Mobile Phones and Caring for People Living with HIV in Iran: Exploring the Role of Context

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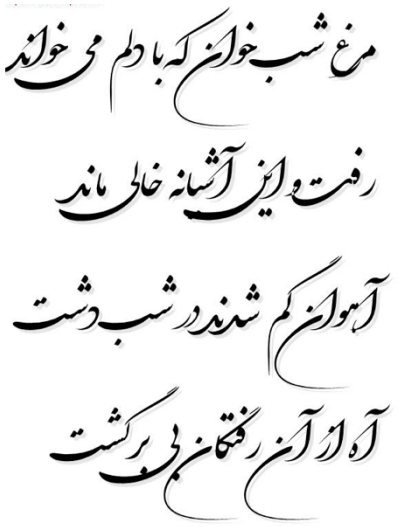
Declaration

I declare that this thesis is entirely my own work, and except where otherwise stated, describes my own research.

Vira Ameli

In memoriam Dr. Mohammad Mel Ameli, my beloved father



The nightingale that sang with my heart

left and this nest remained empty.

The gazelles were lost in the night of plain.

Alas, for those gone without return.

— Hushang Ebtehaj

Abstract

Living with HIV requires lifelong engagement with medical care. However, consistent engagement with antiretroviral therapy can be undermined by multiple forces at the international, national, sociolegal, institutional, and individual levels. Programmes that are aimed at improving engagement with HIV care are introduced into complex care settings that can interact dynamically with the contexts of daily living with HIV. Recently, there has been a surge of research evaluating mobile health (mHealth) support to promote treatment continuity. Such mHealth approaches have shown short-term efficacy in controlled settings, but the long-term effectiveness in real-life contexts remains unclear. This is in part due to the fact that the current body of public health literature predominantly views mHealth through a deterministic lens that examines whether an mHealth programme produces a specific outcome, without examining the recursive relationship and complex interactions with multilevel contexts of HIV care that influence whether such outcomes will occur. Importantly, when moving programmes across settings, it is vital to understand *how* the programme works, *when, why, in what context, and for whom*. In this thesis, I adopt a realist lens of enquiry to examine *how* mHealth interacts with context in such a way to trigger desired mechanisms that in turn can produce intended outcomes. To do so, I collect primary data from Iran and use secondary evidence from various global settings. In DPhil paper I, I contextualise the condition of living with HIV and engaging with antiretroviral therapy in Iran. In DPhil paper II, I conceptualise how specific mHealth features can change the contexts of engaging with HIV care in Iran. In DPhil paper III, I propose a protocol for a pilot trial and a nested realist evaluation of HamRaah, an evidence-based mHealth programme that is viewed by stakeholders to be suited to the contexts of living with HIV and treatment retention gaps in Iran. In DPhil paper IV, I use secondary evidence from various global setting to produce a refined programme theory that explains how, when, for whom, and in what contexts human-supported mHealth can enhance engagement with HIV care.

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of his critical view of the state, to make progress a reality for Iran and its people. As a Professor of Cardiac Surgery, he moved back to Iran from the United States to dedicate his life to the advancement of open-heart surgery in our developing country. Beyond being a surgeon, he was a true teacher, committed to service, and dedicated to training the first generation of cardiac surgeons in Iran. Years after his retirement as the head of the first cardiac surgery unit, I walked through the same hospital campus that I would visit as a child, this time as a public health researcher, but inspired by his devotion that I had witnessed as a child.

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Why nothing works
everywhere for everyone?

— The RAMESES Project

1

Introduction

1.0 Motivation

The discovery of antiretroviral therapy introduced the possibility of 'living with HIV' and ending AIDS. At the time of writing, an estimated 39 million people are living with HIV, of whom an estimated 30 million are receiving antiretroviral therapy (UNAIDS, 2023). This is a significant expansion from two decades ago when less than one million of the estimated 28 million who were living with HIV had access to antiretroviral therapy (World Bank, 2021). But over two decades since the introduction of antiretroviral therapy, AIDS-related mortality and onward transmissions of HIV continue to impact lives globally. In 2022, 630 thousand people died from AIDS-related causes, while one million and 300 thousand people were newly infected with HIV, including 130 thousand children (AIDSinfo & UNAIDS, 2023). Last year, UNAIDS reported that in every minute a life was lost to AIDS, and in every two minutes a young girl was infected with HIV (UNAIDS, 2022). Even in parts of the world where universal access to antiretroviral therapy is offered, AIDS-related mortality and new HIV infections subsist. How to improve care for people living with HIV, in terms of their lifelong engagement with antiretroviral therapy, is therefore an important question.

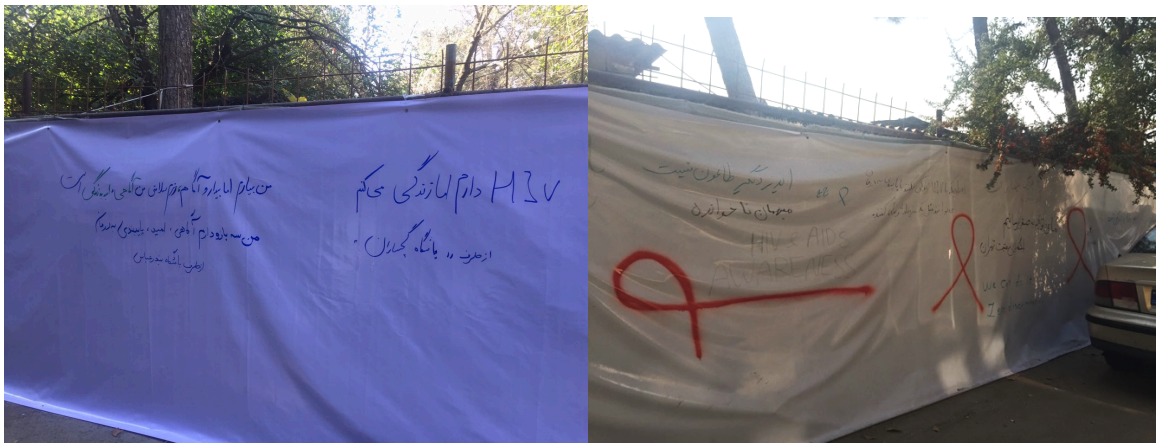

Figure 1.1: Antiretroviral Therapy Awareness Raising Campaign, Tehran, Iran. Writings by members of a peer support [Positive Club] network. Left photo: "A Gatecrasher. AIDS is no longer like plague. With adherence to treatment, people living with HIV can have a normal life. We can bring [AIDS] to zero." Right photo: "I have HIV but I continue to live. I am ill but awake and aware, the secret to my health is awareness and hope for life, I have three arms: awareness, hope, and adherence to treatment". The photo illustrates the hopes of Iranians living with HIV to raise awareness about treatment, emphasising that—with adherence to treatment—people living with HIV can live a normal life and that together, with the available treatment and tools, it is possible to eradicate HIV and AIDS.

Iran offers universal antiretroviral therapy, peer support [positive] clubs for people living with HIV, voluntary counselling and testing services, test-and-treat, once-daily regimens, and widespread harm reduction programmes (HIV Policy Lab, 2021). In 2022, 90 per cent of Iranians who were on treatment had sustained viral suppression, but only 72 per cent of those diagnosed with HIV were on treatment in the past year—a substantial gap in treatment initiation and retention. Last year, 2300 AIDS related deaths and 2900 new HIV infections were reported in Iran. The elimination of preventable new HIV infections and AIDS-related deaths through enhanced access and adherence to treatment remains a national priority, demonstrated through awareness raising campaigns (see Figures 1.1). Thus, it is crucial to investigate how to effectively use existing resources to address the ongoing challenges in terms of engagement with the HIV care and adherence to antiretroviral therapy.

Over the past decade, mobile phones have presented new opportunities to care for people living with HIV. The World Health Organisation (WHO) has endorsed the use of mobile health (mHealth) for augmenting rather than replacing traditional health services (WHO, 2019), highlighting the potential for tailored and differentiated models of care delivery (WHO, 2016). A flurry of research has produced evidence with regard to the efficacy of

various mHealth approaches in supporting people living with HIV to engage with care and adhere to treatment (Finitsis et al., 2014; Haberer, Sabin, et al., 2017; C. Kruse et al., 2019; Mbuagbaw et al., 2015; Pellowski & Kalichman, 2012; Simoni et al., 2015), but evidence is lacking on how these programmes can be applied across settings, scaled-up, and adopted sustainably.

My research project is motivated with a central enquiry in mind: *how can mobile phones be used to enhance the contexts in which HIV care is engaged with globally and in Iran?* Remarkably, a significant knowledge gap exists on the real-world effectiveness of mHealth programmes in term of adoption and scale-up beyond controlled research settings. To investigate the value added by mHealth programmes in any setting, it is important to make sense of *how* these interventions interact with their context, and *what* is their underpinning programme theory. To address these questions, it requires to conceptualise mHealth programmes as complex interventions, introduced into complex health systems, and entangled with the complex contexts of individual reasoning, (re)actions, and behaviours.

The decisions of individuals to engage (or not) with HIV care and their behaviour in terms of whether they adhere (or not) to treatment is embedded within the complex processes of their daily lives and its complex interactions with the wider social systems. In contrast to isolated praxes, these decisions and behaviours are what Pawson defined as 'processes' within 'processes' (Pawson & Tilley, 1997). To understand and intervene at the level of individual behaviours and decisions, we need to uncover the process that produces a behaviour and then introduce a *new* process via the intervention. Complex interventions are often introduced into complex settings (Greenhalgh & Papoutsi, 2018). Thus, to understand how mHealth can improve HIV care, this thesis moves beyond examining the efficacy of mHealth in promoting engagement with HIV care and adherence to treatment, by conceptualising mHealth interventions as complex, and applying a variety of methods to uncover *how* these interventions interact with their context, and *what* is their underpinning programme theory.

The next four sections describe the relevant background literature on the complexities of digital health interventions (Section 1.2), global contexts of living with HIV (Section 1.3), the historical and local context of HIV care in Iran (Section 1.4), the state of the evidence and knowledge gaps on HIV care and mHealth (Section 1.5), and finally the specifics of the research approach used (Section 1.6), followed by a thesis outline (Section 1.7).

1.1 The Challenge of Complexity

In this section I will provide an overview of the lenses through which complexity can be viewed, shedding light on its relevance in terms of digital health interventions and the limitations of current deterministic research approaches before outlining how the role of context is defined and explored in this thesis to enhance our understanding of mHealth as a complex intervention for HIV care. This section sets out the necessary background with regard to how the lens of inquiry I have adopted moves beyond deterministic approaches and engages with the complexities of HIV care and digital health to produce context-sensitive and policy-relevant translational findings.

Complexity can be defined in different ways. The UK Medical Research Council (2021) identifies five attributes that determine the extent to which an intervention is complex: the number of components and interactions involved; the range of behaviours targeted and the variability of outcomes; expertise and skills required by those delivering and receiving the intervention; the number of groups, settings, or levels targeted; the permitted level of flexibility of the intervention or its components (Skivington et al., 2021). However, the listing of specific 'factors' that make an intervention complex does not allow accounting for the emerging nature of interactions and contexts through which interventions are engaged with. It is more apt for the purposes of this thesis to use the more nuanced definition of complexity, as a 'dynamic and constantly emerging set of processes and objects that not only interact with each other but come to be defined by those interactions' (Cohn et al., 2013). This definition of complexity considers that complex interventions can co-evolve, by interacting with and adapting to the system in which they are implemented (Greenhalgh & Papoutsi, 2018).

