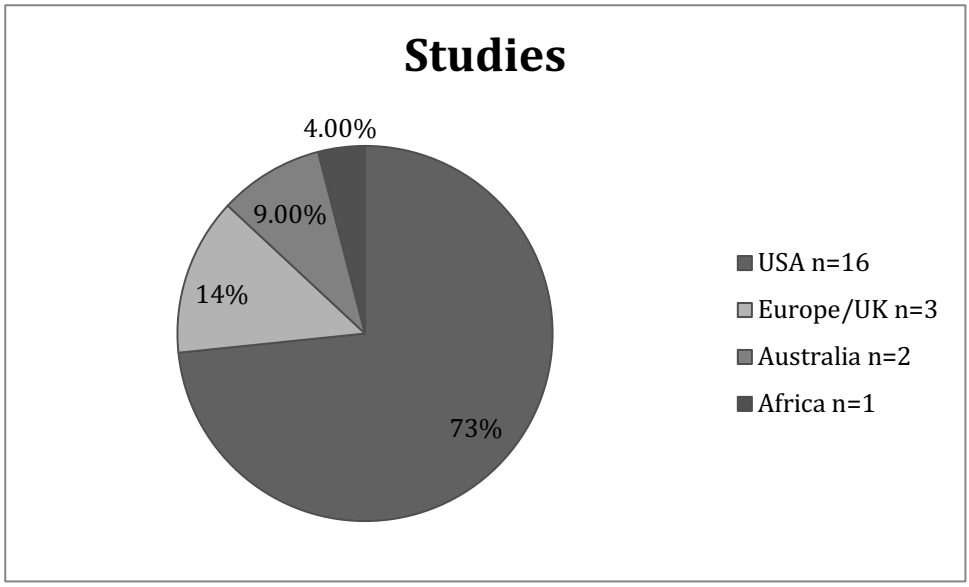


Figure 3 Country distribution of included studies

Adolescent study population ages were skewed towards older (ages 15-19), rather than younger ages. Twenty-one of the included studies reported on adolescents over the age of sixteen years; six of these also reported on those younger than 16 years. Two studies reported exclusively on adolescents under 16 years, which was a videogame developed for HIV and substance use risk reduction targeting 11-14 year-olds (Fiellin et al., 2017 and Montanaro et al., 2015). Abstinence, or delay of sexual debut in younger adolescents under the age of 15 years, was examined in only the Fiellin study (2017) where no difference was found in delay of sexual debut compared to control one year post-videogame intervention. Boys and younger intervention participants showed improved sexual health attitudes overall compared to the control group at 12 months. This effect was not seen in girls or older adolescents.

As regards the research setting, most studies were conducted among post-high school students. Whereas two studies were done in a high-school setting before transitioning to college (Juzang et al., 2011; Rokicki et al., 2017). Reaching adolescents before they transition into potential college settings of increased risk, may minimise the effects of binge-drinking and substance use on the developing brain, while providing the opportunity for early diagnosis of mental disorders.

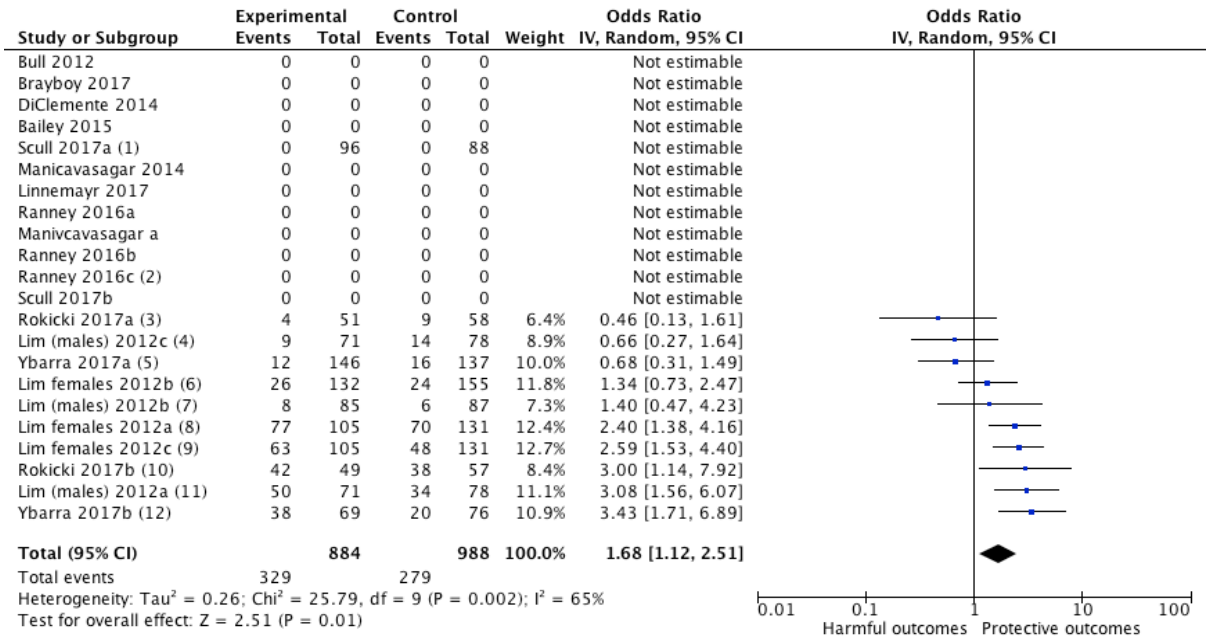
4.4 Sexual and reproductive health studies

Overall, sexual health studies (n=11) reported predominantly behavioural outcomes such as STI testing, condom and contraception adherence and addressed multiple elements simultaneously. Six studies were eligible for pooling (Scull et al., 2017; Lim et al., 2012; Rokicki et al., 2017; Trent et al., 2015; Bull et al., 2015; Ybarra et al., 2017).

Three studies (Cornelius et al., 2013; Lim et al., 2012 and Rokicki et al., 2017) reported knowledge as well as behavioural or biological outcomes. One study addressed HPV vaccine completion (Matheson et al., 2014); another study addressed outpatient clinic attendance as a measure of adherence (Narring et al., 2013).

Condom use was reported as either protected or unprotected (condomless) sex acts. Four studies with 648 participants reported condomless sex acts. Condom use was reported by one large study with 1092 participants.

Figure 4 shows the three studies reporting an odds ratio (Rokicki et al., 2017; Lim et al., 2012 and Ybarra et al., 2017). Moderate heterogeneity (I-squared value = 64%) was found between studies. OR is 1.68 across the studies, and statistically significant with CI=1.12-2.51. Those studies 'not estimable' in the forest plot reported no raw data, only adjusted event values or ratios.STI testing was reported by two studies (Ybarra et al., 2017; Lim et al., 2012). Lim (2012) is examined under a subsequent heading (4.7) of gender subgroups.



Footnotes
(1) knowledge score males and females
(2) wellbeing score
(3) females only, PREGNANCY outcome, bidirectional
(4) males, consulting HCW at 12mo
(5) refers to unprotected sex 3months after intervetion end
(6) females, STI test at 6months
(7) males, STI test at 6months
(8) females, knowledge score improved, at 12 months
(9) females, consulting HCW at 12mo
(10) females only, unprotected sex, bidirectional intervention
(11) males, knowledge score improved, at 12 months
(12) refers to HIV test at 3months post

Figure 4 mHealth evidence: Sexual and reproductive health studies

Ybarra examined condom use and STI test prevalence in sexually active male 14-18 year old participants at 3 months after intervention-end. The intervention was an HIV education

and prevention programme delivered as 5-10 daily SMS, for 5 weeks. They reported both events and adjusted values, with raw data depicted in the forest plot (Figure 3). The adjusted OR for HIV test at three months post-intervention was 3.42 (CI= 1.65-7.09). Sexually active participants in the intervention arm were 3.42 times more likely than control participants to have an HIV test at 3 months. The wide confidence interval illustrates its imprecision: the true effect on HIV testing may be as low as 1.65 times, or as much as 7 times, more likely. Our analysis of raw data yielded a similar OR of 3.43 (CI=1.71-6.89).

The adjusted incident rate ratio (IRR) for condom-protected sex acts was 0.95 (CI=0.45-2.02). The reasons for reporting an adjusted IRR due to skew in data are not well-reported. Our analysis of the raw data shown in Figure 4 yielded an OR of 0.68 (CI=0.31-1.49). This describes the intervention group as being 32% less likely than control to use a condom, with an imprecise, non-statistically significant confidence interval.

The third study, Rokicki et al (2017) examined secondary outcomes of pregnancy self-report after one year, and unprotected sex. The analysis was done among a group of 14-24 year old sexually active female students, and by SMS intervention subgroup. Unidirectional SMS messages delivered to participants were compared with bidirectional communication (Rokicki et al., 2017). The control group received information on malaria rather than SRH. Both uni- and bidirectional interventions were significantly effective in lowering likelihood of pregnancy with adjusted OR's of 0.14 and 0.15, respectively. The study further reports significant improvements in knowledge durability at 15 months with the bi-directional programme compared to the one-way programme. Both interventions were reported as superior to the control (not shown).

Multiple outcomes (knowledge, condom use and pregnancy prevention) could not be pooled due to inconsistent effect sizes reported. By calculating the log OR and 95% confidence interval from the SMD and RR it was possible to estimate the overall effect of mHealth across more studies, by outcome reported, as depicted in Figure 5. The additional components gleaned here were information on pregnancy prevention, STI testing and condom use. Half as many female participants in the intervention group than control self-reported pregnancy in one year (OR of 0.47). This corresponded to 8 per 100 pregnant intervention participants, compared to 16 per 100 in the control, with an imprecise confidence interval of 0.17 to 1.26 (the true effect lies between of 3 to 18 per 100 pregnancies). Effect on STI testing was favourable for mHealth over control, with an OR of 0.45 and a precise, statistically significant CI (0.26-0.78). This would suggest a 55% increased likelihood of STI testing with mHealth. However, this result should be taken

conservatively, as the moderate heterogeneity of 61% signals that this effect may vary in different settings.

The effect of mHealth on condom use showed only 16% increased likelihood of use (OR=0.84); this effect was seen as statistically non-significant (CI=0.56-1.27), again with moderate heterogeneity of 64%. Even though the element of knowledge was initially included in this pooling, the overall effect of mHealth on these multiple aspects of SRH still remains favourable.

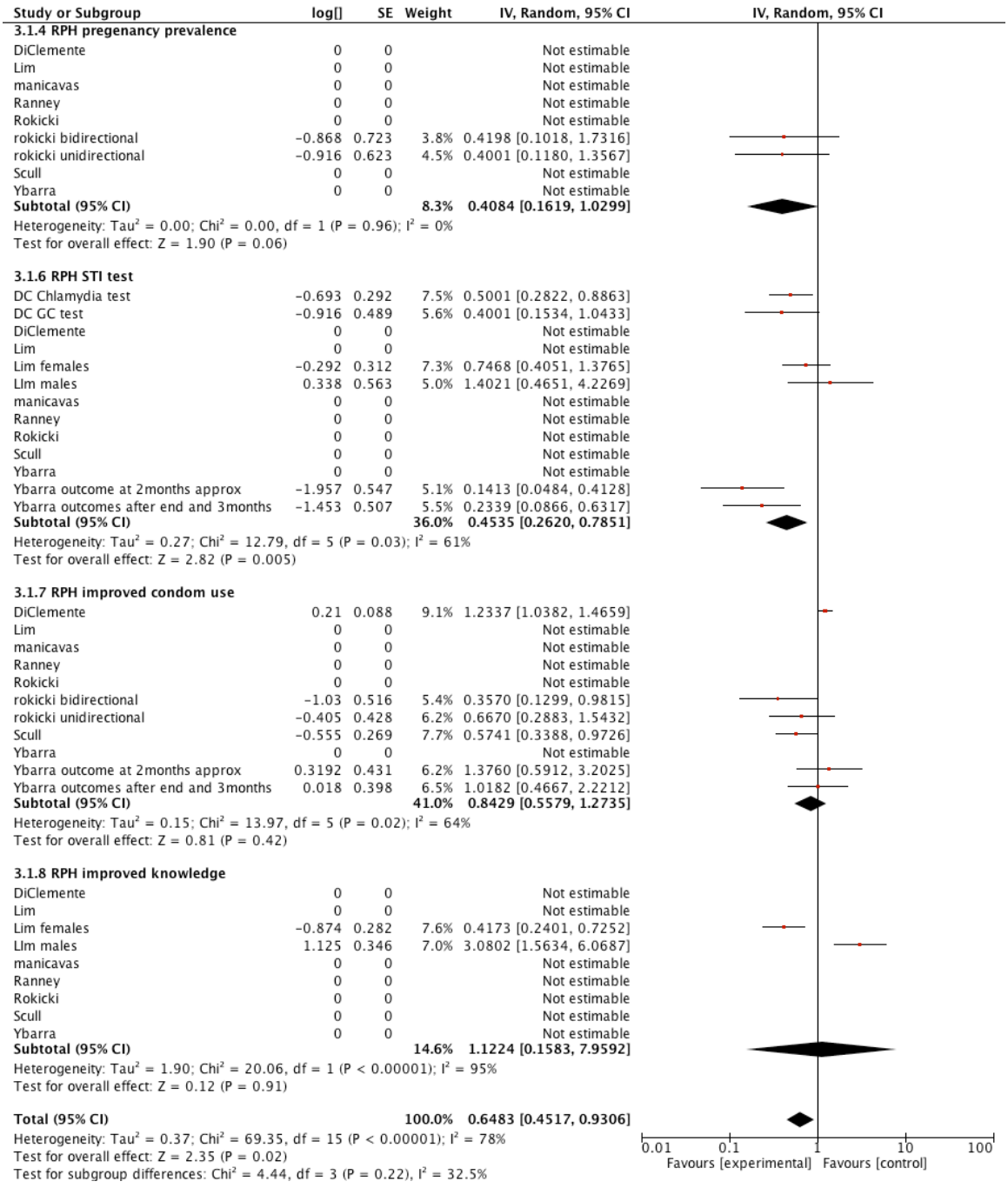


Figure 5 mHealth evidence: multiple sexual and reproductive health outcomes

4.5 Substances other than tobacco

Six studies covered alcohol and substance use exclusively (Montanaro et al., 2015; Haug, 2017; Jeffries et al., 2017; Weitzel et al., 2007; Larimer et al., 2009; Tahaney et al., 2017), while Cornelius (2013) reported on sexual health outcomes as well. Four studies focused on risky single occasion drinking, with individual studies reporting biological outcomes of blood alcohol levels post-intervention (Jeffries et al., 2017) and knowledge (Montanaro et al., 2015).