Crucially, interventions might be considered complex because of the properties of the intervention itself, or the interactions produced within the context in which they are implemented. For instance, a digital health intervention can consist of a relatively simple electronic drug monitoring device to measure medication adherence, but the adherence data can be used in various ways, such as in real-time or at predetermined intervals, to inform remote-care or self-care, introducing complex shifts and dynamic interactions between the patient and the health system (Haberer et al., 2010; Sabin et al., 2010). Simultaneously, the same intervention can include additional components, such as one- or two-way mobile-messaging between patients and providers (Haberer et al., 2016; Sabin, DeSilva, et al., 2015),

introducing new opportunities for patients and providers to communicate; targeting more behaviours and outcomes; leading to more possibilities for the intervention to be adopted and co-evolve within the system. The skill levels of patients and providers to deliver and use the resources offered by the intervention, and the degree of flexibility that is permitted by the intervention guidelines, adds further complexity across implementation settings (Maar et al., 2017).

When implementing a complex intervention in a new setting, there needs to be a degree of flexibility in terms of where, how, and by whom the intervention is delivered, whilst maintaining fidelity to the evidence-base (Craig et al., 2008). Thus, to test interventions in controlled experiments, the evidence-based components of the intervention that constitute the 'active ingredients' and must remain fixed across settings are identified (Hawe et al., 2004). However, the higher the complexity of the intervention, the greater the difficulty in specifying the 'active ingredients', and the greater the need to allow the intervention to adapt to the local context, such as the capacities and needs of local stakeholders (Craig et al., 2008). It is therefore recommended to investigate *how* an intervention works *in relation to its context* and what underlying programme theory is at work (Pawson & Tilley, 1997). In other words, exploring the role of context and understanding what mechanisms are triggered to produce outcomes, provides an explanatory theory that can identify the 'active ingredients' as a *theory* rather than a list of components (Hawe et al., 2004). In his introduction of the realist approach, Pawson described every programme as a 'theory incarnate' (Pawson & Tilley, 1997), whereby unpicking it produces an explanatory framework on *how* a programme works, thereby enhancing its transportability and reproducibility. Importantly, a programme is best explained through a *'middle-range theory'*, which provides insights through abstraction but remains proximate in explanation to the inner workings of the programme (Duddy & Wong, 2023; Wong et al., 2010).

To illustrate, a key study published in the Lancet in 2010 suggested that two-way messaging interventions are efficacious in improving adherence to treatment and viral suppression (Lester et al., 2010). This finding ushered in a new wave of research that tested two-way messaging interventions in different populations and settings (Cornelius et al., 2013; Gross et al., 2019; Mbuagbaw et al., 2013; M. C. , Murray et al., 2013; Nordberg et al., 2021, 2023; Van der Kop et al., 2018). The 'active ingredient' was believed to be the 'bidirectional

messaging', which in some trials and systematic reviews was compared with 'unidirectional messaging' approaches (Finitsis et al., 2014; Nsagha et al., 2020; Wald et al., 2015). The evidence was characterised by high heterogeneity and partial reproducibility whereby interventions designated as 'two-way' messaging appeared to work in some settings and not others. The programme theory, and the larger question of how mobile messaging interventions interacted with their context, remained undiagnosed. The interventions were neither adopted nor scaled-up, fitting in with a larger trend and recurring phenomenon within the field of digital health research whereby technological interventions have very short shelf lives, from the development and research stage to non-adoption and abandonment (Cresswell & Sheikh, 2013; Greenhalgh & Russell, 2010; Sligo et al., 2017; Standing et al., 2018).

1.1.1 The Plight of Digital Health

Two explanations have been provided for the trajectory of digital interventions following the completion of research trials. First, the field of digital health research is imbued with the logic of *technological determinism*: the idea that (a) technological interventions have basic and fundamental properties that affect behaviours and outcomes; and (b) that the impact of such technological interventions can be measured through trials, where effects can be isolated (i.e, technological intervention x will have impact y, and that y can be measured, when controlling for z) (Greenhalgh et al., 2011). Critically, the technological intervention is seen as the foundation for and agent of change, while users are assumed to have little power to influence the technologies themselves (Leonardi, 2012). Thus, the dynamic and recursive relationships that emerge as a result of user interactions with digital programmes are ignored. mHealth for HIV care have predominantly been tested in short-lived trials with no long-term data to inform the emerging interactions with context and the sustainability of the intervention within the wider system (Nittas et al., 2020). In contrast, when CT scanners were introduced, Barley (1986) used structuration theory to demonstrate (via the observable and recurrent patterns of the script in two U.S. hospitals) that CT scanners produced an occasion for new social orders, but importantly were not deterministic of these new orders that emerged dynamically and differently in each hospital (Barley, 1986). Thus, more useful insights can be produced by adopting non-deterministic conceptualisations of technologies and accounting for the

recursively emerging relationships between human actions, technologies, and wider systems (Greenhalgh & Stones, 2010).

Second, while complexity research has become widespread within public health and medicine for over two decades (Carroll et al., 2021), it is important to highlight that engagement with complexity in intervention research has remained perfunctory and suboptimal (Greenhalgh & Papoutsi, 2018). For instance, ethnographic work has found that researchers often frame research topics as 'complex' to justify using one approach, such as qualitative methods (Papoutsi et al., 2021). But while researchers are responding to the expectations of policymakers to receive precise answers with clarity, it is important to produce research that maintains internal validity, without compromising external validity, by accounting for the complex dynamic with the wider policy system (Pearson, 2010; Pearson & Coomber, 2010). To do so, approaches that enable researchers to investigate how an intervention interacts with its context are essential as these will have the ability to unpick how the programme works, and focus efforts to reproduce the intervention mechanisms, rather than intervention components (Hawe et al., 2004).

Through several updates to the original framework published in 2000, MRC has attempted to make more in-depth recommendations for development and evaluation of complex interventions, warning against standardisation and the use of a single research approach. The trade-off between 'precise unbiased answers to narrow questions' and 'more uncertain answers to broader, more complex questions' is recognised, with the recommendation that researchers should prioritise answering questions with greatest use to decision makers, as opposed to questions that are more easily answered with greater clarity. For instance, a clear answer on 'what works' would need to be accompanied by a nuanced answer on 'what works, in what context, for whom, how, why, and to what extent'. Further, 'complex intervention research can take an efficacy, effectiveness, theory-based, and/or systems perspective, the choice of which is based on what is known already and what further evidence would add most to knowledge' (Skivington et al., 2021). To account for complexity, this thesis adopts multiple research approaches and a realist framework of inquiry to investigate efficacy alongside understanding how the intervention intertwines with context in a way that triggers a set of mechanisms that in turn shape the outcomes.

1.1.2 Exploring the Role of Context

In this thesis I adopted a realist lens of enquiry to unpick how mHealth interacts with contexts of HIV care and lifelong antiretroviral therapy. Realist approaches are progressively used to analyse complex problems, praxes, interventions, and policies (Duddy & Wong, 2023), and have been applied to a range of topics, including the usage of data and social prescribing in primary care (Jager et al., 2023; Tierney et al., 2023), collaborative care for prison leavers (Byng et al., 2022), child abuse prevention programmes (Lu et al., 2022), mental-ill health among medical doctors and students (Carrieri et al., 2020), and antimicrobial prescribing pressures (Papoutsi et al., 2017). The principal goal of realist research is to generate an in-depth understanding of complex problems and develop theory-informed recommendations for policy, practice, and research. Long-term conditions are inherently complex as they involve a lifelong treatment and care process and are usually entangled with multiple and multilevel contexts (The RAMESES II, 2017; WHO, 2003; Yakob & Ncama, 2016).

The realist approach to research recognises that a deterministic model cannot predict outcomes in every situation or context (Wong et al., 2010). Instead, it is based on the principle that in certain situations or contexts, individuals are likely to have similar reasonings and (re)actions to the resources available to them (Pawson, 2006). In other words, 'particular contexts influence human choice such that semi-predictable recurring patterns of behaviour occur' (Wong et al., 2010). These recurring patterns of behaviour have been termed 'demi-regularities' in modern economics (Lawson, 1997), or 'reusable conceptual platforms' in evaluation science (Pawson, 2013). Crucially, to produce a reusable programme theory with *explanatory* power, it is essential to recognise that context operates in an emergent and temporal way at multiple levels of the socioecological system. Thus, as opposed to viewing context as a fixed feature or list of 'factors' that can enable or disable an intervention, it is essential to disentangle context as 'relational and dynamic features that shape mechanisms through which interventions work' (J. Greenhalgh & Manzano, 2021). The next two sections will draw on the multiple levels of context that influence living with HIV, globally and in Iran respectively.

1.2 Living with HIV

Globally, the experience of living with HIV is a condition shaped by multiple spheres of influence that dynamically interact throughout individual lifespans and across settings. In this section, I will discuss the dynamic *global* forces that shape access and adherence to lifelong antiretroviral therapy, as these are significant in terms of the extent to which digital interventions can be successful. As a theoretical framework, to shed light on the multiple and interactive levels of context, I draw on Bronfenbrenner's (1979) ecological model (see Figure 1.2) to recognise that behaviours (such as those targeted by digital interventions) are impacted by an interactive set of forces at the micro (individual), meso (organisational), exo (social), macro (national), and chrono (historic) systems (Bronfenbrenner, 1979; Kaufman et al., 2014). Outstandingly, the experience of living with HIV is not only impacted by the local and social contexts, but impacted by a range of international and global structures and policies that can change through time and narrow or widen access to lifesaving medicines and other forms of health and socioeconomic protections (Parker, 1996; Parker et al., 2000). Hence, the chrono (historic) forces impact the targeted outcomes of digital health for HIV care, as does the contexts of living through a global pandemic, which can compound contexts of vulnerability.

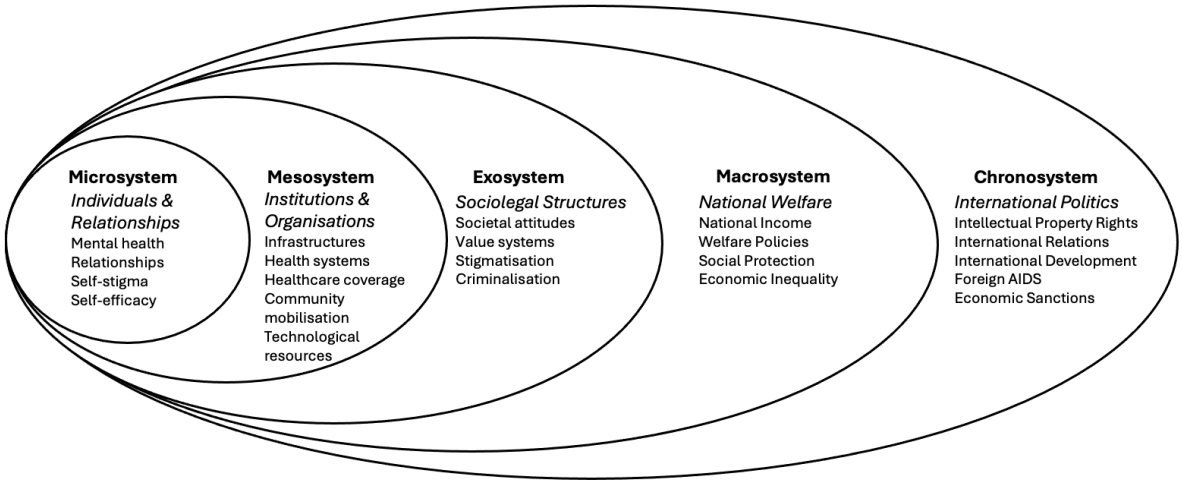

Figure 1.2 Ecological Systems Perspective of multilevel forces that influence engagement with HIV care and treatment. This figure is the author's own illustration of the compiled interactive forces that are discussed below in terms of their direct and indirect impact on antiretroviral access, retention, and adherence.