Three studies addressed intervention impact on risky drinking behaviour, defined as "binge" or risky single-occasion drinking by the study authors.

Most studies (n=6) were ineligible for pooling due to incomplete reporting. An isolated study with clear reporting was an RCT conducted by Haug on 477 participants in Switzerland (Figure 6). Subgroups were analysed according to risk, defined as the number of drinks per episode. Medium risk was defined by the authors as 4-5 drinks, and high risk as 6 or more drinks per episode. The overall intervention effect favoured mHealth, with an OR=0.68, defined as a 32% reduced likelihood of RSOD. The effect of the intervention was even stronger in the group of high risk drinkers, who showed a 72% reduced likelihood of risky single-occasion drinking post-test (OR=0.28). This was both statistically significant and precise. It can be seen that the overall effect was diluted by efficacy in the medium risk subgroup, which unfortunately had more than twice the weighting (due to a larger sample).

Cornelius (2013), not shown, reported minimal intervention effect on risky drug use with a mean difference (MD) of 0.62 lower compared to pre-intervention. This was a pilot repeat measures RCT with a small sample of 71 participants, conducted within a study setting geared at examining primary sexual health outcomes.

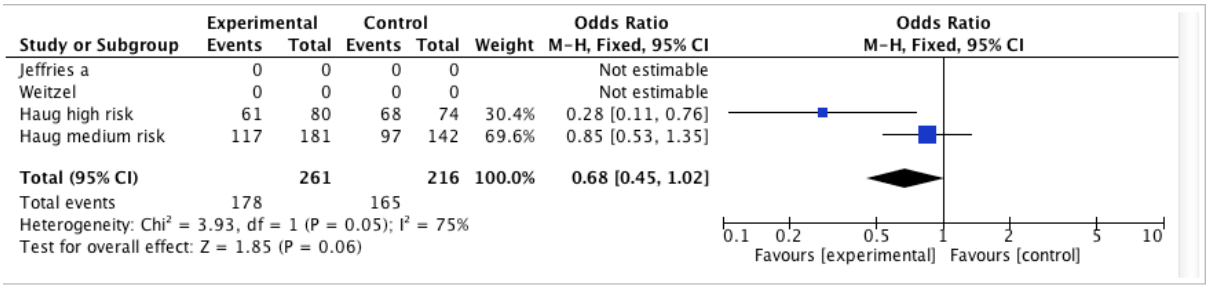


Figure 6 mHealth efficacy for risky drinking behaviour (Haug et al., 2017)

4.6 Mental Health conditions

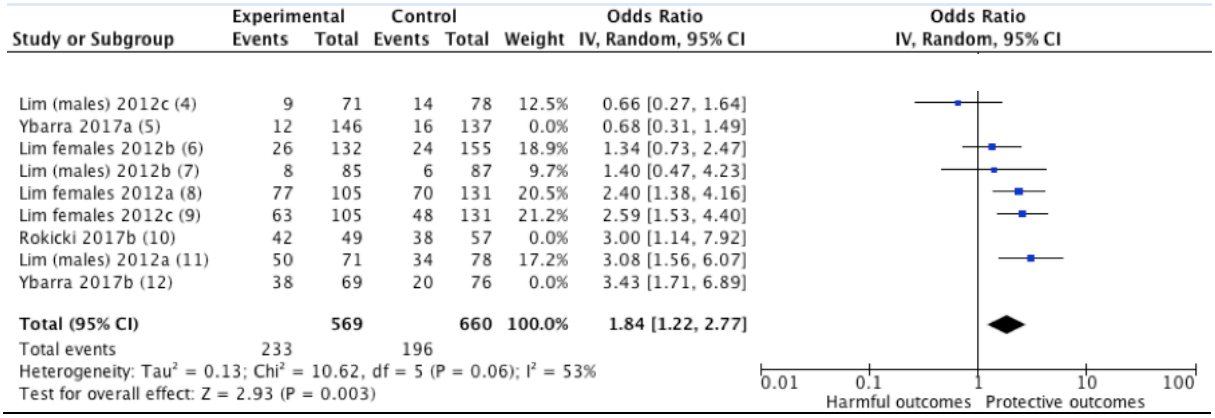
Depression scores reported showed a change in 407 participants across 5 studies, reported as mean difference of 4.01 lower in the mHealth group on validated depression scales (higher scores reflect worse outcomes) with an imprecise CI showing the true effect to lie

anywhere between 8.83 points lower to 0.82 points higher. This wide margin in precision may be due to the different depression scales used in studies, as well as the clinical spectrum of subclinical, to overtly depressed adolescents. This is similarly reflected in a high heterogeneity score of 84%, reflecting the need for caution with interpretation.

The wellbeing score was examined in three studies among 174 participants with a mean difference of 2.17 points higher with mHealth (higher scores reflect improved outcomes). Improved wellbeing ranked higher on the validated scales used in the studies, with an imprecise true effect (CI= -2.86 to 7.2); between 2.86 points lower and 7.2 points higher on the scale.

4.7 Effect of gender

The study by Lim was the only study reporting outcomes by subgroup of gender (Figure 7). Outcomes reported were proportion of protected sex acts, improved knowledge score and STI testing at 6 months, as well as the likelihood of consulting a health care provider at one year post-intervention. Timepoints reported were one year and 6 months post-intervention. Behavioural outcomes of both STI testing as well as consulting a health care worker were better for females than for males, with similar durability of effect persisting up to twelve months. Although females initially scored better for STI knowledge, knowledge retention at twelve months was better for males than for females.



Footnote: 6 and 7) STI test 6 months; 8 and 11) knowledge score 12 months; 9) HCW affiliation 12 months

Figure 7 Gender subgroups (Lim et al., 2012)

However, the improved 12–month knowledge scores in males did not translate into improved protected sex practice in the male group, only in females. This is consistent with published research which shows that although interventions may improve knowledge, this alone does not consistently lead to positive health behaviour, especially with longterm conditions such as HIV and mental health where self-motivation and social support are vital (Kim et al., 2015). Furthermore, effects of improved knowledge may have contrary effects, such as

reduced condom use. Previous literature has accounted for this reduced condom use, by intervention effect of increased monogamy and less risky partners overall. Message framing, such as content focusing on 'pregnancy prevention', rather than 'barrier contraception' may also have unintentional effects such as improved oral contraceptive adherence, with reduction in barrier methods (Rokicki et al., 2017).

Males were also less likely than females to consult health care workers for sexual health concerns. Notably, females were almost twice as likely as males to have spoken to their health care worker about sexual health concerns, or have had an STI test, one year post-intervention. The reported OR of 1.85 was statistically significant and did not cross the line of one (null effect, where control and intervention are equivalent). Furthermore, when analysed in the fixed effects model which assumes that all conditions within the two gender subgroups are the same, the significance increased further to an OR of 1.97. This effect favouring mHealth over standard care remained statistically significant, as confidence intervals in both models did not cross the line of one.

4.8 Effect of follow-up duration

The longest duration of follow-up across all the studies was 36 months (Rokicki et al., 2017). As its overall findings were reported as RR, it could unfortunately not be pooled with the other studies on reproductive health outcomes (all reported OR), so is shown in the lower half of Figure 8. The risk ratio shows an almost 50% reduction in sexual risk behaviour using the intervention. However, this effect is not statistically significant or precise, as the confidence interval is broad (CI 0.21 - 1.21) and crosses the line of 1.

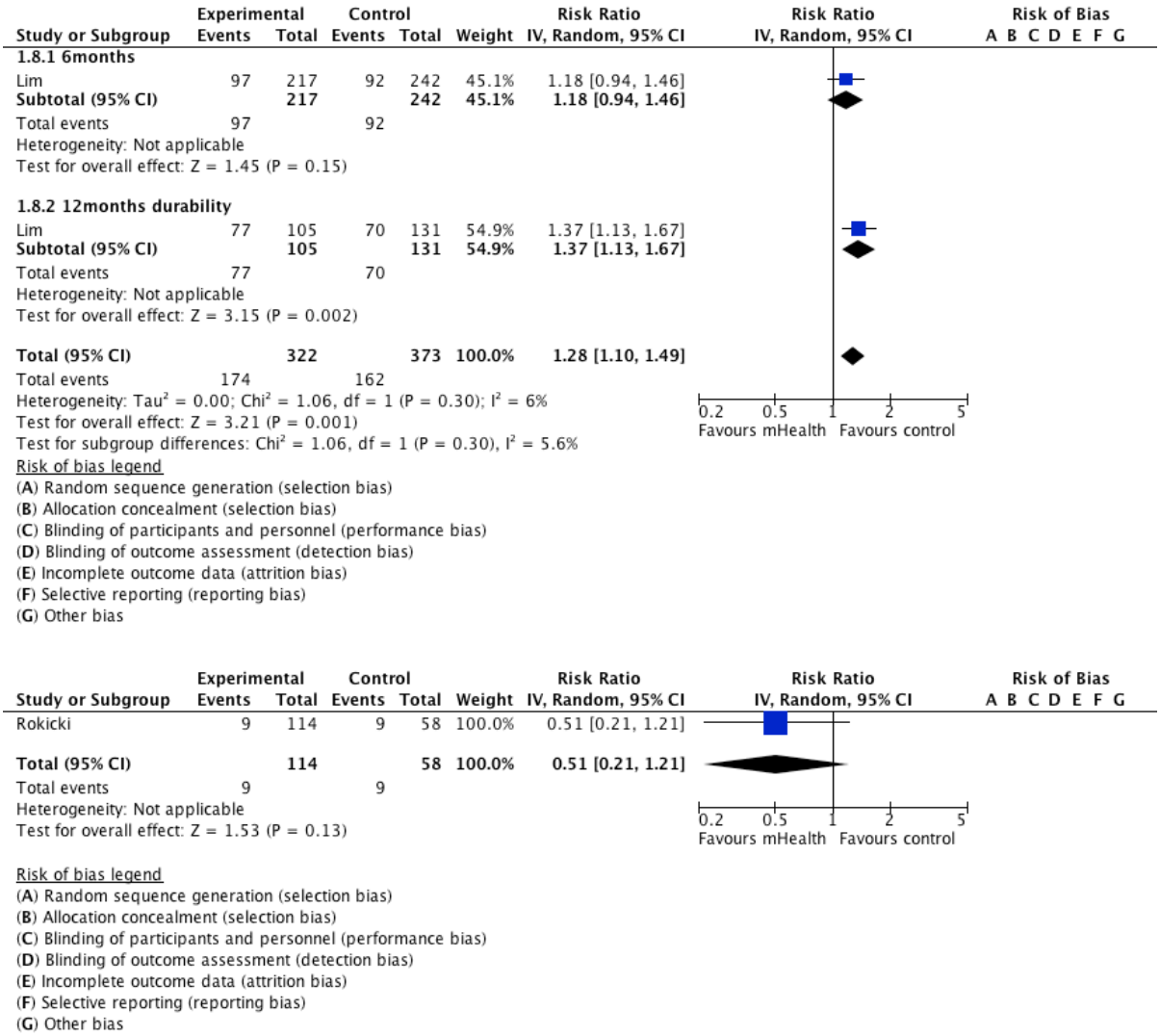


Figure 8 Efficacy for longer follow-up durations (Lim et al., 2012; Rokicki et al., 2017)

4.9 Summary

We found a preponderance of sexual health publications; fewer for mental health; even fewer for drinking and substance use; and none for infectious diseases TB and vaccine-preventable influenza.

Our results indicate that most outcomes reported were behavioural, and self-reported. Time period of follow-up post-intervention was variable, although only two studies reported on participants for more than 12 months, despite the chronic nature of many interventions. This is of some concern as longer periods of observation are preferable when establishing efficacy of interventions. This may also partly explain some of the variable results in the sexual health studies regarding condom use, as follow-up periods varied widely in these studies (from two weeks to 1 year).

Behavioural outcomes included abstinence, condom use, STI testing, risky alcohol and drug use, compliance taking medication and clinic attendance.The vast majority of studies were related to sexual and reproductive health outcomes, assessed commonly as combinations of knowledge improvement and biological or behavioural outcomes. The biological outcomes addressed included pregnancy, depression scores and wellbeing scores. Risk of pregnancy was reliably halved using mHealth in an RCT of 172 participants (OR 0.47).There was a clear improvement in health provider affiliation, especially in females for sexual health concerns. Clinic attendance showed marginal improvement in three studies among 991 participants. The two studies among 742 participants assessing STI testing showed only a small to moderate effect.

The mHealth evidence for improved depression scores was moderate with a change score improved by mean difference (MD) of 4 points, consistent across the studies. Wellbeing showed smaller, consistent improvement.

Risk behaviours encompassed risky sex, risky drug use and risky alcohol use. Risky drug use and sex practice showed small and inconsistent improvements with mHealth. Risky drinking showed considerable improvement with mHealth (32% reduction), and was examined in a larger sample of 477 participants. In the initial search, only Montanaro et al. (2015) and Fiellin et al. (2017) reported on the beneficial effects of videogames on male sexual health knowledge. Improved alcohol risk behaviour and knowledge was related to mastery of the game, rather than time spent playing it. The intervention had no effect in girl and older adolescents, only younger, male participants. Given that both studies showed beneficial effects, this is an area of mHealth that should be explored further. Fiellin et al. and Montanaro et al. were also the only studies targeted at younger adolescents between 11-14 years.

Despite estimations that the largest numbers of adolescents reside in Asia (ITU, 2017), we found no mHealth publications from this region, although there was no language limitation placed on our search. There was no representation of teens in rural or homeless settings, and only one from a school setting with an add-on intervention. Similarly, there was no representation of acute conditions such as unintended injury, violence or suicide.

Chapter 5: Discussion and Conclusion

The study set out to examine the evidence for effective adolescent mHealth interventions for knowledge transfer to LMIC's to implement adolescent immunisation. An initial objective was to map the mHealth evidence for target conditions that contributed significant morbidity to the adolescent global disease burden. This step is referred to as "charting the evidence" in scoping methodology, and requires sufficient well-reported literature (Colquhoun, 2014).

5.1 Factors that affect intervention efficacy

More than seventy percent of 15-24 year-olds globally are reported to be online for at least an hour daily (International Telecommunication Union, 2017). However, the evidence highlights the skew of mHealth research to high-income nations where adolescents are more likely to own smartphones capable of accessing the internet, or may access the internet at home or places of learning. We found three adolescent studies from Africa and Australia, in stark contrast to an adult mHealth systematic review reporting fewer publications from the global North, and an upswing in those from Australia and Africa in the last decade (Fiordelli, Diviani & Schulz, 2013). To our knowledge, no similar systematic review has looked at the global distribution and frequency of mHealth publications among the adolescent age group exclusively, despite their high internet usage.

Our findings also highlight the skew in evidence towards chronic conditions and sexual health topics. The vast majority of studies were related to sexual and reproductive health outcomes, assessed commonly as combinations of knowledge improvement and biological or behavioural outcomes. This finding is consistent with the Fiordelli et al. (2013) review reporting a predominance of chronic, rather than acute, conditions in mHealth literature between 2002 and 2012. Fiordelli recommended then that mHealth for acute conditions should be explored further, due to its unique capability for continuous communication. The Global Burden study has shown that violence and road traffic accidents cause 20% of all adolescent deaths (Mokdad, 2016). Further, road traffic injuries constitute the highest cause of death in younger and older male adolescents; whereas the leading cause of death changes from respiratory causes, to maternal causes in older female adolescents (WHO, 2017). The mHealth capacity for continuous or bidirectional communication may be useful in health promotion, as well as in acute emergencies. However, we found that all of the evidence addressed non-acute conditions. No studies were found on suicide or road traffic accidents.

The gap in the evidence of most concern, given the nature of our scoping project, was the lack of infectious disease publications on adolescent TB. Further, the absence of adolescent mHealth research for infectious disease examining biological and behavioural outcomes

overall is surprising, given advances in drug discovery, and recent outbreaks such as Ebola and Zika virus. Such studies may however have been published since November 2017, or may be in the publication pipeline.

In terms of the study setting, recent reviews report promising adolescent outcomes in school settings for both high income countries and LMIC's, and for non-mHealth (Barry, 2016) as well as mHealth interventions (Champion, 2017). The beneficial effect of mHealth as seen in school settings may be by facilitated by allowing confidential interaction for personally relevant topics, thereby bypassing peer pressure and perceived stigma. Both of the studies we found with mHealth add-ons to a high-school-based curriculum reported positive knowledge and health outcomes (Juzang et al., 2011; Rokicki et al., 2017). Hence we concur with multiple researchers who suggest that mHealth as an add-on holds promise. However, mHealth add-ons to school-based programmes may miss those not in mainstream schools such those living on the street, in correctional facilities and in chronic rehabilitation programmes. More studies examining alcohol and substance use were found conducted among college, rather than high-school, students. The privilege of continuing to tertiary education, or remaining in mainstream secondary education, is tenuous in many rural settings, emerging economies and areas of conflict. The question of how to target adolescents before transition to further education, and outside of traditional school settings, could potentially be an area for important future work.

Most of the studies found used either bidirectional or static text messaging as a follow-up to another standard of care practice. The appeal of smartphones is that they allow personalisation - apps and games may be customised to user preference by a myriad of background settings, sounds and culturally-sensitive avatars for example. The app can usually be accessed on another device. Most users do not keep the same mobile device for more than two years, and phones may be lost, stolen or break down. Using a text-based intervention exclusively with a single mobile telephone number, may therefore be less useful in settings where users change numbers (or SIM cards) frequently. Engagement platforms like WhatsApp may therefore be more relevant in country settings where users share or change SIM cards frequently, yet retain a single profile for access.

As wireless technologies have changed over time, so have social media preferences between younger and older adolescents, as well as boys and girls. Two recent surveys by Pew research organization in the US showed that adolescents spent more time on social media than sending text messages (Lenhart, 2015; Anderson, 2018). Girls preferred visually-orientated social media platforms such as Instagram and Snapchat, while boys of all ethnicities were more likely to play videogames (Lenhart, 2015). Apps and videogames may

therefore hold more potential for targeting younger adolescents than bidirectional texting, for example. Yet our findings do not reflect this change in user preference, as the vast majority of evidence was for text messaging as mHealth modality, despite reasonable infrastructure supporting internet connectivity. Low and middle-income country infrastructure and ownership of older mobile phones among adolescents may limit full exploitation of newer platforms such as WhatsApp. Thus, SMS might still be preferable for countries where connectivity may be poor. In countries such as South Africa, Nigeria and Kenya with good mobile connectivity, there may be a role for exploring the newer platforms in adolescent studies. However, the data costs in these countries remain relatively high compared to Europe and North America (ITU, 2017).

5.2 What does this mean for implementation of adolescent global health interventions?

This study found incomplete reporting of primary studies, which would impact on knowledge transfer at multiple steps. Most studies reported the technology platform, health information system context, user feedback and intervention content aspects increasingly better over time. Whereas facets such as contextual adaptability and replicability, limitations to scaling the intervention, and how individual participants accessed the intervention, remained under-reported. We would argue that these latter aspects are as vital for successful knowledge transfer as for understanding reasons for inconsistent outcomes of infectious disease adherence mHealth interventions. Such information is needed before subsequent systematic reviews are able to map statistical efficacy trends for interventions. An example of the need for detailed reporting, is the earlier reference to the Lester et al. (2010) study that showed promising outcomes for adult ART medication adherence using mHealth in Kenya. This success was replicated by King et al (2015), in a Canadian setting. Yet Mbuagbaw et al (2011) and Shet et al (2014) failed to show similar success for adult ART adherence in Cameroon and India, respectively. It was only when more time had elapsed, that a subsequent systematic review clearly showed efficacy was dependent on the bidirectional nature, and frequency of messages (Anglada-Martinez, 2015). We would therefore encourage all mHealth researchers to report findings in accordance with both the study-specific guidelines (such as STROBE for observational studies; CONSORT for RCT's etc.) and the CONSORT-EHEALTH checklist (Eysenbach et al., 2011).

The small number of studies on younger adolescents under the age of 16 raises the question of whether recruitment is reduced when parental consent is required. Some ethics boards, such as those in the UK and South Africa, require parental consent (as well as adolescent assent) for research on those under the age of 18 years; this exists even for

hard-to-reach minority groups such as young men-who-have-sex-with-men (MSM). The process to waive the widely-accepted ethics requirement of parental consent is laborious, even when these adolescents legally are able to make independent decisions on contraception and obstetric procedures. This begs further investigation and novel ways of approaching regulatory requirements in younger adolescents. In addition, many social network platforms (such as Facebook) have banned any sexual health advertising content to under-18-year-olds due to privacy laws, including recruitment advertisements from validated sexual health research organisations. The low numbers of adolescents under the age of sixteen years in these studies may be therefore be in part due to missed opportunities in recruitment due to regulatory and legislative hurdles, rather than lack of research focus.

Despite making up a third of the population in many countries, there is a significant risk that the great advances in maternal and child health gained through the MDG's stand to be lost by lack of global investment in adolescent health (WHO, 2014c). The latest WHO publication, *Global Accelerated Action for the Health of Adolescents* (WHO, 2017*)* reflects better data reporting by country programmes, and an understanding of the intersectoral collaboration required for health and social policies for adolescents. This is vital as most adolescent social determinants of health such as education and employment, are not within the ambit of the traditional health system. It is of concern that the only current adolescent SDG indicator is pregnancy rate, another sexual health statistic.

5.3 Limitations and recommendations

In this review, some methods of a systematic review were used; however, it remains a scoping review. Its purpose is to inform gaps in the knowledge base and findings should be interpreted bearing in mind that many of the studies were pilots, underpowered for efficacy determination.

Some pilot studies were informative for testing proof of concept; however, inconsistency of authors across successive publications made it relatively difficult to trace the follow-up RCT for example. We found that feasibility studies and pilot studies were not clearly delineated by study title. This lack of clarity became important when keywords and titles were scanned in the initial steps, as pilots and feasibility studies serve different functions in preliminary research, whereas we were interested in health outcomes. In this review, only two studies used reporting guidelines from the CONSORT E-HEALTH checklist for pilot studies, which delineates the initial feasibility and follow-up pilot phases (Eysenbach et al., 2011).

Arksey and O'Malley (2005) invited researchers using the scoping process to publish, comment and build on their initial discussion to advance the methodology. Multiple studies since then have noted that the process took more than a year, and was not necessarily a

“rapid mapping” of literature. This was noted to be the case even when quality assessment was not done (Levac, 2010; Daudt, 2013). We would therefore agree that our scoping process was more in line with the Daudt definition, which entails mapping the literature while “identifying key concepts, research gaps and types and sources of evidence”. However, regardless of definition used, there is a clear need for better reporting guidelines for mHealth, which would benefit both the scoping and systematic review process, both for broadly mapping the literature, and for describing the best available published evidence.

As regards the reporting of scoping reviews generally, we concur with multiple researchers on the value of supplementing Arksey and O’Malley’s initial framework with subsequent publications that build on the methodology (Levac et al, 2010; Daudt, 2013; Peters et al., 2015a). Several Joanna Briggs Institute suggestions such as the use of multiple structured searches, and a multi-disciplinary team approach, would prove useful to follow-up work to this review (Peters et al., 2015b). Further strengths of the Joanna Briggs Institute framework include an approach to multiple research sources (quantitative and qualitative), as well as complex interventions in their model of evidence transfer to various economies and healthcare settings (Peters et al., 2015b).

Furthermore, as in most research, larger, commercial studies were well-funded with bigger numbers, but few had transparent raw data placed into the public space. Some authors were unable or unwilling to provide adolescent data when contacted for age-related information. This occurred either due to the data not being captured, where adolescents fell within a much larger age cohort; or alternatively, that the use of platforms such as Google analytics kept age-related patient data confidential, an unintended effect. Only six eligible studies provided complete supplementary data by appendix or online publication. This may lead to duplication of efforts, where existing data is not easily verified or built upon. A recommendation would be for researchers to report their findings clearly upfront. Specific details on the phase of study design should be captured in the title and the abstract should refer to preliminary work, relevant keywords, and the age disaggregation reported. An example of such a specific reporting checklist for abstracts is the PRISMA abstract checklist shown in Appendix 5 (PRISMA, 2009).

A unique strength of the scoping process remains its iterative nature. We would therefore recommend that more scoping reviews be published, so that others may learn from the process. Arksey and O’Malley intended for the process to be iterative, and formative, with researchers sharing insights and pitfalls experienced during the process, so as to grow the methodology.

In this review, only two studies used mHealth reporting guidelines. The only journal we know of that mandates eHealth and mHealth reporting guideline use for RCT's, is the Journal of Medical and Internet Research. Multiple authors have commented on the specific challenges posed by wireless interventions, which require additional reporting guidance to the widely-adopted study-design specific checklists (Eysenbach, 2002; Moher et al., 2010).The CONSORT-EHEALTH checklist was intended for use in conjunction with the CONSORT statement for reporting RCTS's of mHealth interventions. It was developed to enable replication and peer-learning from mHealth publications (Eysenbach et al., 2011). Unfortunately, as it was merely an extension document, the guideline was rarely used. The WHO therefore developed an mHealth working group (mTERG), and advocates use of their mERA checklist for publications (Agarwal et al., 2016).

As regards the reporting quality found, the mHealth working group set up by the WHO in 2011 was linked to two recent publications advocating for improved reporting in mHealth (Agarwal, Lefevre & Labrique, 2017; Agarwal et al., 2016). This supports our finding that few publications referred to mHealth-specific guidelines, although they may have used study-design-specific guides. We would therefore encourage mHealth study authors to use specific guidelines and checklists for reporting interventions.

Hopefully, increased awareness of the mERA guidelines has a similar effect for adolescent mHealth to the improved reporting quality for sexual and reproductive health publications. We found few eligible studies for our target conditions, despite their significant contribution to adolescent morbidity, and the current adolescent global initiatives (WHO, 2014b). Of most concern, is the lack of relevant adolescent infectious disease studies. Notwithstanding the regulatory challenges regarding consent of younger adolescents, the relative blind spot for their pivotal role in infectious disease transmission needs to be addressed as a matter of priority.

In sum, the research gap for well-reported interventions addressing biological or behavioural outcomes persists outside of the sexual and reproductive health field for adolescents. We postulate that this is related to the dominance of HIV research and funding in the last two decades and the 2011 WHO directive on mHealth for sexual and reproductive health outcomes (WHO, 2011). To address the paucity of non-sexual and reproductive health outcomes within the mHealth sphere and lack of LMIC representation that we found, it would be desirable to have mHealth assessments embedded within large, well-funded, longer follow-up clinical trials. The implication of these findings for knowledge transfer to adolescent infectious disease using mHealth, may be that it remains too early to conclusively comment.

Few studies were reported well, transparently, or by any guideline required to enable replication.

Our study also had limitations. Only five authors responded to email queries for data and clarification. Studies rarely reported details of the setting clearly, and it is possible that some studies were excluded as they were not explicit in reporting how interventions were accessed. Some studies were classified as mHealth, when in fact there was no wireless intervention component, merely an assessment by online questionnaire at follow-up, for example.We found two RCTS that were registered as clinical trials with NIH or clinicaltrials.gov, with clear links to funding. All systematic reviews found were registered with PROSPERO, whereas scoping reviews are not eligible for registration at this time. All studies pooled in the meta-analysis (n=12) used the PRISMA-P diagram to describe flow of study participants from randomization to follow-up, despite the sometimes small numbers.

5.4 Conclusion

Overall, the mHealth studies were not well-reported, with unclear health outcomes and unclearly defined populations (especially for younger adolescents under 16 years). Conversely, the well-reported volume of sexual and reproductive health literature found for adolescents has been encouraging. Our study shows that mHealth interventions geared at adolescents are being produced; yet few target younger adolescents. The variable reporting quality of mHealth publications remains a significant factor limiting knowledge transfer, interpretation of findings,and understanding of the settings in which certain interventions are effective.

At this time, the significant focus on systematic reviews may be misplaced for adolescent mHealth. In much the same way that we use reporting guidelines and registration platforms for systematic reviews, there is a dire need for such tools for scoping reviews (particularly those within mHealth) in order to grow an evidence body of standardised work. Duplicating research efforts while health outcomes worsen is costly in terms of time, money and the wellbeing of young people.

References

Agarwal, S., Lefevre, A.E. & Labrique, A.B. 2017. A Call to Digital Health Practitioners: New Guidelines Can Help Improve the Quality of Digital Health Evidence. *JMIR Mhealth And Uhealth.* 5(10):e136. DOI:10.2196/mhealth.6640.