From the onset of the HIV pandemic, a debate emerged on the relationship between individual behaviours and social forces in determining outcomes (De Guzman, 2001; R. G. Parker, 1996; Seeley et al., 2012). While some scholars have largely focused on individual risk, others have emphasised the impact of structural and social forces in shaping individual choice and decision (Altman, 1999; Farmer, 2021; K. Lee & Zwi, 2007; Parker, 1996). Further, a prominent body of literature sheds light on the structural constraints and power dynamics that are involved in the production of policies and laws at the international and national levels, shaping the HIV epidemic across the globe. Such research has emerged from a variety of disciplinary traditions, thus using different conceptual and language tools (Parker et al., 2000). Scholars in medical anthropology and international development often conceptualise the 'political economy' of the HIV epidemic to underline the historic forces that have shaped politics and economics in ways that have influenced the trajectory of the HIV epidemic (Altman, 1999; Farmer, 2021; Lee & Zwi, 2007; Zwi, 2007; Parker, 1996). On the other hand, global health and policy researchers predominantly frame such issues as 'structural and ecological factors' that impact upon HIV care and treatment coverage (Gupta et al., 2008; Kaufman et al., 2014; Moreno et al., 2014; Pronyk et al., 2016; Rhodes et al., 2005; Rotheram-Borus et al., 2009; Seeley et al., 2012). Despite differences in conceptual, theoretical, and methodological orientations, these researchers consistently outline the interactive and synergistic effects of political, economic, legal, social, psychological, and behavioural forces.

1.2.1 International Politics

At the international politics level (chronosystem), policies such as the enforcement of Intellectual Property Rights (IPRs) by the World Trade Organisation (WTO) through the Trade-Related aspects of Intellectual Property Rights (TRIPs) agreement, persistently prevent the equitable and timely distribution of life saving medications. By 2000, four years after the efficacy of antiretroviral therapy was presented at the 1996 International AIDS Conference in Vancouver, only two percent of people living with HIV were on treatment globally (World Bank, 2021). In November 2001, the WTO adopted an unprecedented declaration on TRIPS to formalise provisions for exceptions to patent laws during public health emergencies (WTO, 2001), but by 2006, a decade after the advent of antiretroviral therapy, only ten percent were

on treatment, and it was not until 2016 when the global coverage of antiretroviral therapy finally reached above 50 percent (World Bank, 2021). It took more than a decade for the price of the cheapest WHO recommended first-line therapy to drop from over 10 thousand USD per person to less than 115 USD, finally affordable for LMICs to provide universal treatment (UNAIDS, 2015). Currently, limited access to the highest quality line of treatment continue to threaten the global HIV response and possibilities of consistent treatment (UNAIDS, 2023).

Medication stock-outs are a prominent feature in many LMICs with the highest burden of HIV, disrupting consistent treatment and threatening the progress made in ending AIDS (Francois, 2019; Hwang et al., 2019; Zakumumpa et al., 2019). Inconsistent procurement can undermine consistent adherence to antiretroviral therapy, thereby heightening the risk of developing and transmitting drug resistant HIV (Lai et al., 2023). Such inconsistencies were found to contribute to the rising prevalence of HIV drug resistance to first-line antiretroviral therapy in LMICs (Gupta et al., 2018). Moreover, for people with HIV to live healthy lives, having access to vaccines and medications that can prevent and treat co-morbidities such as tuberculosis, COVID-19, hepatitis-c, and other infectious and chronic diseases, are as vital as receiving lifelong and consistent antiretroviral therapy (UNAIDS, 2023). Yet, stakeholders have consistently faltered in employing the TRIPS wavers to loosen IPRs and distributing life-saving products, such as COVID-19 vaccines, equitably to low- and middle- income nations (Corporate Europe Observatory, 2022; UNAIDS, 2023).

Lastly, research on international development points to economic inequality and power relations that can threaten the sustainability of the HIV response. Countries targeted by economic sanctions experience pressures on their healthcare capacities (Pinna Pintor et al., 2023). For instance, economic sanctions undermine national harm reduction programme in Iran, thereby pushing opiate users towards injection praxes (Soderholm, 2020); an outcome that is linked to international relations, *unilateral* financial sanctions (that are outside the UN security Council's framework that protect against humanitarian harms), and economic insecurity (Ameli, 2023; Batmanghelidj, 2022). In contrast, countries in Sub-Saharan Africa that rely on international assistance, whereby five countries have reached the UNAIDS 95-95-95 goals, are currently threatened by a widening funding gap that could reverse this progress and jeopardise the global path to end AIDS (UNAIDS, 2023). The World Bank projects that 52 countries, in which 43 percent of people living with HIV are based, will

experience a substantial drop in public spending capacity by 2026. Reductions in public spending are caused by high indebtedness, high interest rates, and debt servicing measures that strip government budgets and undermine public spending capacities, including investments in essential items, such as food and medicine, with negative repercussions on health systems and the HIV response (Development, 2022; Hickel, 2016, 2018). Critically, debt servicing for the world's poorest countries was reported to have reached 171% of all spending on health care, education, and social protection combined (Development, 2022).

1.2.2 National Welfare

Across the globe, at the national level (macrosystem), shrinking financial resources and declining public spending have produced sharp increases in the price of basic goods, such as food and fuel, causing millions of people to become food insecure (FAO, 2023). Such scarcity and precarity increases HIV vulnerability, not only by increasing risk taking behaviours, such as sex-work and unsafe injection drug use, but also by diminishing capacities to remain engaged with treatment and care, both for adults and children (Bigna et al., 2014). Despite living in historically unprecedented times of global accumulation and consumption, food insecurity is rising in many countries, including the Central African Republic, where people living with HIV who experience malnourishment are more likely to discontinue their HIV treatment (UNAIDS, 2022). Likewise, insecure housing is contributing to inconsistent treatment engagement, adherence, and viral suppression rates (Arum et al., 2021; Berthaud et al., 2022; Stone et al., 2022).

During fragile conditions, social protection measures can shield against the multiple threats to health and well-being. Cash-transfer policies can protect against structural vulnerabilities, such as poverty, lack of healthcare, unemployment, and disempowerment (Owusu-Addo et al., 2018; WHO, 2010). By mitigating economic shocks, these policies have an added protective effect on psychological well-being and nutritional health, which are basic foundations for consistent engagement with antiretroviral therapy and optimal adherence (Chipanta et al., 2022). However, social protection measures lose their potency during economic crisis. For instance, waves of economic sanctions in Iran have triggered waves of currency devaluation and chronic inflation, thereby producing conditions of devaluing the

national cash transfer and social protection programmes, thus pushing people into poverty and health insecurity (Batmanghelidj, 2022; Salehi-Isfahani, 2020; Shahrokni, 2021).

1.2.3 Sociolegal Structures

People living with HIV are impacted by policies and structures of legal injustice at the sociolegal level (exosystem) (Global Commission on HIV and the law, 2012). In addition to policies and vulnerabilities that directly impact access to HIV related treatment and care, many laws are discriminatory against specific populations who fear prosecution and choose not to seek medical care and treatment. For instance, in 2019, the UNAIDS reported that 92 countries uphold laws that either directly criminalise HIV status non-disclosure or do so as part of wider laws (UNAIDS, 2020b). Criminalised groups, including people who use drugs, sex workers, men who have sex with men, and transgender persons, and refugees are more vulnerable to punitive laws and less likely to seek HIV testing and treatment, leading to higher incidence of HIV and AIDS-related mortality within countries with punitive legal systems (DeBeck et al., 2017; Lyons et al., 2020, 2023; Reeves et al., 2017). As a result, even in the absence of antiretroviral therapy supply barriers, an antiretroviral therapy demand problem is driven through discriminatory policies, praxes, and laws, currently leaving a quarter of people living with HIV without treatment (UNAIDS, 2022). Moreover, political ideologies can reinforce policies that produce gendered vulnerabilities, for instance by limiting access to safe abortions and failing to protect against gender-based-violence (Global Commission on HIV and the law, 2012). In contrast, countries that have clear laws and advance non-discrimination have been more successful in achieving higher levels of HIV status knowledge, treatment coverage, and viral suppression rates (Kavanagh et al., 2020, 2021).

Behind such laws and policies are social values and belief systems, such as HIV-related stigmatisation, which is a social discrediting process that can profoundly limit possibilities of engaging with health services, and adhering to treatment (Katz et al., 2013; Rueda et al., 2016). How stigma is defined and approached can itself have significant consequences. Initially, explanations of stigma were provided by sociologists, most notably Goffman's work, which conceptualised stigmatisation in relation to socially constructed norms, directed towards attributes that are considered 'deeply discrediting' *relative* to the 'usualness of another'

(Goffman, 1963). Such work highlighted that these attributes, which include any range of behaviours or conditions, do not possess inherent positive or negative values and cannot be inherently 'creditable nor discreditable'. Yet, despite the weight placed on the inherently dynamic and socially constructed nature of such 'discrediting dispositions', critics have noted that psychology, criminology, and public health research (emanated from Goffman's conceptualisation) define stigma as a fixed individual difference or cultural value (Devine et al., 1999; Jones, 1984; Parker & Aggleton, 2003), thereby inherently reinforcing the idea of 'deviance', rather than shedding light on structural, discriminatory, and economic inequalities (Castro & Farmer, 2005; Parker & Aggleton, 2003; R. G. Parker et al., 2000). Intervention work that derives from this research indirectly engages in an unhelpful 'labelling' practice and uses informational and educational approaches to dismantle fear and promote empathy with 'otherised' individuals (Feyissa et al., 2019; Hajebi et al., 2022; Martin et al., 2022; Nyblade et al., 2018; Stangl et al., 2013), rather than adopting approaches that redress structures of inequality and empower people living with HIV.

1.2.4 Institutions and Organisations

At the level of institutions and organisations (mesosystem), poor infrastructures and under-developed health-systems threaten treatment access, adherence, and monitoring. Yet, the HIV response has demonstrated that community organisation and mobilisation can overcome some aspects of lacking infrastructure for healthcare. For instance, in Western and Central Africa, coverage of antiretroviral therapy among adults living with HIV has more than doubled since 2015 (from 36% to 82%), primarily driven through community organisations, mobilising resources and programmes, including the scale-up of differentiated testing and treatment strategies (UNAIDS, 2023). Across large geographical and rural distances, linkage to medical care has been shown to be improved by providing financial and transportation assistance (Bärnighausen et al., 2013; Govindasamy et al., 2012). In Kenya, decentralising services has shown to improve viral suppression rates (Otiso et al., 2017), but more evidence is needed on how to move towards more decentralised services effectively in other countries (Haghighat et al., 2019)(Haghighat et al., 2019). In such contexts, remote service delivery to rural areas using mobile phones and technological tools has been shown to improve adherence and viral

suppression (Fynn et al., 2006; Lester et al., 2010; Nhavoto et al., 2015)(Fynn et al., 2006; Lester et al., 2010; Nhavoto et al., 2015). Remarkably, despite limited infrastructures, Eastern and Southern Africa, the region with the highest burden of HIV, has the highest levels of status knowledge, treatment coverage, and viral suppression in the world (UNAIDS, 2023)(UNAIDS, 2023).

Even in high-resource settings, institutional and national policies such as universal health coverage can determine the extent of treatment accessibility and consistency. For instance, in the United States, where universal health coverage is lacking and financial coverage for HIV treatment is fragmented (Kates et al., 2021)(Kates et al., 2021), only 58 per cent of diagnosed people living with HIV are retained in medical care, and only 66 percent are virally suppressed, while 87 percent are aware of their status (CDC, 2019)(CDC, 2019). In other high-income settings, such as the European Union, where universal health coverage is accessible to the general population, more than 90 per cent of people living with HIV have achieved viral suppression, and most countries are on track to meet the 95-95-95 goals (UNAIDS, 2023)(UNAIDS, 2023). However, recent findings from the EU illustrate that minorities and migrant populations face precarious HIV care and late diagnosis (Nöstlinger et al., 2022)(Nöstlinger et al., 2022), a finding that is particularly pronounced among migrant women (Owusu et al., 2023)(Owusu et al., 2023). Further, policies that expand privatisation of health services, whereby services are increasingly outsourced to for-profit companies, are found to correspond with significantly increased rates of treatable mortality in England (Goodair & Reeves, 2022)(Goodair & Reeves, 2022), and reduced quality of social care services (Bach-Mortensen et al., 2022, 2023)(Bach-Mortensen et al., 2022, 2023).

1.2.5 Individuals and Relationships

An extensive body of literature has examined vulnerabilities at the level of individuals (microsystem). From the outset, an HIV diagnosis can negatively impact individual's mental wellbeing and motivation for treatment (Earnshaw et al., 2013; Lee et al., 2002)(Earnshaw et al., 2013; Lee et al., 2002), thereby jeopardising the course of treatment initiation and retention (Kalichman et al., 2019; Katz et al., 2013)(Kalichman et al., 2019; Katz et al., 2013). People living with HIV experience a disproportionate burden of mental ill health, such as depression

and anxiety that can interfere with consistent engagement with HIV care (Gonzalez et al., 2011; Uthman et al., 2014). Even at sub-clinical levels, depression has been shown to trigger disengagement from care and disruption of treatment, while cumulative clinical depression has been shown to accelerate disease progression and elevate the risk of mortality (Gonzalez et al., 2011; J. C. Mills et al., 2019). Internalising beliefs about oneself, such as internalising stigma and shame are the key contributing factors to mental ill health among people living with HIV, jeopardising health seeking behaviours, self-care (C. Brown et al., 2010; Onono et al., 2020), and in some cases increasing the risk of suicide following diagnosis (Ferlatte et al., 2017; Y. T. Tsai et al., 2023). More generally, 'illness–related self-discrepancy' occurs when the currently diagnosed 'actual' self is perceived to be inconsistent with the conceptualised healthy 'ideal' self (Higgins, 1987), leading to experiencing shame, anxiety, depression, and mental ill-health (Higgins, 1989). While the discrepancy between the 'actual' and 'ideal' self appears to be an intra-personal belief, emanating from inside one's mind, recent research shows that internalisation of stigma and self-limiting beliefs have interpersonal and socio-structural roots and must be tackled at the social and structural levels (Pantelic et al., 2017, 2019).

Behavioural patterns, such as social isolation and unsafe drug use, can be triggered by internalised stigma, depression, and anxiety, which can further contribute to the cycle of mental ill-health and low engagement with care (Earnshaw et al., 2020; Kalichman et al., 2013, 2020; Pellowski et al., 2016). Importantly, social isolation can be caused by an absence of social support, or as a result of fearing HIV status disclosure, denial coping, and perceived lack of social support (Carrico et al., 2006; Gerke, Step, et al., 2020; Mabachi et al., 2020; Murphy et al., 2015; Mykhalovskiy, 2011; Turan et al., 2016; Zang et al., 2014). Importantly, interpersonal relationships, intimate-partner violence, and gender-based violence compound and lead to psychological, behavioural, and coping responses that negatively interact with seeking HIV care and daily adherence (Hampanda, 2016; Onono et al., 2020). Key life events, such as bereavement have also been shown to lead to a deterioration of mental health and an increase in disengagement from care and treatment by a factor of 24. (Brinkley-Rubinstein et al., 2013).

Medication-related barriers include the side-effects of medications, which present a key challenge (Mills et al., 2006), especially in places where options for preferred regimens

remain limited. Antiretroviral side effects range from inconvenient (such as diarrhoea and flatulence) to severe, including lipoatrophy, gynaecomastia, and long-term toxicity (Agwu & Fairlie, 2013); however, these effects are minimised following transition to improved first-line (Dolutegravir-based) regimens that have been shown to improve adherence to and retention on treatment (Da Silva, 2022). According to the WHO, more countries are adopting these regimens (WHO, 2019b); the most recent UNAIDS update reported that at the end of 2022, seventy-three countries were using these regimens, in contrast to thirty-three at the end of 2021 (UNAIDS, 2023). These changes in medication side-effects are believed to reduce interruptions in treatment. A decade ago, a study from South Africa found that about one in five people admitted to hospitals presented with advanced HIV disease, indicating that they had previously initiated and interrupted their antiretroviral therapy, while a further 21% of people admitted to hospitals were on antiretroviral therapy, but with an unsuppressed viral load (Meintjes et al., 2015). Today, it has been estimated that overall, about a quarter of people interrupt treatment at some point after starting antiretroviral therapy, for periods that range from a few days to more than six months (WHO, 2023).

This section has outlined various underlying causes of treatment interruption globally, including psychological and interpersonal barriers; infrastructural and institutional challenges; societal stigma and legal injustice; intellectual property rights impacting access and quality of available regimens; and economic and power dynamics within and between nations that threaten the sustainability of the HIV response. The focus of the next sections will be on the specific context of Iran.

1.3 HIV Care in Iran

In this section, I will provide an overview of the multi-level perspectives of HIV care in Iran. I will provide a brief history and summary of the characteristics of the HIV epidemic in Iran, the national response, and the social, legal, and institutional praxes that are the background to HIV care, into which this research project is aiming to introduce a digital health intervention.

Iran is a middle-income country located in West Asia, with a population of 85 million. Until 2021, the UNAIDS categorised Iran within the Middle East and North Africa Region (MENA), but since 2022 it has been categorised within the Asia and Pacific Region (APAC).

All presentations of data, including historic trends, now use the new regional designation within UNAIDS databases (UNAIDS, 2022). I primarily consider Iran within the MENA region in this thesis. However, by sitting at the crossroads of MENA and APAC, with a majority Muslim population, Iran shares sociocultural characteristics with countries in both regions. The MENA region has a low HIV prevalence (less than 0.1 per cent), but an alarmingly rising rate of new HIV infections and AIDS-related mortality (AIDSinfo & UNAIDS, 2023). The prevalence of HIV in Iran is similarly low (less than 0.1 per cent); however, the rate of new infections and AIDS-related mortality have declined over the past two decades. In terms of HIV transmission, and incidence to mortality ratio (see Figure 1.3), Iran shares characteristics with countries in the APAC region due to similar drug use patterns.

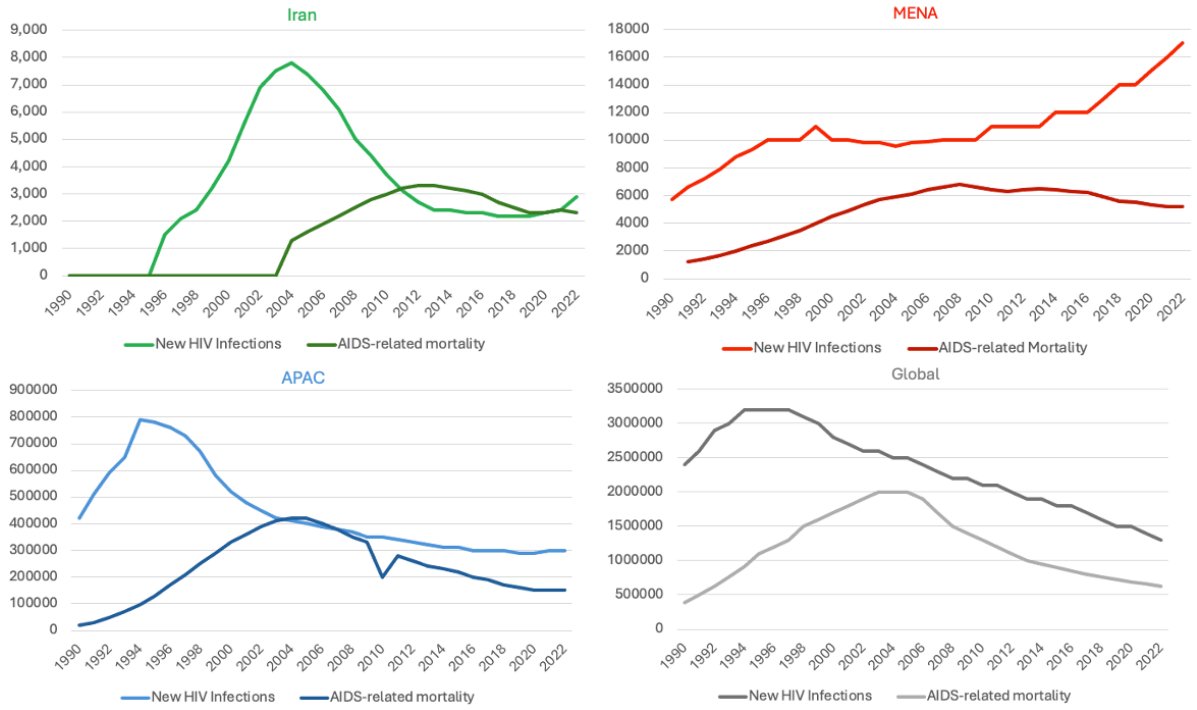

Figure 1.3 HIV Incidence-to-Mortality Ratio, National, Regional, Global. Author's own illustration (Source of extracted data: AIDSinfo, UNAIDS). Note: Iran's rate of new HIV infections (before 1995) and AIDS-related mortality (before 2003) were below 500, thus not captured in the UNAIDS databases. In 2022, following a period of under-diagnosis during the COVID-19 pandemic that kept people away from referring to health centres for testing, the rate of new HIV infections increased in Iran.

1.3.1 Historical Perspective

The first reported case of AIDS in Iran was registered in 1986, when a young haemophiliac boy who had received contaminated imported blood was diagnosed with HIV. Consequently, the onset of the HIV epidemic in Iran was linked to France's 'blood scandal' (BMJ, 1998). AIDS was perceived by many in Iran as a 'foreign' disease, and the series of HIV cases identified among Haemophiliac recipients of the imported contaminated blood products facilitated this viewpoint, resulting in lack of action in the following years (The France 24 Observers, 2015). Yet, given Iran's dynamic history of drug use (see Figure 1.4), it was not surprising that by 1996, an increasing number of HIV diagnoses were made among people who injected drugs and their sexual partners. More importantly, it began to emerge that the biggest predictor of being HIV positive was having been in jail, where injection drug use was far more widespread than previously thought (T. Rosenberg, 2010a). In response, the medical community called for more screenings and the Ministry of Health set out to screen inmates who used drugs as the first population at risk of HIV. Reportedly, the prevalence of HIV was above 90 per cent among inmates who injected drugs in three prisons, all located in the city of Kermanshah, located by the Western border of Iran and one of the cities most affected by Saddam Hussein's invasion of Iran and the aftermaths of an eight-year war (Behrouzan, 2010, 2016).

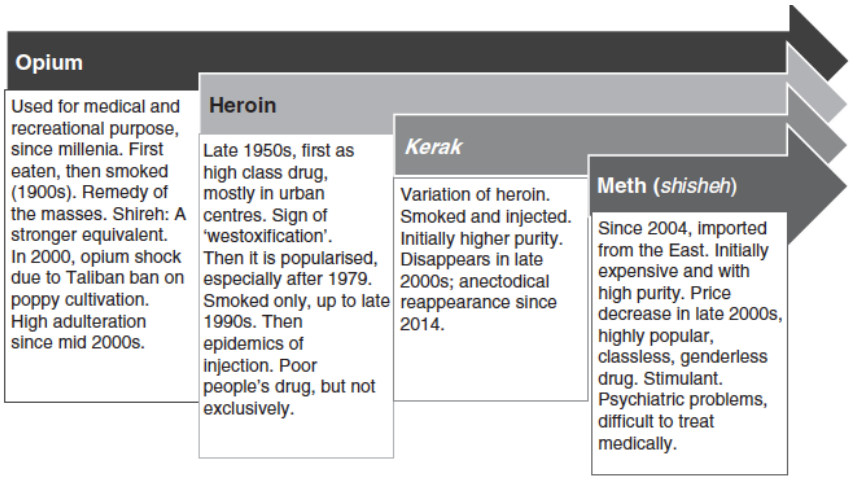

Figure 1.4 Changes in Drug Use Patterns in Iran (1800-2015), reproduced from (Ghiabi, 2019)

The results signalled the coexistence of two epidemics: an HIV epidemic and an unsafe injection epidemic. The concentration of both epidemics within prisons presented a threat—

but also an opportunity for a contained pilot harm reduction programme (Ghiabi, 2019). A collaboration began between Iran's Ministry of Health, the Prisons Organisation, and the newly opened UNODC office for the first experimental harm reduction programme in three prisons. Inside prisons, methadone clinics grew in number (see Figure 1.5), while simultaneously the Islamic conjugal visiting days (which offered private rooms for inmates to meet their spouses and maintain sexual relations) were used as a means and justification for distributing condoms amongst inmates (Behrouzan, 2010). Outside prisons, scale-up of harm reduction grew (see Figure 1.6), while establishing a National AIDS Committee. By 2010, homeless shelters were offering vending machines for clean needles (Rosenberg, 2010b), free condoms were provided by clinics and a decentralised universal antiretroviral therapy programme was offered across the country (see Section 1.4.4).