Agarwal, S., Perry, H.B., Long, L.-A. & Labrique, A.B. 2015. Evidence on feasibility and effective use of mHealth strategies by frontline health workers in developing countries: systematic review. *Tropical Medicine & International Health.* 20(8):1003-1014. DOI:10.1111/tmi.12525.

Agarwal, S., LeFevre, A.E., Lee, J., L'Engle, K., Mehl, G., Sinha, C. & Labrique, A. 2016. Guidelines for reporting of health interventions using mobile phones: mobile health (mHealth) evidence reporting and assessment (mERA) checklist. *Bmj.* 352. DOI:10.1136/bmj.i1174.

Ahmed, T., Lucas, H., Khan, A.S., Islam, R., Bhuiya, A. & Iqbal, M. 2014. eHealth and mHealth initiatives in Bangladesh: A scoping study. *BMC Health Services Research.* 14(1):260. DOI:10.1186/1472-6963-14-260.

Alonso-Coello, P., Schünemann, H.J., Moberg, J., Brignardello-Petersen, R., Akl, E.A., Davoli, M., Treweek, S., Mustafa, R.A. et al. 2016. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. *bmj.* 353:i2016.

Amicizia, D., Domnich, A., Gasparini, R., Bragazzi, N.L., Lai, P.L. & Panatto, D. 2013. An overview of current and potential use of information and communication technologies for immunization promotion among adolescents. *Human Vaccines & Immunotherapeutics.* 9(12):2634-2642. DOI:10.4161/hv.26010.

Anderson, S., Allen, P., Peckham, S. & Goodwin, N. 2008. Asking the right questions: Scoping studies in the commissioning of research on the organisation and delivery of health services. *Health Research Policy and Systems.* 6(1):7. DOI:10.1186/1478-4505-6-7.

Anderson, M. 2018. Teens, Social Media & Technology 2018. *Pew Research Center, May 2018.*http://assets.pewresearch.org/wpcontent/uploads/sites/14/2018/05/31102617/PI_2018.05.31_TeensTech_FINAL.pdf.

Anglada-Martinez, H., Riu-Viladoms, G., Martin-Conde, M., Rovira-Illamola, M., Sotoca-Momblona, J.M. & Codina-Jane, C. 2015. Does mHealth increase adherence to medication? Results of a systematic review. *International Journal of Clinical Practice.* 69(1):9-32. DOI:10.1111/ijcp.12582.

Annan, K. 1997. Inter-agency project on Universal Access to basic communication and information services, 3rd Session, United Nations Commission on science and technology for development, Geneva. Republished online *On the Digital Divide* Nov. 5, 2002. http://www.un.org/News/ossg/sg/stories/sg5nov-2002.htm.

Aranda-Jan, C.B., Mohutsiwa-Dibe, N. & Loukanova, S. 2014. Systematic review on what works, what does not work and why of implementation of mobile health (mHealth) projects in Africa. *BMC public health.* 14(1):1.

Arksey, H., O'Malley, L. 2005. Scoping Studies: Towards a Methodological Framework. *International journal of social research methodology*. 8(1): 19-32.

Asah, S.T. 2015. Post-2015 Development Agenda: Human Agency and the Inoperability of the Sustainable Development Architecture. *Journal of Human Development & Capabilities.* 16(4):631-636. DOI:10.1080/19452829.2015.1103712.

Bailey, J., Pavlou, M., Copas, A., McCarthy, O., Carswell, K., Rait, G., Hart, G., Nazareth, I. et al. 2015. The Sexunzipped trial: optimizing the design of online randomized controlled trials. *Journal of medical internet research.* 15(12):e278. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/481/CN-01047481/frame.html.

Bangure, D., Chirundu, D., Gombe, N., Marufu, T., Mandozana, G., Tshimanga, M. & Takundwa, L. 2015. Effectiveness of short message services reminder on childhood immunization programme in Kadoma, Zimbabwe - a randomized controlled trial, 2013. *BMC public health.* 15:137. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/678/CN-01109678/frame.html

Besoain, F., Perez-Navarro, A., Cayla, J.A., Avino, C.J. & de Olalla, P.G. 2015. Prevention of sexually transmitted infections using mobile devices and ubiquitous computing. *Int J Health Geogr.* 14:18. DOI:10.1186/s12942-015-0010-z.

Black, A.D., Car, J., Pagliari, C., Anandan, C., Cresswell, K., Bokun, T., McKinstry, B., Procter, R. et al. 2011. The Impact of eHealth on the Quality and Safety of Health Care. *PLoS Medicine.* 8(1). DOI:10.1371/journal.pmed.1000387.

Blackstock, O.J., Patel, V.V. & Cunningham, C.O. 2015. Use of Technology for HIV Prevention Among Adolescent and Adult Women in the United States. *Current HIV/AIDS Reports.* 12(4):489-499. DOI:10.1007/s11904-015-0287-3.

Borenstein, M., Hedges, L.V., Higgins, J.P. & Rothstein, H.R. 2009. *Introduction to meta-analysis.* Hoboken, NJ: WileyDOI:10.1002/9780470743386.

Brandt , A.M. 2013. How AIDS Invented Global Health. *New England Journal of Medicine.* 368(23):2149-2152. DOI:doi:10.1056/NEJMp1305297.

Bröder, J., Okan, O., Bauer, U., Bruland, D., Schlupp, S., Bollweg, T.M., Saboga-Nunes, L., Bond, E. et al. 2017. Health literacy in childhood and youth: a systematic review of definitions and models. *BMC Public Health.* 17(1):361. DOI:10.1186/s12889-017-4267-y.

Branson CE, C.P., Mukherjee P. . 2013. Text Message Reminders to Improve Outpatient Therapy AttendanceAmong Adolescents: A Pilot Study. *Psychol Serv.* Vol. 10(No. 3):298–303. DOI:10.1037/a0026693.

Brayboy, L., Mills, B., Sepolen, A., Mezoian, T., Wheeler, C. & Clark, M. 2017. Girl talk: a smartphone application to teach sexual health education to adolescent girls. *Obstetrics and gynecology. Conference: 64th annual clinical and scientific meeting of the american college of obstetricians and gynecologists. United states. Conference start: 20160514. Conference end: 20160517.* 127:22s-23s. Available:http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/143/CN01250143/frame.html

Brinkel, J., Krämer, A., Krumkamp, R., May, J. & Fobil, J. 2014. Mobile phone-based mHealth approaches for public health surveillance in sub-Saharan Africa: a systematic review. *International journal of environmental research and public health.* 11(11):11559-11582.

Buhi, E.R., Klinkenberger, N., Hughes, S., Blunt, H.D. & Rietmeijer, C. 2013. Teens' use of digital technologies and preferences for receiving STD prevention and sexual health promotion messages: implications for the next generation of intervention initiatives. *Sex Transm Dis.* 40(1):52-54. DOI:10.1097/OLQ.0b013e318264914a.

Bull, S.S., Levine, D.K., Black, S.R., Schmiege, S.J. & Santelli, J. 2012. Social media-delivered sexual health intervention: a cluster randomized controlled trial. *Am J Prev Med.* 43(5):467-474. DOI:10.1016/j.amepre.2012.07.022.

Cairns, K.E., Yap, M.B.H., Pilkington, P.D. & Jorm, A.F. 2014. Risk and protective factors for depression that adolescents can modify: A systematic review and meta-analysis of longitudinal studies. *Journal of Affective Disorders.* 169:61-75. DOI:10.1016/j.jad.2014.08.006.

Capurro, D., Cole, K., Echavarría, M.I., Joe, J., Neogi, T. & Turner, A.M. 2014. The use of social networking sites for public health practice and research: A systematic review. *Journal of Medical Internet Research.* 16(3). DOI:10.2196/jmir.2679.

Casey, B., Jones, R.M. & Hare, T.A. 2008. The adolescent brain. *Annals of the New York Academy of Sciences.* 1124(1):111-126. DOI:10.1196/annals.1440.010.

Champion, K.E., Newton, N.C., Spring, B., Wafford, Q.E., Parmenter, B.J. & Teesson, M. 2017. A systematic review of school-based eHealth interventions targeting alcohol use, smoking, physical inactivity, diet, sedentary behaviour and sleep among adolescents: A review protocol. *Systematic Reviews.* 6(1). DOI:10.1186/s13643-017-0645-x.

Chib, A., Wilkin, H., Ling, L.X., Hoefman, B. & Van Biejma, H. 2012. You have an important message! Evaluating the effectiveness of a text message HIV/AIDS campaign in Northwest Uganda. *J Health Commun.* 17 Suppl 1:146-157. DOI:10.1080/10810730.2011.649104.

Curioso, W.H. & Mechael, P.N. 2010. Enhancing 'M-Health' With South-To-South Collaborations. *Health Affairs.* 29(2):264-267. DOI:10.1377/hlthaff.2009.1057.

da Costa, C., Walker, B. & Bonavia, A. 2015. Tuberculosis Vaccines – state of the art, and novel approaches to vaccine development. *International Journal of Infectious Diseases.* 32:5-12. DOI:http://dx.doi.org/10.1016/j.ijid.2014.11.026

Das Gupta, M., Engelman, R., Levy, J., Gretchen, L., Merrick, T. & Rosen, J.E. 2014. *The Power of the 1.8 billion, ADOLESCENTS, YOUTH AND THE TRANSFORMATION OF THE FUTURE, State of world population, 2014.* UNFPA, https://www. unfpa. org/sites/default/files/pub-pdf/SWOP.

Davis, R., Campbell, R., Hildon, Z., Hobbs, L. & Michie, S. 2015. Theories of behaviour and behaviour change across the social and behavioural sciences: a scoping review. *Health psychology review.* 9(3):323-344. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4566873/pdf/rhpr-9-323.pdf.

De Jongh, T., Gurol‐Urganci, I., Vodopivec‐Jamsek, V., Car, J. & Atun, R. 2012. Mobile phone messaging for facilitating self‐management of long‐term illnesses. *The Cochrane Library.*

Degeling, C., Mayes, C., Lipworth, W., Kerridge, I. & Upshur, R. 2015. The Political and Ethical Challenge of Multi-Drug Resistant Tuberculosis. *Journal of Bioethical Inquiry.* 12(1):107-113. DOI:10.1007/s11673-014-9595-3.

Dempsey, A.F. & Zimet, G.D. 2015. Interventions to Improve Adolescent Vaccination: What May Work and What Still Needs to Be Tested. *Am J Prev Med.* 49(6 Suppl 4):S445-454. DOI:10.1016/j.amepre.2015.04.013.

Devi, B.R., Syed-Abdul, S., Kumar, A., Iqbal, U., Nguyen, P.-A., Li, Y.-C. & Jian, W.-S. 2015. mHealth: An updated systematic review with a focus on HIV/AIDS and tuberculosis long term management using mobile phones. *Computer Methods and Programs in Biomedicine.* 122(2):257-265. DOI:http://dx.doi.org/10.1016/j.cmpb.2015.08.003.

Dick, B. & Ferguson, B.J. 2015. Health for the world's adolescents: a second chance in the second decade. *Journal of Adolescent Health.* 56(1):3-6.

Dorsey, E.R. & Topol, E.J. 2016. State of Telehealth. *New England Journal of Medicine.* 375(2):154-161.

Eysenbach, G. 2002. Issues in evaluating health websites in an Internet-based randomized controlled trial. *J Med Internet Res .* 4(3). DOI:10.2196/jmir.4.3.e17

Eysenbach, G& CONSORT-EHEALTH GROUP.2011. CONSORT-EHEALTH: Improving and Standardizing Evaluation Reports of Web-based and Mobile Health Interventions. *J Med Internet Res.* 13(4). DOI:10.2196/jmir.1923

Eze, G.U. & Adeleye, O.O. 2015. Enhancing Routine Immunization Performance using Innovative Technology in an Urban Area of Nigeria. *West Afr J Med.* 34(1):3-10.

Falzon, D., Timimi, H., Kurosinski, P., Migliori, G.B., Van Gemert, W., Denkinger, C., Isaacs, C., Story, A. et al. 2016. Digital health for the End TB Strategy: developing priority products and making them work. *The European Respiratory Journal.* 48(1):29-45. DOI:10.1183/13993003.00424-2016.

Fiellin, L.E., Hieftje, K.D., Pendergrass, T.M., Kyriakides, T.C., Duncan, L.R., Dziura, J.D., Sawyer, B.G., Mayes, L. et al. 2017. Video Game Intervention for Sexual Risk Reduction in Minority Adolescents: Randomized Controlled Trial. *Journal of Medical Internet Research.* 19(9):e314. DOI:10.2196/jmir.8148.

Fiordelli, M., Diviani, N. & Schulz, P.J. 2013. Mapping mHealth Research: A Decade of Evolution. *J Med Internet Res.* 15(5):e95. DOI:10.2196/jmir.2430.

Fortuin, J., Salie, F., Abdullahi, L.H. & Douglas, T.S. 2016. The impact of mHealth interventions on health systems: a systematic review protocol. *Systematic Reviews.* 5(1):200.

Free, C., Phillips, G., Felix, L., Galli, L., Patel, V. & Edwards, P. 2010. The effectiveness of M-health technologies for improving health and health services: a systematic review protocol. *BMC Research Notes.* 3:250-250. DOI:10.1186/1756-0500-3-250.

Free C., Phillips, G., Watson L., Galli L., Felix L., Edwards P., et al. 2013. The Effectiveness of Mobile-Health Technologies to Improve Health Care Service Delivery Processes: A Systematic Review and Meta-Analysis. *PLoS Med* 10:1e1001363. Available: https://doi.org/10.1371/journal.pmed.1001363 [Accessed 19 May 2018].

Ginsberg, A. 2010. Tuberculosis drug development Progress-challenges and the road ahead. *Tuberculosis.* 90:162-167. DOI:10.1016/j.tube.2010.03.003.

Ginsberg, A.M., Ruhwald, M., Mearns, H. & McShane, H. 2016. TB vaccines in clinical development. *Tuberculosis.*http://dx.doi.org/10.1016/j.tube.2016.05.013:1-5. DOI:http://dx.doi.org/10.1016/j.tube.2016.05.013.

Gore, F.M., Bloem, P.J., Patton, G.C., Ferguson, J., Joseph, V., Coffey, C., Sawyer, S.M. & Mathers, C.D. 2011. Global burden of disease in young people aged 10–24 years: a systematic analysis. *The Lancet.* 377(9783):2093-2102.