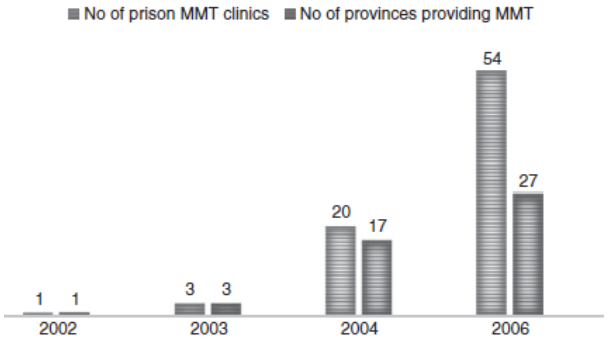

Figure 1.5 Methadone Clinics in Prisons. Source: Drug Control Headquarters Annual Report, reproduced from (Ghiabi, 2109).

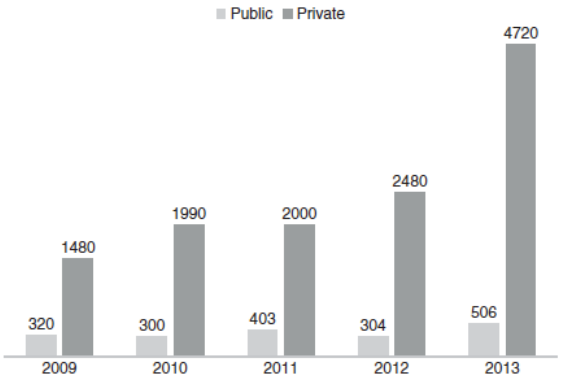

Figure 1.6 Methadone Clinics Scale-up. Source: Drug Control Headquarters Annual Report, reproduced from (Ghiabi, 2109). Note: These Methadone clinics are a mix of free, insurance-covered, and out-of-pocket services.

Such measures helped derail a potential health crisis, considering that in the early 2000s there was a shift towards injection, following the Taliban's take-over of power in Afghanistan, poppy seed production halted, leaving Iranian Opium users with little choice but to switch to the cheaper and stronger injectable drugs (Ameli, 2014; Ghiabi, 2019). The number of injecting users increased to 300 thousand by 2002 (Nissaramanesh et al., 2005), but the timely implementation of harm reduction programmes helped mitigate the threat of a larger HIV epidemic (T. Rosenberg, 2010a). Crucially, the harm reduction paradigm was adopted by lawmakers, who, following the 1979 revolution that established the Islamic Republic, opted for severe punitive measures, such as making drug possession a capital offence (Ghiabi, 2019; Nissaramanesh et al., 2005). As the limits of enforcement were realised, a medicalised view of drug use replaced the criminalised approach (Rahnama et al., 2014), ultimately restricting the capital offence (to distributions of more than 50 kilograms of narcotics like Opium, 2 kilograms of heroin or 3 kilograms of crystal meth), replacing incarceration with methadone replacement therapy (now offered by numerous governmental and non-governmental centres as shown in Figure 1.6) (Erdbrink, 2018). Efforts are still needed to move away from compulsory drug treatment and towards voluntary rehabilitation services (UNODC, 2020), but significant decriminalisation and medicalisation efforts have already produced a less threatening context for people who use drugs to engage with health services, including HIV treatment. Indeed, the prevalence of HIV among people who use drugs declined from 13.8 to 4.2 per cent while the size of the population who injects also decreased (UNAIDS, 2020a).

1.3.2 Community Perspective

At the onset of the epidemic, a series of reports indicated that the majority of former inmates who were living with HIV committed suicide upon re-entering their communities (Behrouzan, 2010). These reports suggested that suicide, rather than AIDS-related causes, became the primary cause of death among Iranians diagnosed with HIV in the late 1990s. The heavy burden of stigma, especially in border cities and among the more conservative ethnic minorities, contributed to family disownment, severe isolation, internalised shame, and

ultimately suicide (Karamouzian et al., 2014). In response, there was a need for programmes that could mitigate the consequences of HIV stigma through intervening at the family and community levels, by providing education and counselling (T. Rosenberg, 2010b, 2010a). Iran's health system had a history of community delivered healthcare, thereby the medical community mobilised community resources to provide culturally sensitive support and counselling to HIV-affected families (J. Rosenberg et al., 2011). This work was followed by the development of triangular clinics, which provided treatment for drug use, HIV and other sexually transmitted diseases; a model that diffused stigma by avoiding direct reference to HIV/AIDS, resulting in a higher acceptance of HIV services and uptake of treatment (Mokri & Schottenfeld, 2008). This model, which received a best practice achievement award by the WHO in 2004, facilitated delivery of HIV care by intervening at the community and family levels; targeting the microsystem through a medicalised approach (Rahnama et al., 2014). Evidently the high rates of suicide were reduced as engagement with treatment and support increased, but this medicalised approach simultaneously side-lined efforts that could raise public awareness of HIV and tackle stigma at the macroscale (Behrouzan, 2010).

As a consequence of limited public debates regarding HIV, enacted and internalised stigma associated with HIV in Iran remain high (Rasoolinajad et al., 2018). Iranian society has a collectivist culture, resulting in the experience of collective shame and concerns about family honour. Simultaneously, modern Iranian society has rapidly transitioned towards more individualistic value-systems and lifestyles, as a result of increasing access to education, modernisation of the workforce, and an expanding middle-class (before the past decade of sanctions and chronic inflation pushed people into poverty) (Harris, 2017; Salehi-Isfahani, 2020). For instance, women make up more than 50 percent of university students; the per centage is even higher for female students in science and technology degrees, which is significant given that Iran is one of the countries with the highest per capita number of engineering graduates (Dobbs et al., 2016). Yet, these statistics are occurring in parallel to emerging and evolving modern transitions that remain embedded within a traditional value system and conservative social norms regarding gender, sexuality, drug use, and consequently HIV (Ferdows, 1983; Mir-Hosseini, 1999; Shahrokni, 2020)isengagement, was reported by 96.9 percent of Iranians living with HIV, a proportion that is substantially higher than any country in the world (UNAIDS, 2022). Recognizing the need to raise public awareness, Iran

has now joined a global partnership to escalate efforts that can address stigma and discrimination by establishing formal processes to seek redress and providing legal assistance to victims of discrimination and key populations affected by HIV (UNAIDS, 2022).

1.3.3 Legal Perspective

As a Shi'a majority Muslim country, the Islamic law that is in effect in Iran offers possibilities for variegated reasonings through Shi'a Jurisprudence (f*eqh*), which is a philosophical practice of deep argumentation over issues at the macro and micro scales, adopting either of two approaches: a dynamic jurisprudence (*feqh-e puyā*), which calls for contemporary reinterpretations of the Shari'a law by evaluating the current junctures of society and time; or a fixed jurisprudence (*feqh-e istā*), which is a more traditional practice that seeks to adhere more proximately to Shari'a rules (Axworthy, 2013). Such dynamic reasonings have produced fatwas and new laws focused on decriminalisation. Chiefly, the fatwa delivered by Ayatollah Khomeini (the founder of the Islamic Republic) recognised gender confirmation and transgender rights, once in 1964 in his writings and once in 1982 following the revolution, when gender confirmation surgeries began to be offered in Iran (Pirnia & Pirnia, 2022).

In contrast to this decriminalisation act, drug possession was criminalised as a capital offence, despite existing fatwas at the time that opposed making drug possession a capital offence, including the fatwa by Ayatollah Khomeini himself, who at the time was the religious leader and opposed the more strict reasoning that introduced capital punishment for drug possession (Borhani & Ahmadzadeh, 2019). Therefore, policy-making through *fegh* can be dependent on the odds of one argument being adopted over another. By 2017, it had taken almost three decades for capital punishment to be removed for personal drug possession (as explained in section 1.4.1). It is thus relevant to consider that beyond the bifurcation of dynamic versus traditional jurisprudence, a further debate exists on minimal (*feqh-e hadd-e aqali*) versus maximal (*feqh-e hadd-e askari*) involvement of *feqh* in the domain of policymaking, especially sociocultural matters, and its extension to public's lifestyle (Tabaar, 2018)(Tabaar, 2018). These can be a forum for debate in which the limits of *feqh*'s involvement in matters that are currently criminalised can be discussed with cultural and

religious sensitivity, and with significant implications in terms of preventing HIV and supporting individuals living with HIV.

1.3.4 Institutional Perspective

At the outset of the 1979 revolution, it was estimated that more than 50 per cent of Iran's population lived in rural areas (Statistical Centre, Iran). To improve access to healthcare and to reduce disparities between rural and urban areas, a pyramidal network of primary care was established to connect 'Health Houses' to 'Primary Health Centres' (see Figure 1.7), with an efficient referral system that could maintain patient records and track public health outcomes (Rosenberg, 2011). Public health services were provided by community health workers, who were recruited from the communities they would serve, thereby delivering care that was dually efficient and culturally acceptable (Harris, 2017). The public health gains of the 1980s and 1990s included: achieving universal immunisation, eradicating polio and measles, sharply reducing maternal and infant-mortality rates, and 'the most rapid national decline in birth-rates in world history', from an average of seven to two children per mother by the end of the century (Harris, 2017).

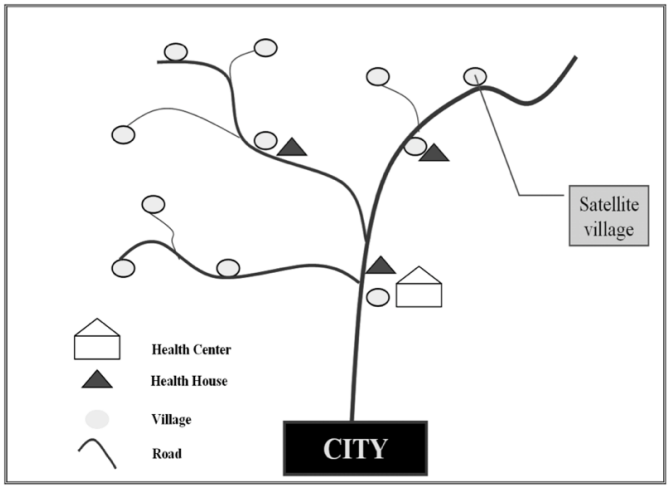

Figure 1.7: Primary Health Care Network, connecting Health Houses pyramidally to Health Clinics (Source: J. Rosenberg, 2011)

Four decades after the revolution, developments in terms of education, workforce, and urbanisation, have reduced both the sizes of rural areas and the rural populations to less than 30 per cent, while the health system is increasingly focused on secondary and tertiary care through a mix of public and private services. There exists a growing need to address the

chronic health demands of an aging and urban population with more efficiency and care coordination(Tabrizi et al., 2017). The decline of primary health care, combined with the growing burden of chronic health issues, has resulted in fragmentation of care that is delivered by multiple specialists, with a reduced emphasis on prevention and primary care approaches (National Health Report, 2021). This contemporary context demands more efficiency and continuity—characteristics that could be enhanced through the introduction of technological approaches—if the design fits the wider system, the needs of patients and providers, and the exigencies of various health conditions (Greenhalgh et al., 2017; Tabrizi et al., 2017).

To use digital interventions for HIV care in Iran, the national HIV response and the contexts of living with HIV must be carefully considered. To maintain discrete HIV-related patient information and prevent enacted stigma against people living with HIV and their families, the PHC network was purposely sidestepped, and instead the triangular clinics model was used to provide combined counselling and care for drug use, sexually transmitted diseases (STDs), and HIV. An institution wholly dedicated to HIV services would raise suspicion and stigma in small communities, while combining services would circumvent specific associations (Behrouzan, 2010). The current national strategic plans (NSPs) for HIV service delivery are built on the foundations of triangular clinics, offering core services at Voluntary Counselling Testing centres (VCTs). The NSP includes the collaboration of multiple governmental institutions, as depicted in Figure 1.8.

HIV testing, counselling, treatment, and care services are integrated at the VCTs. For people living with HIV who need further support, the VCTs refer patients to Positive Clubs (PCs). Run and organised by peers, the PCs offer a highly supportive and non-discriminatory environment. The care and support services offered by PCs provide a perfect opportunity to build upon via digital health approaches. The PC services aim to:

- reduce loss to follow up;
- provide support for adherence;
- provide support for partner notification and disclosure (also offered by VCTs);
- provide family counselling and support;
- reduce internalised stigma;
- provide psychosocial support;
- offer empowerment classes, education and awareness raising.

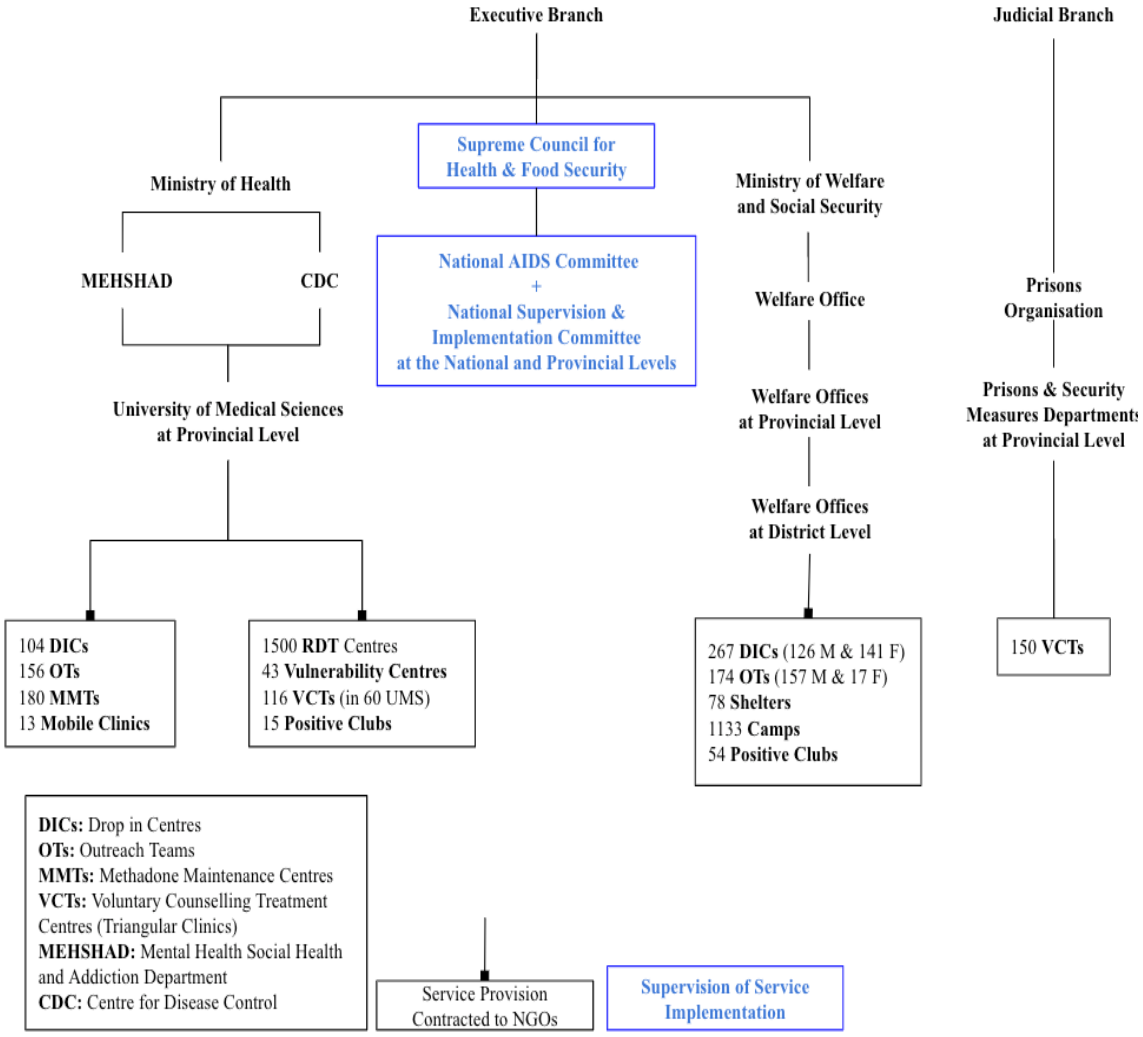

Figure 1.8 HIV Management and Service Implementation. This figure maps the national HIV management programme that encompasses multiple organisations (governmental, non-governmental and private) that are structured with a division of responsibilities as defined by the National Strategic Plan (NSP) for HIV. Supervision of the implementation of the NSP is monitored by the National AIDS Committee and a national Supervising of the Implementation of Programmes (SIP) committee which at the national level is based under the Supreme Council for Health and Food Security and includes members from every relevant governmental ministry and organisation. At the provincial level, SIP is operated through Universities of Medical Sciences, and provincial welfare or prisons offices. (Source: Author's own compilation using data collected through the evaluation of the national HIV programme that was conducted for the Global Fund during this doctorate, from January to October of 2020.) Note: these services are all free at the point of delivery.

Internationally, Iran collaborates with the Global Fund to Fight AIDS, Tuberculosis and Malaria, receiving technical assistance to ensure that the programming is up to date with the latest science. I served as a part of a team of international consultants for the Global Fund to evaluate the national programming for HIV and AIDS. Even though more than 90 per cent of the funding for the HIV programming is secured domestically, the collaboration is a fruitful venue in which Iranian physicians and policymakers can keep up to date with the latest international recommendations to ensure sustainability of services in terms of treatment and prevention. Further, the funding from the Global Fund has been used for auxiliary services, such as the establishment of a viral resistance lab (first in the MENA region) to ensure that antiretroviral resistance is contained, in addition to the procurement of mobile buses that offer test-and-treat to populations at risk for HIV and deliver treatment to those who may be lost to follow up due to drug use or homelessness. The data collated for Figure 1.8 was collected by myself as part of the consultancy that was conducted for the Global Fund.

1.3.5 Epidemic Transitions

Within the past decade, as a result of successful harm reduction programmes and universal antiretroviral therapy, HIV transmission and unsafe injection practices have seen a significant decline, and the prevalence of HIV has fallen from 13.8 to 4.3 per cent among people who use drugs (UNAIDS, 2020a). However, ongoing efforts are needed to increase diagnosis, linkage to treatment, and consistent engagement with HIV care (National AIDS Committee, 2020).

The HIV epidemic which initially was interwoven with the injection drug use epidemic, is increasingly now increasingly driven through sexual transmissions (Leylabadlo et al., 2016). Further, the epidemic burden has been shifting from men to women. Before 2017, 65.8% of transmissions occurred through the use of shared needles by people who inject drugs, the largest key population living with HIV, while sexual and vertical transmissions accounted for 19.6% and 1.5% of all cases, respectively. Since 2017, 47% of cases were sexually transmitted, followed by 32% of cases of transmission through injection. The total proportion of women

diagnosed with HIV increased from 4.7% of all cases in 2001 to 16% in 2017 (Najafi et al., 2020; UNAIDS, 2018).

This section has provided the historical, social, legal, and institutional perspective with regard to the ways in which HIV care is offered and engaged with and the contexts through which people living with HIV navigate daily lives in Iran. To examine the impact of these historic, social, legal, institutional, and epidemiological developments in terms of HIV care continuum outcomes and how mobile phones can be used to support HIV care, the next section summarises the relevant background on the HIV care continuum and mobile phone use in HIV care.

1.4 HIV Care and Mobile Phones

In this section I provide an overview of the HIV care cascade, its limitations relative to the HIV care continuum, and its global, regional, and national status, highlighting outcomes of HIV care in Iran. The spectrum of engagement with HIV care is outlined before providing an overview of the predominant interventions that are delivered to improve HIV care and adherence to treatment. Further, a summary of the state of the current evidence and the limitations of existing knowledge with regard to the application of mHealth, and in particular mobile messaging in the field of HIV care, is provided. This summary will set the necessary background regarding the utility of mobile phones for improving HIV care outcomes. In addition, I highlight the gaps in knowledge on how to utilise mobile phones in HIV care, before proceeding to the research approaches used in my research project.

1.4.1 HIV Care

To assess the success and failures of policy and programmes in delivering HIV testing, treatment, and care, data are collected across the HIV treatment cascade, a sequential model that delineates three successive steps through which people living with HIV engage with medical care and treatment, from the point of diagnosis to achieving sustained viral load (UNAIDS, 2022). At the population level, the treatment cascade is a useful framework to analyse the proportion of people who are engaged in the key stages of HIV care and ascertain the local and national points at which service deficiencies exist and interventions are needed.

To date, the UNAIDS has set out two sets of targets to eliminate AIDS related mortality and new HIV infections. These began with the 90-90-90 goals to be reached by 2020 and followed by the 95-95-95 goals to be reached by 2030 (UNAIDS, 2023). The first target aims for having 95 percent of the estimated population living with HIV to be aware of their HIV status trough a confirmed diagnosis. The second target aims to have 95 percent of those who are aware of living with HIV to be actively on treatment, and the third target aims to have 95 percent of those who are on treatment to be virally suppressed. Table 1.1 depicts the global, MENA, Asia and Pacific, and Iran's treatment cascade metrics, as of 2022.

Table 1.1 HIV Treatment Cascade Metrics, National, Regional, Global (Source: UNAIDS, 2023)

Region/Country	Estimated Adult Prevalence of HIV	Aware of HIV Status	Receiving HIV Treatment	Achieving Viral Suppression
Global	0.7	86	89	93
MENA	<0.1	67%	75%	90%
APA	0.2	78%	84%	95%
Iran	<0.1	51%	72%	90%

With regard to the 'on treatment' status, the second 95 target is calculated by considering people as lost to follow-up if they have not been seen within 28 days of the last expected clinical contact (for either an appointment or drug pick-up)—essentially measuring the proportion of people who are *actively retained* rather than merely *linked* to treatment (UNAIDS, Indicators Registry). Therefore, the indication that only 72 per cent of Iranian who are aware of their HIV status are actively retained in care suggests that interventions are needed to both link the newly diagnosed to antiretroviral therapy *and* prevent disengagement from available medical care. While Iran reached the third 90 target of viral suppression by 2020, suggesting that *daily adherence* may not be suboptimal among Iranians who are *actively retained* on treatment, but there is a vital need to reduce longer gaps in treatment disengagement, which are more critical in terms of increased risk of viral rebound and developing antiretroviral resistance (Haberer et al., 2015; Lai et al., 2023; von Wyl et al., 2009). To address this crucial problem, mHealth strategies can show promise by staying connected to patients, reducing disengagements and losses to follow-up, and actively linking people to the resources available (such as Positive Clubs and counselling that was discussed

in Section 1.4.4). Further, improved follow-up can prevent viral resistance, and refer those at risk of developing antiretroviral therapy resistance to viral resistance labs (discussed in section 1.4.4) in due course.