Gough, D., Thomas, J. & Oliver, S. 2012. Clarifying differences between review designs and methods. *Systematic Reviews.* 1(1):28. DOI:10.1186/2046-4053-1-28.

Grist, R., Porter, J & Stallard, S. 2017. Mental Health Mobile Apps for Preadolescents and Adoescents: A Systematic Review.*J Med Internet Res.* 19(5):e176. DOI:10.2196/jmir.7332.

Guse, K., Levine, D., Martins, S., Lira, A., Gaarde, J., Westmorland, W. & Gilliam, M. 2012. Interventions using new digital media to improve adolescent sexual health: a systematic review. *J Adolesc Health.* 51(6):535-543. DOI:10.1016/j.jadohealth.2012.03.014.

Gurman, T.A., Rubin, S.E. & Roess, A.A. 2012. Effectiveness of mHealth behavior change communication interventions in developing countries: a systematic review of the literature. *Journal of health communication.* 17(sup1):82-104.

Guyatt, G.H., Oxman, A.D., Vist, G., Kunz, R. & Falck-Ytter, Y. 2008. Rating quality of evidence and strength of recommendations GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 336. DOI:10.1136/bmj.39489.470347.AD.

Hall, C.S., Fottrell, E., Wilkinson, S. & Byass, P. 2014. Assessing the impact of mHealth interventions in low- and middle-income countries – what has been shown to work? *2014.* 7. DOI:10.3402/gha.v7.25606.

Hamine, S., Gerth-Guyette, E., Faulx, D., Green, B.B. & Ginsburg, A.S. 2015. Impact of mHealth Chronic Disease Management on Treatment Adherence and Patient Outcomes: A Systematic Review. *J Med Internet Res.* 17(2):e52. DOI:10.2196/jmir.3951.

Harris, R.C., Sumner, T., Knight, G.M. & White, R.G. 2016. Systematic review of mathematical models exploring the epidemiological impact of future TB vaccines. *Human Vaccines & Immunotherapeutics.* 10.1080/21645515.2016.1205769:00-00. DOI:10.1080/21645515.2016.1205769.

Hermans, S.M., Elbireer, S., Tibakabikoba, H., Hoefman, B.J. & Manabe, Y.C. 2017. Text messaging to decrease tuberculosis treatment attrition in TB-HIV coinfection in Uganda. *Patient Preference and Adherence.* 11:1479-1487. DOI:10.2147/PPA.S135540.

Higgs, E.S., Goldberg, A.B., Labrique, A.B., Cook, S.H., Schmid, C., Cole, C.F. & Obregón, R.A. 2014. Understanding the role of mHealth and other media interventions for behavior change to enhance child survival and development in low-and middle-income countries: An evidence review. *Journal of health communication.* 19(sup1):164-189.

Higgins JPT, Green S. Eds. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]; 2011. [Internet]. Available from http://www.cochrane-handbook.org. Accessed July 15 2016.

Hospital, M.M., Wagner, E.F., Morris, S.L., Sawant, M., Siqueira, L.M. & Soumah, M. 2016. Developing an SMS Intervention for the Prevention of Underage Drinking: Results From Focus Groups. *Subst Use Misuse.* 51(2):155-164. DOI:10.3109/10826084.2015.1073325.

International Telecommunication Union (ITU)., I.T.U. 2017. Measuring the Information Society 2017. *Geneva: ITU.* 1. https://www.itu.int/en/ITUD/Statistics/Documents/publications/misr2017/MISR2017_Volume1.pdf[Accessed 19 May 2018].

Iribarren, S.J., Schnall, R., Stone, P.W. & Carballo-Diéguez, A. 2016. Smartphone Applications to Support Tuberculosis Prevention and Treatment: Review and Evaluation. *JMIR mHealth uHealth.* 4(2):e25. DOI:10.2196/mhealth.5022.

Jeffries, C., Ross, P., Matoff-Stepp, S., Thompson, R., Harris, J., Uhrig, J. & Cheever, L. 2017. Ucare4life: mobile texting to improve HIV care continuum outcomes for minority youth. *Topics in antiviral medicine. Conference: 23rd conference on retroviruses and opportunistic infections, CROI 2016. United states. Conference start: 20160222. Conference end: 20160225.* 24(E-1):427. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/329/CN-01250329/frame.html.

Juzang, I., Fortune, T., Black, S., Wright, E. & Bull, S. 2011. A pilot programme using mobile phones for HIV prevention. *J Telemed Telecare.* 17(3):150-153. DOI:10.1258/jtt.2010.091107.

Kalan, R., Wiysonge, C.S., Ramafuthole, T., Allie, K., Ebrahim, F. & Engel, M.E. 2014. Mobile phone text messaging for improving the uptake of vaccinations: a systematic review protocol. *BMJ open.* 4(8):e005130.

Kaufmann, S.H., Hussey, G. & Lambert, P.-H. 2010. New vaccines for tuberculosis. *The Lancet.* 375(9731):2110-2119.

Keith, R.E., Crosson, J.C., O'Malley, A.S., Cromp, D. & Taylor, E.F. 2017. Using the Consolidated Framework for Implementation Research (CFIR) to produce actionable findings: a rapid-cycle evaluation approach to improving implementation. *Implementation Science.* 12(1):15. DOI:10.1186/s13012-017-0550-7.

Khalil, H., Peters, M., Godfrey, C.M., McInerney, P., Soares, C.B. & Parker, D. 2016. An Evidence-Based Approach to Scoping Reviews. *Worldviews Evid Based Nurs.* 13(2):118-123. DOI:10.1111/wvn.12144.

Kim, S.H., McDonald, S., Kim, S., Foster, C. & Fidler, S. 2015. Importance of Self-Motivation and Social Support in Medication Adherence in HIV-Infected Adolescents in the United Kingdom and Ireland: A Multicentre HYPNet Study. *AIDS Patient Care STDS.* 29(6):354-364. DOI:10.1089/apc.2014.0335.

King, E., Kinvig, K., Steif, J., Qiu, A.Q., Maan, E.J., Albert, A.Y., Pick, N., Alimenti, A. et al. 2017. Mobile Text Messaging to Improve Medication Adherence and Viral Load in a Vulnerable Canadian Population Living With Human Immunodeficiency Virus: A Repeated Measures Study. *J Med Internet Res.* 19(6):e190. DOI:10.2196/jmir.6631.

Kobak, K.A., Mundt, J.C. & Kennard, B. 2015. Integrating technology into cognitive behavior therapy for adolescent depression: A pilot study. *Annals of General Psychiatry.* 14(1). DOI:10.1186/s12991-015-0077-8.

Kuruvilla, S., Bustreo, F., Kuo, N., Mishra, C., Taylor, K., Fogstad, H., Gupta, G.R., Gilmore, K. et al. 2016. The Global strategy for women's, children's and adolescents' health (2016–2030): a roadmap based on evidence and country experience. *Bull World Health Organ.* 94(5):398-400. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4850541/pdf/BLT.16.170431.pdf.

Labrique, A.B., Vasudevan, L., Kochi, E., Fabricant, R. & Mehl, G. 2013. mHealth innovations as health system strengthening tools: 12 common applications and a visual framework. *Glob Health Sci Pract.* 1(2):160-171. DOI:10.9745/GHSP-D-13-00031.

Labrique, A., Vasudevan, L., Chang, L.W. & Mehl, G. 2013. H_pe for mHealth: more "y" or "o" on the horizon? *International journal of medical informatics.* 82(5):467-469. DOI:10.1016/j.ijmedinf.2012.11.016.

Laski, L. 2015. Realising the health and wellbeing of adolescents. *BMJ. British medical journal.* 351.

Lenhart, A. 2015. Teens, Social Media & Technology Overview 2015. *Pew Research.*

Leon, N., Schneider, H. & Daviaud, E. 2012. Applying a framework for assessing the health system challenges to scaling up mHealth in South Africa. *BMC Medical Informatics and Decision Making.* 12:123-123. DOI:10.1186/1472-6947-12-123.

Levac, D., Colquhoun, H. & O'Brien, K.K. 2010. Scoping studies: advancing the methodology. *Implementation Science : IS.* 5:69-69. DOI:10.1186/1748-5908-5-69.

Lim, M., Hocking, J., Aitken, C., Fairley, C., Jordan, L., Lewis, J. & Hellard, M. 2012. Impact of text and email messaging on the sexual health of young people: a randomised controlled trial. *Journal of epidemiology and community health.* 66(1):69-74. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/479/CN-00832479/frame.html

Lund, S., Nielsen, B.B., Hemed, M., Boas, I.M., Said, A., Said, K., Makungu, M.H. & Rasch, V. 2014. Mobile phones improve antenatal care attendance in Zanzibar: a cluster randomized controlled trial. *BMC Pregnancy Childbirth.* 14:29. DOI:10.1186/1471-2393-14-29.

Malloy-Weir, L.J., Charles, C., Gafni, A. & Entwistle, V.A. 2015. Empirical relationships between health literacy and treatment decision making: A scoping review of the literature. *Patient Educ Couns.* 98(3):296-309. DOI:10.1016/j.pec.2014.11.004.

Manicavasagar, V., Horswood, D., Burckhardt, R., Lum, A., Hadzi-Pavlovic, D. & Parker, G. 2014. Feasibility and effectiveness of a web-based positive psychology program for youth mental health: randomized controlled trial. *J Med Internet Res.* 16(6):e140. DOI:10.2196/jmir.3176.

Matheson EC, D.A., Gagliano M, Thompson JA, Blood-Siegfried J. 2014. Increasing HPV vaccination series completionrates via text message reminders.*J Pediatr Health Care.* 28(4):e35-e39. DOI: 10.1016/j.pedhc.2013.09.001.

Mbuagbaw, L., Mursleen, S., Lytvyn, L., Smieja, M., Dolovich, L. & Thabane, L. 2015. Mobile phone text messaging interventions for HIV and other chronic diseases: an overview of systematic reviews and framework for evidence transfer. *BMC Health Services Research.* 15:33. DOI:10.1186/s12913-014-0654-6.

McIntosh, J.R.D., Jay, S., Hadden, N., Whittaker, P. J. 2017. Do E-health interventions improve physical activity in young people: a systematic review. Public Health. 148:140-148. DOI: 10.1016/j.puhe.2017.04.001.

Moher, D., Schulz, K., Simera, I., &Altman, D. 2010. Guidance for developers of health research reporting guidelines. *PLoS Med.*7(2):e1000217. DOI:10.1371/journal.pmed.1000217.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D. & Liberati, A. 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 4. DOI:10.1186/2046-4053-4-1.

Mokdad, A.H., Forouzanfar, M.H., Daoud, F., Mokdad, A.A., El Bcheraoui, C., Moradi-Lakeh, M., Kyu, H.H., Barber, R.M. et al. 2016. Global burden of diseases, injuries, and risk factors for young people's health during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet.*

Montanaro, E., Fiellin, L.E., Fakhouri, T., Kyriakides, T.C. & Duncan, L.R. 2015. Using Videogame Apps to Assess Gains in Adolescents' Substance Use Knowledge: New Opportunities for Evaluating Intervention Exposure and Content Mastery. *J Med Internet Res.* 17(10):e245. DOI:10.2196/jmir.4377.

Morris, J., Wang, W., Wang, L., Peddecord, K.M. & Sawyer, M.H. 2015. Comparison of reminder methods in selected adolescents with records in an immunization registry. *J Adolesc Health.* 56(5 Suppl):S27-32. DOI:10.1016/j.jadohealth.2015.01.010.

Mustanski, B., DuBois, L.Z., Prescott, T.L. & Ybarra, M.L. 2014. A Mixed-Methods Study of Condom Use and Decision Making Among Adolescent Gay and Bisexual Males. *AIDS and Behavior.* 18(10):1955-1969. DOI:10.1007/s10461-014-0810-3.

Narring F, J.P., Dominicé DM, Camparini RN, Humair J, Broers B, et al. 2013. Text-messaging to reduce missed appointmentin a youth clinic: a randomised controlled trial. *J Epidemiol Community Health.* 67(10):888-891. DOI:10.1136/jech-2013-202510.

Ncube, M. 2013. Infrastructure deficit, financing needs and the post-2015 MDG framework in Africa. *I D S Bulletin.* (5-6):72-80.

Nglazi, M.D., Bekker, L.-G., Wood, R., Hussey, G.D. & Wiysonge, C.S. 2013. Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: a systematic review. *BMC Infectious Diseases.* 13:566-566. DOI:10.1186/1471-2334-13-566.

Odone, A., Ferrari, A., Spagnoli, F., Visciarelli, S., Shefer, A., Pasquarella, C. & Signorelli, C. 2015. Effectiveness of interventions that apply new media to improve vaccine uptake and vaccine coverage: A systematic review. *Human vaccines & immunotherapeutics.* 11(1):72-82.

Oluoch, T., Kwaro, D., Ssempijja, V., Katana, A., Langat, P., Okeyo, N., Abu-Hanna, A. & de Keizer, N. 2015. Better adherence to pre-antiretroviral therapy guidelines after implementing an electronic medical record system in rural Kenyan HIV clinics: a multicenter pre-post study. *Int J Infect Dis.* 33:109-113. DOI:10.1016/j.ijid.2014.06.004.

Oosthuizen, M.A., Jinabhai, C.C., Terblanche, A.P.S. & Becker, P.J. 2008. A transition in health status from childhood to adulthood and associated lifestyle risk factors: a 13-year interval follow-up study in South Africa. *International Journal of Environmental Health Research.* 18(1):65-72. DOI:10.1080/09603120701309203.

Oyo-Ita, A., Wiysonge, C.S., Oringanje, C., Nwachukwu, C.E., Oduwole, O. & Meremikwu, M.M. 2016. Interventions for improving coverage of childhood immunisation in low- and middle-income countries. *Cochrane Database of Systematic Reviews.* 10.1002/14651858.CD008145.pub3(7). DOI:10.1002/14651858.CD008145.pub3.

Patton, G.C., Coffey, C., Cappa, C., Currie, D., Riley, L., Gore, F., Degenhardt, L., Richardson, D. et al. 2012. Health of the world's adolescents: a synthesis of internationally comparable data. *The Lancet.* 379(9826):1665-1675.

Peters, M.D., Godfrey, C.M., Khalil, H., McInerney, P., Parker, D. & Soares, C.B. 2015a. Guidance for conducting systematic scoping reviews. *International journal of evidence-based healthcare.* 13(3):141-146.

Peters, M., Godfrey, C., McInerney, P., Soares, C., Khalil, H. & Parker, D. 2015b. The Joanna Briggs institute Reviewers' Manual 2015: Methodology for JBI scoping reviews.