Importantly, a critical limitation of the care cascade is that measurements at each step are cross-sectional, precluding the ability to longitudinally track losses to follow-up and changes over-time at the individual level (Colasanti et al., 2016). To better examine how these measurements translate to structural barriers in provision of medical care or psychosocial barriers in engagement with medical care this thesis is informed by the steps conceptualised in the HIV care continuum. While also assessed cross-sectionally, this continuum is primarily used in the United States to more granularly ascertain the problems related to losing people living with HIV following diagnosis (Gardner et al., 2011). It appears to be a better model for showing key steps and highlighting the level of engagement with HIV care, relative to the UNAIDS care cascade (Colasanti et al., 2016). The spectrum of engagement is more enlightening within qualitative discussions on engagement and disengagement from care (see Figure 1.9). But in terms of measurements, just as the cascade, prevalence-based continuum measures each step as a proportion of estimated population size of people living with HIV, while diagnosis-based replaces the prevalence denominators with the number of people who are diagnosed with HIV. The key steps consist of diagnosis, linkage to care, receipt of care, retention in care, adherence to treatment, achievement and maintenance of viral suppression and can show a spectrum of engagement with care. These steps are the direct targets of interventions that seek to move people living with HIV towards being fully adherent to HIV treatment. The next section will discuss some of these interventional approaches, before moving onto the utility of mobile phones for improving HIV care and treatment outcomes.

Figure 1.9 Spectrum of Engagement with HIV Care Continuum, recreated by author from (Gardner et al., 2011). The key steps between linkage to care, to retention in care, and adherence to treatment can be supported through mHealth that links people living with HIV to providers.

1.4.2 Improving Engagement

Numerous interventions have been tested to improve engagement with HIV care and adherence to treatment in a variety of settings. Broadly categorised, these interventions are either delivered at the structural level or at the individual level. At the structural level, the barriers to accessing and engaging with HIV care and treatment are multiple and multilevel (as discussed in Sections 1.3 and 1.4). Insights from economics, behavioural psychology, and social theories are applied frequently in the development and implementation of interventions that target HIV care (Galárraga et al., 2013). Economic incentives in the form of conditional or unconditional cash transfers, and social protection, are effective strategies to address poverty, social vulnerability, and HIV outcomes (Pega et al., 2017; Richterman & Thirumurthy, 2022)(Pega et al., 2017; Richterman & Thirumurthy, 2022). Factors such as fragile supply chains leading to stock-outs, long distances to clinics, and long clinic wait times are known to undermine successful treatment outcomes (Haberer, Sabin et al., 2017). Improvements in delivery of care can substantially improve outcomes. For instance, decentralising HIV services improves retention in care (Kredo, Ford, Adeniyi, & Garner, 2013). Similarly, reducing the frequency of clinic visits and medication refill schedules can streamline care, reducing the burden on over-worked clinic staff and crowding at hospitals and clinics (Barker et al., 2017). These approaches can be especially effective in resource-limited settings, where there is a shortage of clinical staff.

At the individual level, interventions are predominantly underpinned by the information-motivation-behavioural skills (IMB) model of health. The IMB model assumes three primary constructs influence behaviour change: information and knowledge about the behaviour; the individual's motivation to perform the behaviour; and the behavioural skills necessary to perform the behaviour (J D Fisher, Fisher, Misovich, Kimble, & Malloy, 1996). Based on this model, education interventions aim to provide information to patients on various aspects of HIV treatment and medication adherence. These interventions primarily aim to build knowledge and increase health literacy. Notably, a systematic review shows that when these interventions are tailored to patient concerns and delivered using relevant metaphors, they can be more effective (Perazzo et al., 2017). Counselling interventions can similarly be informational, using problem-solving tools to collaboratively improve engagement with HIV care. Based on the IMB model, common counselling approaches used to prevent

disengagement from care and treatment include Cognitive Behavioural Therapy (CBT) models (Bere et al., 2017) and Motivational Interviewing (MI) (Holstad et al., 2012). Through several sessions, patients are counselled to identify their thoughts and feelings, resolve potential discrepancies between intentions and actual actions, and increase motivation to change behaviours that are inconsistent with those intentions. Crucially, while such strategies are goal oriented and aim to promote behaviour change at the individual level, the WHO recommends counselling and education strategies that use a peer-delivered and family-centred approaches to build support around the individual (WHO, 2015a). Psychosocial approaches used in Iran are successful examples of building such support (see Section 1.4.4). Evidence from South Africa shows adherence clubs are a notable example of social support strategies that have been shown to be highly efficacious (Luque-Fernandez et al., 2013). Further, there is promising evidence from Sub-Saharan Africa on the optimised delivery of counselling with software and technology-enhanced tools, such as laptops or tablets (Remien et al., 2013; Robbins et al., 2015). These interventions leverage existing resources, but may require shifting already constrained human and technological resources, with limited reproducibility across settings (Haberer, Sabin et al., 2017).

1.4.3 Mobile Phones

Mobile phones can be employed in various ways to provide remote care for long-term conditions (with the potential to combine some of the approaches discussed in the previous section) (Abrams et al., 2015; Kew Kayleigh & Cates Christopher, 2016; Nhavoto et al., 2015). To improve engagement with the HIV care continuum, a flurry of research targeting individual-level adherence behaviour has been produced (Devi et al., 2015; T. Horvath et al., 2012; S. B. Lee & Valerius, 2020). Despite the lack of a standard definition, mHealth is an expanding field, especially following the COVID-19 pandemic, in which the provision for remote care became an urgent need. Most commonly, mHealth refers to the use of mobile communication functionalities and applications (apps), for a wide range of healthcare purposes (Aranda-Jan et al., 2014).

In this thesis, I will focus on caring for people living with HIV, using the mobile messaging feature. For the purposes of adherence support, mobile messaging interventions

have been the most commonly utilised feature, assessed primarily through RCTs to examine efficacy across global settings (Chaiyachati et al., 2014; Mbuagbaw, Sivaramalingam, et al., 2015). The first of these studies was a trial of a two-way mobile-messaging intervention, called WelTel Kenya, which improved adherence through a weekly message of asking patients: 'How are you?'. Since then, a number of studies showed efficacy of two-way mobile messaging to improve antiretroviral therapy adherence (Garofalo et al., 2016; Ingersoll et al., 2015; Mbuagbaw et al., 2011). Several systematic reviews confirmed the efficacy of 'text-messaging' in improving adherence (Finitsis et al., 2014; Lima et al., 2016; Mayer et al., 2017). One systematic review and meta-analysis that included 86 studies of all interventions that targeted adherence, found mobile messaging strategies to be the most effective (Kanters et al., 2017). Finally, the WHO recommended mobile messaging as an effective intervention to Click or tap here to enter text.support antiretroviral therapy (WHO, 2015a). To consider the characteristics that make these programmes most effective, a meta-analysis found that mobile interventions have a larger effect when messages are '(1) sent less frequently than daily, (2) support bidirectional communication, (3) include personalised message content, and (4) are matched to participants' antiretroviral therapy dosing schedule' (Finitsis et al., 2014). However, conflicting evidence on the effectiveness of mobile-messaging intervention in terms of directionality and characteristics remained unresolved (Haberer, Sabin et al., 2017; Mayer & Fontelo, 2016; E. J. Mills et al., 2012).

At the onset of this doctorate, it became evident that a crucial gap in knowledge and an important research question to address is: *how* mobile-messaging interventions work, *for whom, in what contexts, and why*. Importantly, beyond being one-way or two-way, mobile messaging holds versatile capacities for remote care, by offering an efficient and easy means of communication that can be standardised or personalised, technology-based, or human-supported, informational, or interactive. These differences in using mobile messaging can determine how care will be organised, how contexts of treatment delivery will be changed, what mechanisms will be produced, and what outcomes will be shaped. Yet, most studies fail to fully describe the explanatory theories that underpin mobile messaging interventions. Further, the content of two-way communication, whether such content is standardised, and who delivers this content is often left unreported. Consequently, the theories of change that

explain how mobile messaging leads to improved adherence remains too abstract and the reproducibility of these trials remains challenging.

This gap in knowledge is underpinned by the type of evidence that is not available (i.e. how these interventions produce their effects and how can they be replicated), despite the wealth of evidence that confirms the efficacy of 'mobile messaging' in terms of improving adherence behaviour. In response, this thesis attempts to add to the knowledge gap by investigating how these interventions *could* interact with the context of HIV care by collecting primary data from Iran and secondary data from global settings. The next section will describe the research approach and design in detail.

1.5 Research Approach

This DPhil thesis attempts to advance the scientific as well as the practical knowledge of mHealth intervention designs as applied to HIV care. Despite the growth of evidence in terms of the efficacy of mHealth approaches, remarkably little consensus exists on *how* these interventions operate and *how* they interact with their contexts. In this thesis, I claim that such a lack of consensus is due to a deterministic view of mHealth interventions and a lack of emphasis on the recursive and emerging relationship of context with mHealth approaches, and in particular mobile messaging strategies. By applying a realist logic of analysis to primary data collected from Iran and by conducting a realist synthesis of secondary global evidence, the final product of this thesis is a middle-range realist programme theory that can be further developed and tested (confirmed, refined or refuted) in Iran and other global contexts.

Realist inquiry begins with an initial programme theory and ends with a more refined version that explains the variations of relationships between contexts, mechanisms, and outcomes (Pawson, 2013). Importantly, there is a distinction between realist programme theory, that explains the inner workings of a specific intervention, and formal theories within psychosocial sciences (e.g. social learning theory or attachment theory). Formal theories are drawn from the literature and are often too abstract and distant from the intervention to permit empirical testing (Wong, 2017). In contrast, realist programme theories can be rooted in or draw on formal theories but focus on explaining context sensitive outcomes in such a way that permits empirical testing. As such, realist programme theories are *middle-range*: i.e. specific

enough to permit empirical testing, but abstract enough to provide useful, explanatory transferability to other contexts where the same mechanisms may be operating. A programme theory can enhance the reproducibility of intervention outcomes across settings as it produces knowledge that enables a programme to be configured across contexts in a way to trigger the core mechanisms that produce the desired outcomes. To do so, a detailed knowledge of the condition that would be targeted through the intervention is needed first, before understanding what features of the intervention are needed, and what value these would propose to the context in which the condition is experienced (Greenhalgh et al., 2017).

As a conceptual framework to structure and present this thesis, I draw on the first three domains of the NASSS (non-adoption, abandonment, scale-up, spread, sustainability) framework, developed by Greenhalgh and colleagues, with roots in sociotechnical theory (Berg, 1999; Harrison et al., 2007), that moves beyond a deterministic view of technologies and considers how technologies influence and are influenced by multiple and interactive levels of context. The framework can be applied 'at the micro (individual users), meso (organisations and systems), and macro (national policy and social context) levels' (Greenhalgh et al., 2017). It consists of 'seven domains (see Figure 1.10), each of which may be simple (few components, predictable), complicated (many components but still largely predictable), or complex (many components interacting in a dynamic and unpredictable way)' (Abimbola et al., 2019). This research project is conducted at the micro (individual) level. Therefore, to present the findings, I draw on the first three domains of NASSS that correspond to the three main research aims and standalone papers at the level of individuals living with HIV: (1) the condition [Paper I], (2) the technology [Papers II & III], and (3) the value proposition [Paper IV]. As such, an ex-post drawing on the NASSS (presented in Figure 1.10) informs the structure of this thesis as highlighted in the following sections.