Piette, J.D., Aikens, J.E., Trivedi, R., Parrish, D., Standiford, C., Marinec, N.S., Striplin, D. & Bernstein, S.J. 2013. Depression self-management assistance using automated telephonic assessments and social support. *The American Journal Of Managed Care.* 19(11):892-900. Available: http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=24511987&site=ehost-live.

Puccio, J.A., Belzer, M., Olson, J., Martinez, M., Salata, C., Tucker, D. & Tanaka, D. 2006. The use of cell phone reminder calls for assisting HIV-infected adolescents and young adults to adhere to highly active antiretroviral therapy: a pilot study. *AIDS Patient Care STDS.* 20(6):438-444. DOI:10.1089/apc.2006.20.438.

Ranney, M.L., Freeman, J.R., Connell, G., Spirito, A., Boyer, E., Walton, M., Guthrie, K.M. & Cunningham, R.M. 2016. A Depression Prevention Intervention for Adolescents in the Emergency Department. *Journal of Adolescent Health.* 59(4):401-410. DOI:10.1016/j.jadohealth.2016.04.008.

Reback, C.J., Grant, D.L., Fletcher, J.B., Branson, C.M., Shoptaw, S., Bowers, J.R., Charania, M. & Mansergh, G. 2012. Text messaging reduces HIV risk behaviors among methamphetamine-using men who have sex with men. *AIDS Behav.* 16(7):1993-2002. DOI:10.1007/s10461-012-0200-7.

Rice, B., Huettner, S., Perrin, J. & Trent, M. 2016. Responsiveness and reliability: Understanding text messaging communication in a pelvic inflammatory disease intervention. *Journal of adolescent health.* 58(2 suppl. 1):S30-s31..

Rokicki, S., Cohen, J., Salomon, J.A. & Fink, G. 2017. Impact of a text-messaging programon adolescent reproductive health: A cluster-randomized trial in Ghana. *American Journal of Public Health.* 107(2):298-305. DOI:10.2105/AJPH.2016.303562.

Rose, T., Barker, M., et al. 2017. A Systematic Review of DIgital Interventions for Imporving Diet and Physical Activity Behaviors of Adolescents.*Journal of Adolescent Health.* 61(6):669-677. DOI:10.1016/j.jadohealth.2017.05.024.

Russell, S. 2012. Effectiveness of text message reminders for improving vaccination appointment attendance and series completion among adolescents and adults. *Value in health.* 15(4):A248.

Sawyer, S.M., Afifi, R.A., Bearinger, L.H., Blakemore, S.-J., Dick, B., Ezeh, A.C. & Patton, G.C. 2012. Adolescence: a foundation for future health. *The Lancet.* 379(9826):1630-1640.

Shet, A., De Costa, A., Kumarasamy, N., Rodrigues, R., Rewari, B.B., Ashorn, P., Eriksson, B. & Diwan, V. 2014. Effect of mobile telephone reminders on treatment outcome in HIV: evidence from a randomised controlled trial in India. *Bmj.* 349:g5978. DOI:10.1136/bmj.g5978.

Scull, T.M., Kupersmidt, J.B., Malik, C.V. & Keefe, E.M. 2017. Examining the efficacy of an mHealth media literacy education program for sexual health promotion in older adolescents attending community college. *J Am Coll Health.* DOI:10.1080/07448481.2017.1393822.

Slack, L. 2014. The post-2015 Global Agenda - a role for local government. *Commonwealth Journal of Local Governance.* 10.5130/cjlg.v0i0.4069(15):173-177. DOI:10.5130/cjlg.v0i0.4069.

Smillie, K., Van Borek, N., van der Kop, M.L., Lukhwaro, A., Li, N., Karanja, S., Patel, A.R., Ojakaa, D. et al. 2014. Mobile health for early retention in HIV care: a qualitative study in Kenya (WelTel Retain). *Afr J AIDS Res.* 13(4):331-338. DOI:10.2989/16085906.2014.961939.

Smillie, K., Van Borek, N., Abaki, J., Pick, N., Maan, E.J., Friesen, K., Graham, R., Levine, S. et al. 2014. A qualitative study investigating the use of a mobile phone short message service designed to improve HIV adherence and retention in care in Canada (WelTel BC1). *J Assoc Nurses AIDS Care.* 25(6):614-625. DOI:10.1016/j.jana.2014.01.008.

Stockwell, M.S., Kharbanda, E.O., Martinez, R.A., Vargas, C.Y., Vawdrey, D.K. & Camargo, S. 2012. Effect of a text messaging intervention on influenza vaccination in an urban, low-income pediatric and adolescent population: A randomized controlled trial. *JAMA - Journal of the American Medical Association.* 307(16):1702-1708. DOI:10.1001/jama.2012.502.

Tahaney, K.D. & Palfai, T.P. 2017. Text messaging as an adjunct to a web-based intervention for college student alcohol use: A preliminary study. *Addictive Behaviors.* 73:63-66. DOI:10.1016/j.addbeh.2017.04.018.

Ten Dam, H., Toman, K., Hitze, K. & Guld, J. 1976. Present knowledge of immunization against tuberculosis. *Bulletin of the World Health Organization.* 54(3):255.

Trent M, T.C., Tomaszewski K. . 2015. Text messaging support for urban adolescents and young adults using injectablecontraception: outcomes of the depotext pilot trial *J Adolesc Health* 57(1):100-106.

Tossmann, H.-P., Jonas, B., Tensil, M.-D., Lang, P. & Strüber, E. 2011. A controlled trial of an internet-based intervention program for cannabis users. *Cyberpsychol Behav Soc Netw.* 14(11):673-679. DOI:10.1089/cyber.2010.0506.

United Nations Department of Economic and Social Affairs, U. 2013. "What do we mean by youth?" Factsheet Available: http://www.unesco.org/new/en/social-and-human-sciences/themes/youth/youth-definition [Accessed 21 November 2016].

Uppada, D.R., Selvam, S., Jesuraj, N., Lau, E.L., Doherty, T.M., Grewal, H.M., Vaz, M. & Lindtjørn, B. 2016. Incidence of tuberculosis among school-going adolescents in South India. *BMC Public Health.* 16(1):1.

Viner, R.M., Coffey, C., Mathers, C., Bloem, P., Costello, A., Santelli, J. & Patton, G.C. 2011. 50-year mortality trends in children and young people: a study of 50 low-income, middle-income, and high-income countries. *The Lancet.* 377(9772):1162-1174.

Wagner, E., Morris, S., Siqueira, L. & Sawant, M. 2013. Examiningthe effectiveness of an alcohol-targeted text messaging intervention with minority adolescents. *Alcoholism: Clinical and Experimental Research.* 37:284a. Available: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/166/CN-01027166/frame.html

Weitzel, J., Bernhardt, J., Usdan, S., Mays, D. & Glanz, K. 2007. Using wireless handheld computers and tailored text messaging to reduce negative consequences of drinking alcohol. *Journal of studies on alcohol and drugs.* 68(4):534-537.

Wiysonge, C.S., Ngcobo, N.J., Jeena, P.M., Madhi, S.A., Schoub, B.D., Hawkridge, A., Shey, M.S. & Hussey, G.D. 2012. Advances in childhood immunisation in South Africa: where to now? Programme managers' views and evidence from systematic reviews. *BMC Public Health.* 12:578-578. DOI:10.1186/1471-2458-12-578.

World Health Organization, W.H.O. 2011. mHealth: New horizons for health through mobile technologies: second global survey on ehealth. Global Observatory for eHealth series—Volume 3. 2011. *Mental Health Action Plan.*

World Health Organization, W.H.O. 2013. Maternal, newborn, child and adolescent health. *Documents on the integrated management of childhood illness [IMCI](online). Available from URL:* http://www*. who. int/maternal_child_adolescent/documents/imci/en/index. html.*

World Health Organization, W.H.O. 2014a. WHO calls for stronger focus on adolescent health. *WHO Media centre.*

World Health Organization, W.H.O. 2014b. Adolescents: health risks and solutions. *Fact sheet.* (345).

World Health Organization, W.H.O. 2014c. Health for the world's adolescents: a second chance in the second decade: summary.

World Health Organization, W.H.O. 2015. *Global tuberculosis report 2015.* World Health Organization.

World Health Organization, W.H.O. 2017.*Global Accelerated Action for the Health of Adolescents (AA-HA!): guidance to support country implementation.* Summary. Geneva: WHO; 2017 (WHO/FWC/MCA/17.05). Licence: CC BY-NC-SA 3.0 IGO.

Wu, S.J. & Raghupathi, W. 2012. A Panel Analysis of the Strategic Association Between Information and Communication Technology and Public Health Delivery. *Journal of Medical Internet Research.* 14(5):e147. DOI:10.2196/jmir.2242.

Ybarra, M.L., Prescott, T.L., Phillips, G.L., Bull, S.S., Parsons, J.T. & Mustanski, B. 2017. Pilot RCT Results of an mHealth HIV Prevention Program for Sexual Minority Male Adolescents. *Pediatrics.* 140(1). DOI:10.1542/peds.2016-2999.

APPENDIX 1 FINAL AND INITIAL SEARCH STRATEGY (PUBMED)

Initial search:

Set 1 Adolescence

Adolescent [MeSH] (13-18 yrs.)

OR

Young adult [MeSH] (19-24 yrs.)

OR

Adolescence OR adolescent OR teenager OR teenage OR teen OR pubertal OR Youth OR young adult OR young people

AND

Set 2mHealth

"Telemedicine"[Mesh]

OR

Cellular Phone [MeSH]

OR

Text Messaging [MeSH]

OR

Medical Informatics Applications [MeSH]

OR

Reminder Systems [MeSH]

OR

Mobile Applications [MeSH]

OR

Telemedicine OR Digital health OR Mhealth OR M-health OR eHealth OR e-health OR mobile health OR telehealth OR telecare

OR

(Health OR medicine) AND (Mobile based OR Mobile technology OR Text messaging OR Text OR texting OR messages OR Messaging OR SMS OR MMS OR Mobile phones OR Mobile phone based OR Cell phones OR Cellular phones OR Smartphone OR mobile devices OR Mobile apps OR Mobile applications OR Web-based OR Internet-based OR e-counselling OR portable electronic applications OR telephone-based OR telecommunication OR social media)

AND

Set 3 Health Promotion

Preventive Health Services [MeSH]

OR

Health Communication [MeSH]

OR

Patient Compliance [MeSH]

OR

Health education OR health promotion OR patient education OR health communication OR peer-to-peer communication OR health behavior change OR health behaviour change

AND

Set 4 Immunization

"Immunization"[Mesh]

OR

Immunization OR Immunisation OR vaccination OR immunostimulation OR Immunologic Stimulation OR Immunological Stimulation OR Immunological Sensitization OR vaccines

AND

Set 5 Tuberculosis

Mycobacterium Infections [MeSH]

OR

TB OR tuberculosis OR mycobacterium Infections

AND

Set 6 Infectious Diseases

Communicable Diseases [MeSH]

OR

Infectious Diseases OR communicable diseases

Final Search:

S1	"Health Promotion" OR "Health Communication" OR "Health Education" OR "Health Behavior" OR "Medication Adherence" OR “Patient Compliance" OR “information seeking behavior” OR “Health behavior change” OR “patient education” OR “patient compliance”
S2	"Telemedicine" OR "Smartphone" OR "Cell Phones" OR "Social Media" OR "Text Messaging" OR mHealth OR “mobile health” OR “Digital health” OR ehealth OR “mobile device” OR “mobile phone” OR “cell phone” OR SnapChat OR Instagram OR WhatsApp OR “web 2.0” OR twitter OR facebook OR "Mobile Applications" OR “short message service”
S3	"Adolescent" OR adolescence OR "Young Adult" OR "Minors"
S4	undernutrition OR anaemia OR malnutrition OR suicide OR “mental disorders” OR “mood disorder” OR "depressive disorder" OR depression OR "bipolar disorder" OR "substance-related disorder" OR smoking OR “tobacco use” OR “alcohol use” OR “underage drinking” OR injury OR "Road traffic accidents" OR "Traffic Accidents" OR “Unintentional injury” OR “Penetrating Wounds” OR Wounds OR violence OR "infectious disease" OR “infectious disease transmission” OR "communicable disease" OR pneumonia OR bronchopneumonia OR meningitis OR diarrhea OR gastroenteritis OR malaria OR tuberculosis OR “human immunodeficiency virus” OR HIV OR immunis* OR vaccine OR vaccination OR immunization OR "Reproductive health" OR "Sexual health" OR "Unsafe sex
S5	“randomized controlled trial” OR “controlled clinical trial” OR “randomized controlled trials” OR “random allocation” OR “double-blind method” OR “single-blind method” OR “clinical trial” OR “clinical trials” OR "clinical trial" OR singl* OR doubl* OR trebl* OR blind* OR placebos OR placebo* OR random* OR “research design” OR “comparative study” OR “comparative studies” OR “evaluation studies” OR “evaluation study” OR “follow-up studies” OR “prospective studies” OR controlled OR controls OR control OR prospectiv* OR volunteer* OR cohort OR “mixed methods” OR “meta analysis” OR “meta-analysis”
S6	S1 AND S2 AND S3 AND S4 AND S5
S7	S6 NOT ("Qualitative Research" OR "Surveys and Questionnaires" OR “qualitative study” OR “qualitative method” OR survey OR “survey method” OR questionnaire)

APPENDIX 2 ELIGIBILITY PROMPT TOOL FOR INCLUSION/EXCLUSION

	Inclusion Criteria: if 'NO" to any of these questions, exclude	**YES**	**Unsure**	**NO**
1	Is the intervention accessed on wireless technology, such as mobile phones/ smartphone/laptop/PDA? (rather than e.g. desktop, home- or facility-based computer etc.)			
2	Is the intervention aimed at one of the target conditions? (TB, HIV, SRH, self-harm, violence, substance abuse, suicide, depression)			
3	Is the study an RCT / MMSD / quasi-experimental / before-and-after trial design? (rather than editorial, focus group/ survey / commentary)			
4	Is there a control group receiving standard of care or another mHealth intervention?			
5	Do participants 10-19 years of age make up at least 50% of the sample size?			
	Exclusion Criteria: if 'YES" to any of these questions, exclude	**YES**	**Unsure**	**NO**
1	Is there exclusive use of telephone or voice calls as a means of communication? (rather than e.g. SMS, social media, website, WhatsApp, Facebook etc.)			
2	Is any part of the study pending for complete reporting of results?			
3	Is insufficient detail reported for the study to be replicated? (e.g. sample size, effect size)			
4	Is the intervention targeted at vaccine-preventable disease other than influenza or HPV?			
5	Do participants older than 19 years make up more than 50% of the sample?			
	NB. TICKS IN SHADED AREAS SUGGEST EXCLUSION OR DISCUSSION	DATE: _____		

FIRST REVIEWER's INTIALS ☐☐

SECOND REVIEWER's INTIALS ☐☐

IN AGREEMENT? YES ☐ NO / ADJUDICATION ☐

FINAL DECISION: INCLUDE FOR FULL-TEXT SCREEN ☐ EXCLUDE ☐

COMMENTS:_____

_____

_____

Date:_____

APPENDIX 3 DATA EXTRACTION FORM

Author	Year	Reviewer

1. General Information

Date, reviewer	
Reference citation	
Publication type	
Potentially eligible studies from the reference list	Yes (1) No (2)
Notes:	

2. Study characteristics

	Eligibility criteria	**Location in text**
<u>Disease</u> targeted	HIV (1) TB (2) RTA(3) RPH (4)VIOLENCE (5) DEPRESSION(6) SUICIDE (7) VPD INFLUENZA (8) VPD HPV (9)	*pg* *fig*
Location/Language of paper	*Location* *WB Classification LMIC (1)* *WB MIC (2)*	*pg* *fig*
Study type	*Specify:*	*pg* *fig*
Systematic review reference	*Yes (1)* *No (2)*	*pg* *fig*
Participants *(age-ranges / proportion of adolescents if broader sample)*	10 – 14 years (1) 15 – 19 years (2) Other (3)	*pg* *fig*
Types of outcome measures	Health knowledge (1) Risk behaviour (2) Medication adherence (3) Appointment management (4) on-time or increased Provider relationship (5) Treatment outcome measure (VL, scale) (6) Other (7)	*pg* *fig*
INCLUDE☐ EXCLUDE☐		
Notes:		

DO NOT PROCEED IF STUDY EXCLUDED FROM REVIEW

3. Characteristics of included studies

Methods

	Descriptions as stated in report/paper		Location
Aim of study			*pg* *fig*
Study Design *(specify)*	*Cohort (1)* *Mixed Methods (4)* *Cross Sectional (2)* *RCT (3)* *Pre-post /quasi-experimental (4)*		*pg* *fig*
Unit of allocation *(by individuals, cluster/ groups)*	Individuals (1) Clusters (2)		*pg* *fig*
Duration	**Start date** *(recruitment* **End date** *to last follow-up)*		*pg*
Ethics approval obtained / needed	1☐ **2**☐ **3**☐ YesNoUnclear		*pg*
Notes:			

Quantitative study characteristics

Population and setting

	Description *Include comparative information for each intervention or comparison group if available*		**Location**
Population description			*pg* *fig*
Setting *(including location and social context)*			*pg* *fig*
Inclusion criteria			*pg* *fig*
Exclusion criteria			*pg* *fig*
Method of recruitment of participants			*pg* *fig*
Informed consent obtained	1☐ **2**☐ **3** ☐ Yes No Unclear		
Notes			

Participants

	Description as stated in paper	Location in text
Total enrolled		*pg* *fig*
Withdrawal/exclusions		
Age	Age range eligible: OR Age-disaggregated data with at least 50% sample between ages 10-19 years:	*pg* *fig*
Sex		
Location/Access	1☐rural 2☐urban 3☐airtime provided	*pg* *fig*
Phone/technology	1☐Own 2☐Shared 3☐Study	*pg* *fig*
Subgroups measured		*pg* *fig/table*
Notes		

Outcome measures

	Description	Location in text
Intervention		
Modality		
Prevalence/Incidence of Condition		
Comparator *(specify comparator as SOC or another mHealth modality, validated?)*	1☐ Yes 2☐No	
Point of treatment provision	1☐add-on 2☐outpatient 3☐inpatient	
Notes:		

Risk of bias assessment

High risk of:	Description and assessment
Selection bias? *pg fig/table*	
	1☐Yes 2☐No 3☐Unclear
Performance bias? *pg fig/table*	
	1☐Yes 2☐No 3☐Unclear
Detection bias? *pg fig/table*	
	1☐Yes 2☐No 3☐Unclear
Attrition bias? *pg fig/table*	
	1☐Yes 2☐No 3☐Unclear
Reporting bias?*pg fig/table*	
	1☐Yes 2☐No 3☐Unclear
Are study results valid? *pg fig/table*	
	1☐Yes 2☐No 3☐Unclear

Other relevant information

	Descriptions/figures as stated
Key conclusions from the authors *pg* *fig/table* *pg* *fig/table*	
Notes *pg* *fig/table* *pg* *fig/table* *pg* *fig/table* *pg* *fig/table* *pg* *fig/table* *pg* *fig/table*	

APPENDIX 4 SCOPING REVIEW STUDY PROTOCOL

The impact of mHealth on adolescent global health outcomes: a scoping review of mHealth initiatives

Please refer to Sections 3.1-3.5 of the thesis Methods for a description of the changes between this initial study protocol and completed scoping review.

Background

HIV, tuberculosis (TB) and malaria collectively account for 60% of the global disease burden (WHO 2015 report). A third of the world's population, about 2 billion people, have latent TB infection (LTBI), meaning that they are infected with TB bacteria that are contained by the immune system and have not progressed to active disease. HIV co-infection with LTBI rapidly accelerates progression to active TB disease, but also complicates diagnosis of TB. In 2014, tuberculosis alone killed 1.5 million of the 9.6 million people with active tuberculosis disease. Twenty-five percent of these deaths occurred in HIV-positive people, the vast majority living in Sub-Saharan Africa (WHO TB report 2015).

This disease burden places immense pressure on health systems in developing countries. Prevention of infection by means of an effective vaccine is an important public health tool and offers the best hope of eradication (Wiysonge, 2012; Kim, 2012; Cobelens, 2012). Globally, immunisation against vaccine-preventable disease (VPD) saves between 2 and 3 million lives per year (Odone, 2015). There is however not yet a safe, publicly accessible vaccine that offers lasting protection against HIV, TB or Malaria. The only registered anti-tuberculous vaccine, BCG, is administered at birth and does not offer lasting protection against tuberculosis into adulthood (Kaufmann, Hussey & Lambert, 2010).

Many promising infectious disease vaccines for HIV and TB now target adolescents (Harris et al 2016). Some of these vaccines are already in late-stage development, with registration anticipated in the next few years (Ginsberg, Ann M. et al., 2016). As adolescents are neglected by health systems, the opportunity to shape enduring positive health behaviour that reduces chronic disease in later life and assists early diagnosis and reduced transmission of infectious disease, is often missed (Viner 2011, Patton 2012). Information is therefore urgently needed on how best to communicate health promotion messages to adolescents, so that health workers may effectively engage with adolescents to implement the vaccines when approved (Patton 2016).

Mobile phone technology has become recognised for its ability to improve health service delivery through improved communication, education and behaviour change (Gurman, Rubin & Roess, 2012).The greatest increase in mobile phone ownership has been in developing countries and its potential in reaching vulnerable populations has led to rapid integration in health care delivery. This integration of mobile or wireless technology into health systems for improved healthcare delivery is known as mHealth (Mechael, 2009). mHealth has been identified as an effective tool for improved vaccine implementation (Wiysonge, 2012; WHO, 2015), as well as for adult infectious disease management through improved adherence, visit reminders, education, communication of results, data collection and follow-up care (Devi et al., 2015). Adolescents are the group with growing access to wireless technologies that include WAP-enabled mobile phones, smartphones, tablets and laptops (Amacizia, 2013). With the fastest-growing use of mobile phones globally being among youth, m-Health interventions may be especially suited to this group for communication of positive health-related information (Kata, 2009).

Rationale

Much of the evidence for improved health outcomes using mHealth comes from developed countries, and for target groups such as caregivers of younger children, health professionals, and adult patients (Free, 2011), while adolescents have been neglected as mHealth beneficiaries. Moreover, the same mHealth interventions may not show similar results when applied to different health conditions, or in different socio-cultural settings. For example, two-way short-message service (SMS) that improved adherence to antiretroviral (Mitchell, Pirie & Ingram) treatment did not show similar success for TB treatment adherence (Nglazi et al., 2013). As yet, there remains no clear evidence for the link between mHealth and behaviour change or why some interventions work, and others do not (Davis, 2015; Mbuagbaw 2015; Aranda-Jan 2014; Labrique 2013).

Unfulfilled infectious disease targets of the Millennium Development Goals have been carried through to the Sustainable Development Goals (SDGs) and SDG 3 has prioritized infectious disease efforts for developing countries with the hope of eradicating infectious disease by 2030 (WHO Global TB report 2015). For the first time in 2016, adolescents have been included in the WHO's updated Global Strategy "because they are central to everything we want to achieve and…by helping adolescents to realise their rights to health, well-being, education and full and equal participation in society, we are equipping them to attain their full potential as adults" (Ban Ki-moon, United Nations Secretary General, quoted in the WHO

Global Strategy 2015).

The period of adolescence, defined as between 10 and 19 years of age (United Nations Department of Social and Economic Affairs, 2013), is a highly social age that corresponds with waning immunity from childhood vaccination and often-missed booster vaccines for VPD such as pertussis and meningococcal meningitis (Amicizia, 2013). Identifying what has worked previously for improving health-seeking behaviour for common adolescent conditions will be vital for curbing transmission of infectious disease when the long-awaited vaccines against TB, HIV and malaria become available to the public. The purpose of this scoping review is therefore to examine the state of the evidence for adolescent mHealth success globally, in order to gain insights into the types of interventions that work best at targeting adolescents for positive health outcomes. These insights will be used to propose a framework for the design and implementation of adolescent mHealth infectious disease management in low and middle-income countries.

Literature Review

mHealth for infectious disease management

Mobile phone technology has become recognised for its ability to improve health service delivery through improved communication, education and behaviour change (Gurman, Rubin & Roess, 2012).The integration of mobile or wireless technology into health systems for improved healthcare delivery and health promotion is also known as mHealth (Mechael, 2009). mHealth may include health information systems, clinical decision-making tools such as apps[3], reminder services, short message services (SMS) and telephone calls or any other wireless communication for the purpose of improving health implementation and outcomes (Aranda-Jan, Mohutsiwa-Dibe & Loukanova, 2014; Fortuin et al., 2016).

mHealth has been shown to be effective for a range of improved health outcomes that include disease surveillance, health information for patients, supply chain management and provider decision aids (Free, 2010; Kalan, 2014; Oyo-Ita, 2016); it has also been shown to

[3]A mobile application, most commonly referred to as an app, is a type of application software designed to run on a mobile device, such as a smartphone or tablet computer. Mobile applications frequently serve to provide users with similar services to those accessed on PCs. Apps are generally small, individual software units with limited function. (source: https://www.techopedia.com/definition/2953/mobile-application-mobile-app)

be effective for adult HIV and TB disease management through improved adherence, visit reminders, education, communication of results, data collection and follow-up care (Devi et al., 2015). Information and communication technology through mobile phones, the internet, social networking sites and instant messaging have provided means to an expanded social environment, and many young people are at the forefront of adopting these means of communication. However, their benefits of communication and entertainment are weighed against harmful information, cyberbullying, sleep disturbance and other physical effects from over-use (Gore et al., 2011). Owing to its low cost, ease of use, growing mobile phone coverage among youth, and ability to deliver health messages directly to the target patient, mHealth may be uniquely placed in addressing the adolescent health knowledge and behaviour, even in rural areas with poor clinic access. Its great potential in reaching vulnerable populations has led to rapid integration in health care delivery, especially in developing countries, where mobile phone ownership has grown the most in the last decade (Wu & Raghupathi, 2012).

In as much as the growth in mobile phone ownership and wireless coverage is a major opportunity for mHealth, its sustainability in developing countries is threatened by a "digital divide" (Wu & Raghupathi, 2012). The divide between those rural, older, less affluent communities in developing countries and those younger, more urban, living in more affluent communities means that those who stand to benefit most from disruptive technologies, are least likely to use the technology(Ahmed, 2014; Dorsey, 2016). Despite evidence of mHealth's positive impact upon infectious and non-infectious disease in both developed and developing contexts, it remains under-utilised and is rarely scaled to capacity in low and middle-income countries (Brinkel, 2014; Hall, 2014; Falzon, 2016).

The role of immunisation in infectious disease management

Immunisation refers to the planned administration of a series of oral or injectable vaccines. Vaccines are substances able to stimulate a protective immune response, in order to reduce the effects of infectious illness (Ginsberg, A., 2010).There are countless barriers to effective immunisation - among them stigma, access, incomplete vaccine coverage (in the case of multiple doses), harmful information about vaccine safety and other context-specific reasons (Degeling et al., 2015). When there are too few adequately immunised people in a community, it increases risk of infection for the whole community, or "herd" (Agarwal 2015; Szilagy 2006), especially for those who are at risk of infection, but cannot be immunised due

to pregnancy, allergy or extremes of age (too young or too old), for example.

Incomplete immunisation, missed boosters, and waning immunity after childhood immunisation causing reduced herd immunity, all contribute to the current global resurgence in VPD like measles and pertussis. Immunisation programmes linked with other relevant health services has potential to improve morbidity and mortality directly, as well as providing an opportunity for broader services such as health promotion and screening (Wiysonge et al., 2012). Immunisation incentives therefore remain a global priority as a target of the Sustainable Development Goals (Asah, 2015). Furthermore, adolescent immunisation has been specifically identified as a target with potentially the greatest public health benefits for infectious disease management (Agarwal, 2015; Harris 2016).

The role of mHealth for adolescent global health

The World Health Organisation (WHO) defines “adolescents” as those aged 10–19 years, and “youth” as those aged 15-24 years (United Nations Department of Economic and Social Affairs, 2013), definitions which this paper will adhere to. Adolescents have been overlooked in global health initiatives due to the assumption that theirs is the healthiest period of life (Blum, 2004). Adolescents pose unique health systems challenges in terms of coverage and positive health knowledge (Viner et al., 2011) and addressing their wellbeing becomes vital as this enables independence, completion of schooling with better employment options, and healthy relationships (Gore et al., 2011; Sawyer et al., 2012). The transition from adolescence into healthy, productive adulthood requires access to health education, quality appropriate health services, and supportive home and community environments (Laski, 2015). In addition, negative health attitudes developed in adolescence (like poor nutrition and lack of exercise, road traffic accidents, undetected depression, eating disorders, substance and tobacco use, for example) underpin chronic disease and physical disability in later life, as well as directly affecting the health and early childhood development of their potential children (Patton, 2012; Laski, 2015).

Understanding and promoting health behaviour among adolescents is essential because they constitute the future health and economic potential of especially low and middle-income countries (UNICEF, 2002; Wiysonge, 2012). This is especially so in Sub-Saharan Africa (SSA) where their number makes up 30% of the population (Dick, 2015), and their wellbeing becomes integral to later workforce productivity (WHO Global strategy report, 2015). Countries have neglected the future potential of these young people over the past 50 years, and need to invest in their improved health and economic development (Das Gupta et al., 2014).

Adolescents are the group with growing access to wireless technologies, a trend present across the spectrum of per capita income and geo-spatial location (Agarwal et al., 2015). Wireless technologies prevalent among adolescents include WAP-enabled mobile phones, smartphones, tablets and laptops (Amacizia, 2013).

With the fastest-growing use of mobile phones globally among youth, m-Health interventions may be especially suited to them for communication of positive health-related information (Kata, 2009). This may be especially so among the vulnerable group of male adolescents whose burden of disease has been least affected by public health initiatives (Viner, 2011; WHO 2015).

What remains unclear is what specific m-Health interventions work best across the broad spectrum of mHealth modalities to target adolescents. Other specific mHealth modalities such as Unstructured Supplementary Service Data (USSD) or free applications may hold more appeal in higher data cost settings than SMS reminders and telephone calls, for example, which have previously been shown to improve healthcare appointment attendance in adults (Gurol-Urganci, 2013). Though it makes sense that adolescents should prefer web 2.0 communication social networking platforms such as Facebook and Twitter that allow continuous updating (as they are cheap and allow more text characters than SMS, for example) there is little evidence to support this, especially for low and middle-income countries (Wolfe, 2005). Given the recent proliferation of mHealth initiatives targeted at adolescents, it would be useful to examine their successes and failures to understand what has worked, and why (Aranda-Jan, Mohutsiwa-Dibe & Loukanova, 2014; Mbuagbaw et al., 2015). The knowledge gained could potentially facilitate rollout of adolescent vaccines for high-burden infectious disease, already in late-stage development, once they are registered for use (Harris et al., 2016).

Aim

The project aims to determine if the use of mHealth enhances infectious disease management among adolescents in low and middle-income countries, and how this knowledge may be transferred to the implementation of adolescent immunisation programmes, particularly for TB. The aims will be achieved by addressing multiple, related research questions using published evidence, grey literature as well as consultation with relevant health practitioners:

1. What specific mHealth intervention modalities appeal to adolescents, and why?
2. How do the successful modalities differ between developed and developing countries, and for infectious and non-infectious disease?
3. What are the implications of the above for designing and implementing mHealth interventions for TB immunisation among adolescents in developing countries?

Methodology

In order to close the knowledge gap between successful adolescent mHealth interventions and their implementation in developing countries, a scoping review will be conducted of all relevant primary studies and systematic reviews on mHealth interventions targeting the adolescent population. A scoping review is a specific style of literature review, able to rapidly and systematically map key concepts underscoring a research area as well as the types and main sources of evidence (Arksey and O'Malley, 2005). This knowledge is essential for understanding gaps in the evidence base, and scoping reviews are therefore often done to determine the feasibility of a full systematic review (Levac, Colquhoun & O'Brien, 2010). The framework for conducting scoping reviews is described in the literature, and the mandatory steps of refining the research question (Stage 1), literature review and selection (Stage 2 and 3), data extraction (Stage 4) and concise reporting of results (Stage 5) will be followed (Arksey and O'Malley, 2005; Armstrong 2011). Given the breadth of the topic to be covered, the optional Fifth Stage of consultation with health experts may also be followed (Levac, Colquhoun & O'Brien, 2010). The findings will be considered in the context of adolescent infectious disease management, particularly tuberculosis immunisation.

Study participant eligibility

Primary studies used in this scoping review will include adolescents of any gender, location, or ethnicity with access to a mobile phone or wireless device in any country, used for a health-related outcome. Ethics approval is not applicable, as no participants will be recruited.

Type of intervention

We will examine mHealth interventions targeting the most common adolescent conditions, as identified by most recent Global Burden of Disease Study (Mokdad et al., 2016). The GBD tracks the burden of age-and gender-specific causes of death and morbidity in 188 countries, across environmental (air pollution, sanitation, handwashing), behavioural (alcohol and drug use, unsafe sex, road accidents, interpersonal violence), mental health and metabolic causes, for a period of twenty years (Mokdad et al., 2016). mHealth interventions for the 4 highest causes of disability and death in adolescents (road injuries, mental health disorders and suicide, violence, selected infectious diseases and iron-deficiency anaemia) will be targeted.

mHealth modalities may include health information systems, clinical decision-making tools such as apps, reminder services, short message services (SMS) and telephone calls or any other wireless communication for the purpose of improving health implementation and outcomes (Fortuin et al., 2016). There will be no limitation placed on the type of mHealth modality, as this scoping review aims to identify the evidence for mHealth interventions for adolescents as well as any differences between successful developing- and developed-country interventions.

Outcomes

Commonly-used outcome indicators such as mortality, morbidity, and cost to health systems, may not be available in published evidence due to the very recent focus on adolescent wellbeing and given that age-aggregated data is limited (Dick 2015; WHO 2015). An assessment of improved health outcome will thus be done by grouping mHealth intervention outcomes into descriptive outcome categories, such as self-actualisation, self-reported health knowledge, effect on socialisation, community positioning, and mediation of improved

relationships between health-care-workers and adolescents (Petit, 2012). The descriptive mHealth outcome categories will be reviewed against the quality of evidence supporting them.

The primary outcome of this review will be an assessment of whether there is improved management of the commonest global adolescent conditions when using mHealth. The knowledge gained from the literature will be used to consider how mHealth implementation programmes for infectious disease management in developing countries may be designed. This will be done by examining the evidence profile for the descriptive outcome categories of mhealth modalities targeting the commonest adolescent conditions in order to answer the research questions (What specific mHealth intervention modalities appeal to adolescents, and why? How do the successful modalities differ between developed and developing countries, and for infectious and non-infectious disease? What are the implications of the above for designing and implementing mHealth interventions for TB immunisation among adolescents in developing countries?).

Secondary outcomes include identifying further research needs, and identifying opportunities and barriers to scaling up mHealth interventions in developing countries.

Search Strategy

An overview will be conducted of primary studies and systematic reviews published in peer-reviewed journals from January 1990 until January 2017, with no language limitation. The following electronic databases will be searched: Pubmed (NLM), Scopus, CINAHL, EBSCOhost, Africa-Wide, psychINFO, Web of Science (Thomson Reuters), Cochrane Library (including Cochrane Central Register of Controlled Trials (CENTRAL), Academic Search Premier, Communication and Mass Media Complete, Computer and Applied Sciences Complete and NHS Health Technology Assessment Database. The studies will be selected using predefined search terms comprising both free text word and medical subject heading (MeSH) for Pubmed (Appendix 1), and adapted appropriately for other databases. The terms will describe m-Health, the adolescent population, and the most relevant adolescent health promotion interventions.

The reference lists of identified studies will be hand searched for relevant articles and a citation index such as Scopus will be used to identify relevant articles being cited, and their references. This will be expanded until a point of saturation is reached. Unpublished sources will also be evaluated in the form of conference proceeding and abstracts, institutional

websites including the World Health Organisation (WHO), and other international working groups for clinical evidence guidelines.

The search strategy will be developed with a Health Sciences Information specialist, and updated before the final search.

Inclusion and exclusion criteria for study and systematic review selection

Conventional systematic reviews risk excluding large bodies of evidence due to stringent inclusion and exclusion criteria (Leon, Schneider & Daviaud, 2012). This scoping review will aim to include as much relevant evidence for policy makers, disease control planners and health practitioners to understand and effectively implement adolescent mHealth interventions in their particular context.

We will include studies and systematic reviews where the mHealth intervention is the primary component being evaluated. Studies with additional non-mHealth measures (for example, health visits or counselling) that differ between the control and intervention groups, will be excluded.

Included studies will target adolescents themselves, and not schoolteachers, caregivers or other health providers. Studies should report clearly on the mHealth modality used, and state study objectives *a priori.* For inclusion of systematic reviews, at least one primary study should be a randomised controlled trial, and contain a transparent assessment by the authors of quality and risk of bias in order to strike a balance between methodological rigour and the broad review parameters required to effectively map the literature.

Review selection

All articles identified by the search will be screened by title and abstract and the full-text drawn if relevant, or more information is needed. All relevant full-text articles will be saved in Endnote software manager and all duplicate material will be deleted. The process of identification, screening, and inclusion of relevant studies will be depicted by flow diagram (PRISMA, 2009).

Data extraction and management

A data extraction form will be piloted on four selected reviews or primary studies, with reviewers meeting to discuss insights and refine the data extraction tool. Data will be extracted independently in duplicate by the author and her primary supervisor and verified by a third adjudicator (her co-supervisor) if no consensus can be reached.In the case of multiple reviews covering the same population and all meeting inclusion criteria, the most comprehensive or recent review will be used. One reviewer will enter the final data into statistical software package (Cochrane Collaboration Review Manager Version 5.1). Data will be crosschecked by a second reviewer independently before analysis.

The data will be presented in a summary of findings table showing the number and type of included studies; participant details; countries in which the primary studies were done; mHealth modality and wireless technology targeted; reporting quality regarding allocation concealment, blinding of outcome assessors, loss to follow-up, and other sources of bias. Key conclusions, possible limitations and knowledge gaps will also be presented in tabulated form. The measures of effect per intervention will be provided as a forest plot with 95% confidence intervals and I-squared value for heterogeneity

Dealing with missing data

The authors of primary studies will be contacted telephonically or by email when study designs, methods, outcomes or statistical data reported are unclear. If the data has not been obtained despite multiple attempts, it will be noted in the narrative.

Assessing methodological quality

Poor quality of included primary studies and reviews adversely affects the reliability, and thereby the transferability of results outside the clinical trial environment (Guyatt 2011; Coello-Alonso 2016). This scoping review will thus implement rigorous methods of quality assessment throughout the review process. The Cochrane Risk of Bias Tool (Cochrane Group 2011, Higgins 2011) will be used to assess methodology of primary quantitative studies, and report the quality as being of high, medium, low, or unclear quality. Qualitative studies will be assessed by the Joanna Briggs Institute Qualitative Assessment and Review Instrument (JBI-QARI 2011). The AMSTAR (Assessment of methodological quality of systematic reviews) tool will review 11 criteria for detection of bias in systematic reviews.

Reviews may be scored as high quality (8-11 items), moderate quality (4-7) and low quality (3 or less items).

The quality assessment forms will be piloted on four selected studies. One reviewer will independently assess the studies, which will be checked by the second reviewer. Quality assessment discordance between the two initial reviewers will be adjudicated by the third reviewer.

Data Synthesis of Quantitative Studies

Meta-analysis, the statistical process of pooling comparable results to determine effect size, will only be done if the primary studies are similar enough as regards participant, intervention, comparator and outcome elements. It is unlikely that meta-analysis for most quantitative data obtained will be possible, due to varying outcomes. Forest plots will thus illustrate the range of effect sizes for the different mHealth modalities; even if the standardised effect size cannot be obtained for meta-analysis, all effect sizes with 95% confidence will be provided in the narrative.If any required data is unclear or incomplete, the authors will be contacted for clarification.

A summary of findings (SOF) table will be used to show the findings for each primary outcome. One reviewer will group findings from primary studies into broad descriptions related to improved adolescent health outcomes. The second reviewer will then verify that the narrative of the primary studies matches that of first reviewer's SOF table descriptions.

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach advocated by the GRADE Working Group, will be used to assess the quality of evidence for all included primary studies (Guyatt et al., 2008). This will be reported in the evidence profile of the SOF table for each outcome description as being of high, moderate, low or very low quality.

A sensitivity analysis will be conducted by including only studies assessed as low risk of bias in a repeat meta-analysis, where possible. This will allow assessment of the sensitivity of the results to overall quality of the data.

Heterogeneity of studies included in reviews will be assessed before inclusion in the meta-analysis. A cut-off I-square value of 50% will render them excluded from the pooled meta-analysis as an indication of high heterogeneity.

Subgroup analysis may be conducted across the following variables:

- Risk- high or average
- Location- rural or urban
- World Bank definition of low or middle-income country

Dissemination of findings

Following completion of the scoping review, the results are planned for publication in a scientific journal, and as a chapter of the student reviewer's Masters thesis.

The review protocol will be registered with PROSPERO before commencement.

Discussion

The proposed scoping review may advance scoping review methodology as an effective, systematic research approach to address complex questions that could otherwise not be answered by the explicit approach of a systematic review. As it is able to effectively and quickly map the literature, it will help to identify further gaps in the existing mHealth evidence base, and prompt further research. Finally, this review has the potential to inform the design of a relevant, accessible adolescent immunisation mHealth intervention, thereby including adolescents and developing countries as stakeholders in the global health arena.

APPENDIX 5 PRISMA FOR ABSTRACTS CHECKLIST

TITLE	CHECKLIST ITEM	REPORTED ON PAGE #
1. Title:	Identify the report as a systematic review, meta-analysis, or both.	
BACKGROUND		
2. Objectives:	The research question including components such as participants, interventions, comparators, and outcomes.	
METHODS		
3. Eligibility criteria:	Study and report characteristics used as criteria for inclusion.	
4. Information sources:	Key databases searched and search dates.	
5. Risk of bias:	Methods of assessing risk of bias.	
RESULTS		
6. Included studies:	Number and type of included studies and participants and relevant characteristics of studies.	
7. Synthesis of results:	Results for main outcomes (benefits and harms), preferably indicating the number of studies and participants for each. If meta-analysis was done, include summary measures and confidence intervals.	
8. Description of the effect:	Direction of the effect (i.e. which group is favoured) and size of the effect in terms meaningful to clinicians and patients.	
DISCUSSION		
9. Strengths and Limitations of evidence:	Brief summary of strengths and limitations of evidence (e.g. inconsistency, imprecision, indirectness, or risk of bias, other supporting or conflicting evidence)	
10. Interpretation:	General interpretation of the results and important implications	
OTHER		
11. Funding:	Primary source of funding for the review.	
12. Registration:	Registration number and registry name.	