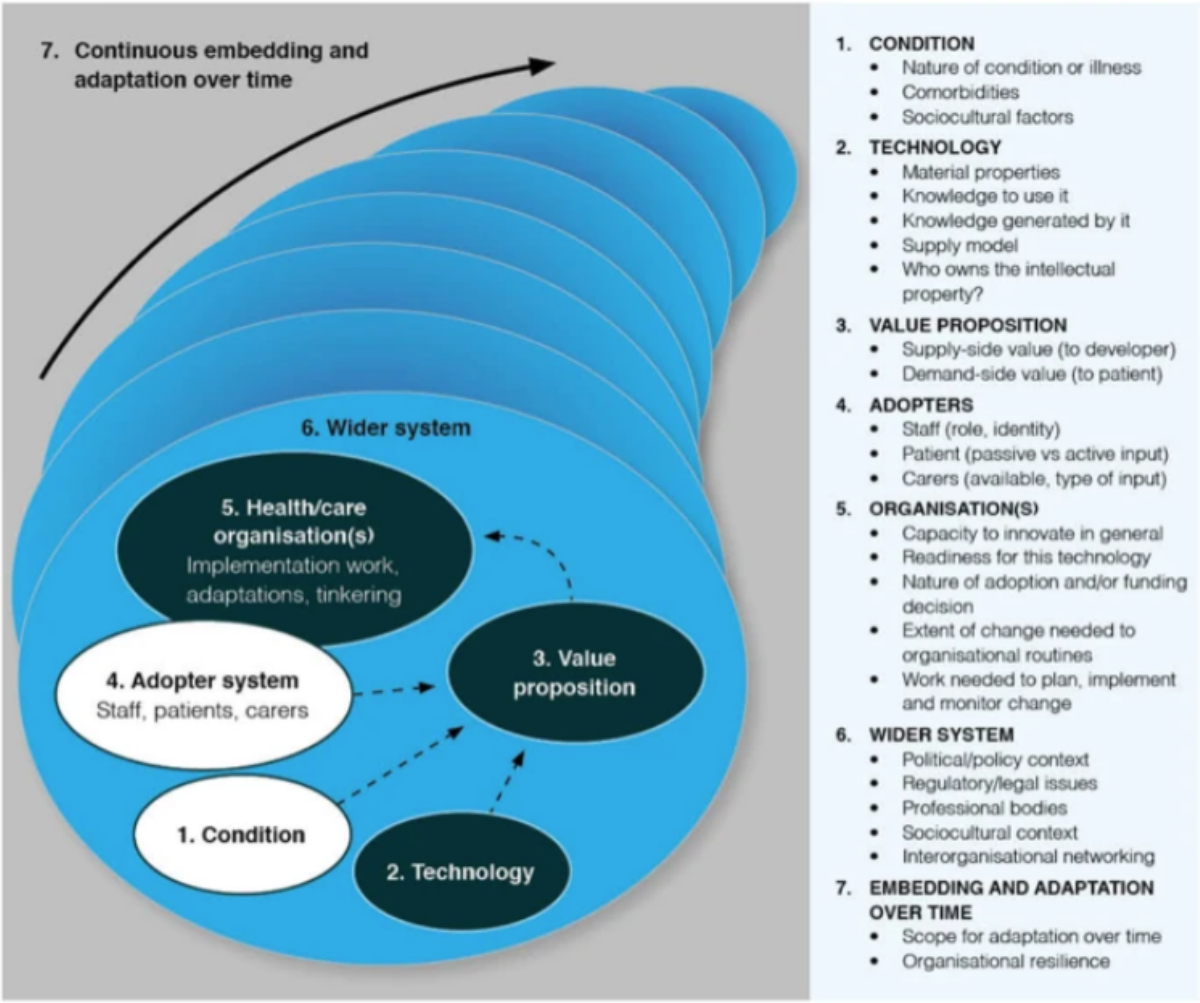

Figure 1.10 The NASSS Framework, for studying or ex-post theorisation of non-adoption and abandonment of technologies by individuals and the challenges to scale-up, spread, and sustainability of such technologies in health and care organisations, reproduced from (Abimbola et al., 2019).

1.5.1 Research Aims

This research project consists of three overarching aims, which have produced four standalone papers, thus corresponding to the requirements for the DPhil by publication track. Simultaneously, the three aims are aligned with the first three domains of the NASSS framework, which are highlighted here and discussed thematically within the discussion section of the thesis (Chapter 6).

Research Aim 1: To contextualise (dis)engagement from HIV care and antiretroviral therapy for people living with HIV in Iran.

This aim was addressed in *DPhil Paper I*, a qualitative study with a realist logic of analysis was conducted to contextualise living with HIV and engaging with HIV lifelong treatment within the socioecological context of HIV in Iran. This paper addresses the first domain of the NASSS framework: *the condition* by studying the nature of illness and its sociocultural influences.

Research Aim 2: To conceptualise and propose how an mHealth intervention can change the contexts of HIV care and engagement with antiretroviral therapy in Iran.

This aim was addressed in *DPhil papers II and III*, a qualitative study with a realist logic of analysis was conducted to conceptualise how specific mHealth features and provisions can change the contexts of engaging with HIV care in Iran. This paper addresses the second domain of the NASSS framework: *the technology*, by conceptualising how the material features of two-way mHealth mobile messaging with providers can be adopted in the context of HIV care in Iran. Further, DPhil paper III used these findings to propose an mHealth intervention called *HamRaah* (together-in-path in Persian) to be tested in a pilot RCT for efficacy, feasibility, and acceptability—in addition to a nested realist intervention. This paper proposed the initial realist programme theory which was later refined in a realist synthesis.

Research Aim 3: To conceptualise an evidence-based and theory-informed programme theory of two-way provider-supported mHealth for HIV care.

This aim was addressed in *DPhil paper IV*, a realist synthesis, which progressively focused on the added value of two-way messaging, when connected to a human provider. The synthesis was informed by findings of the research questions addressed in parallel to this review and as part of the abovementioned aims. This paper addresses the third domain of the NASSS framework: *the value proposition*, by demonstrating the value of having a human-supported versus technology-based mHealth for HIV care.

1.5.2 Research Design

This research project has consisted of primary and secondary research that have been conducted in parallel and sequentially, with iterative refinements within and between the two parallel arms. To structure this thesis, and further recognise the non-deterministic role that mHealth can play in the context of living with HIV, the three main questions of the thesis align with the first three domains of the NASSS framework (see Figure 1.11) at the individual (micro) level of people living with HIV.

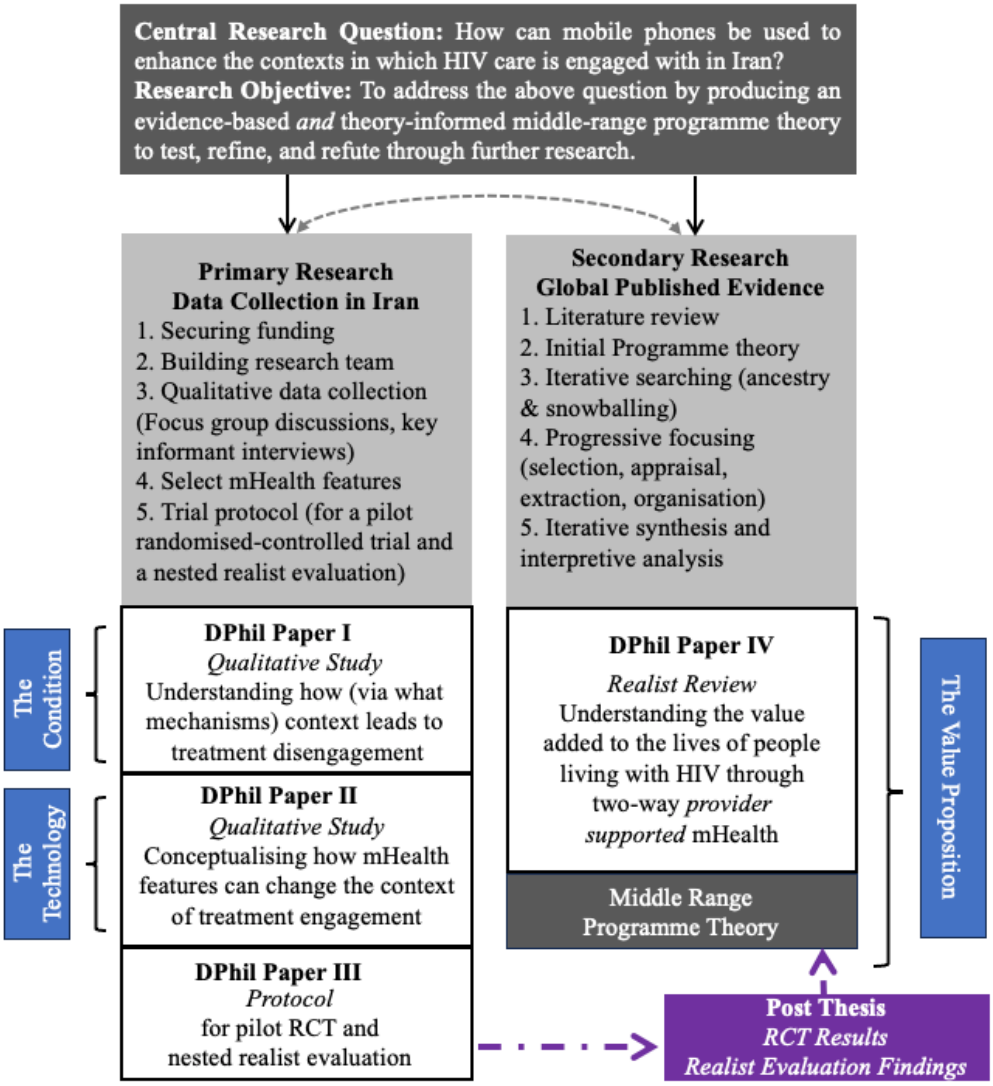

Figure 1.11 Iterative Study Design. Curved arrow represents the iterative relationship between the findings and processes of the parallel arms of primary and secondary research. The blue boxes represent the ex-post alignment and conceptualisation through the NASSS framework. The purple box represents the findings that will be finalised after the submission of this thesis.

1.5.3 Research Collaboration

I formed this research project through a collaboration between experts and researchers across Tehran University of Medical Sciences, Iranian Research Center for HIV/AIDS, Center for Global Health at Massachusetts General Hospital, Department of Global Health at Boston University School of Public Health, School of Social and Political Sciences at University of Edinburgh, in addition to the University of Oxford's Department of Social Policy and Intervention and the Department of Primary Care Health Sciences (Box 1.1). I secured the funding for this study through the call for proposals made by Tehran University of Medical Sciences (TUMS) bi-annual research fund. The collaboration begun at the cusp of the Joint Comprehensive Plan of Action (JCPOA), commonly referred to as the Nuclear Agreement. While this is not the first or last of such research collaborations since the revolution of 1979, the open attitude towards cooperation that existed from 2015 to 2018 helped invigorate more enthusiasm around joint work.

Box 1.1 Study Collaboration Supervisors and Experts

Prof. Jane Barlow, Department of Social Policy and Intervention, University of Oxford
Dr. Geoff Wong, Nuffield Department of Primary Health Care Sciences, University of Oxford
Dr. Franziska Meinck, School of Social and Political Sciences, University of Edinburgh
Prof. Jessica Haberer, Center for Global Health at Massachusetts General Hospital
Prof. Lora Sabin, Department of Global Health at Boston University School of Public Health
Prof. Minoo Mohraz, Iranian Research Center for HIV/AIDS, Tehran University of Medical Sciences

Further, I was lucky to have the mentorship of methodological and content experts with regard to evidence-informed and policy-relevant research methodology (JB and FM), context-sensitive realist lens of enquiry (GW), mHealth programmes for HIV care (JH and LS), and the context of the HIV epidemic in Iran (MM) (see Box 1.1). Such mentorship helped me navigate new research approaches and consider research questions that are relevant to the HIV programming context of Iran. The combination of the collaboration setup, research methods used, and research questions asked, kept this research sensitive to local policy context and the needs of people living with HIV in Iran. Further, given that this project was conducted entirely with the help of paid local staff who had full-time employment in Iran, much of the ethical dilemmas that surround recruiting temporary local staff or volunteer international researchers on precarious terms were avoided (Kaplan et al., 2020; Steinert et al., 2021). Thus,

this project countered the colonial structures of global health research that reproduce global north-south power asymmetries (Abimbola et al., 2021), whereby research ideas formed by northern researchers are pursued without engagement with local problems, stakeholders, resources, and contexts.

1.5.4 Ontology and Epistemology

Social science research is sometimes conducted at opposing ontological stances (Newman, 2019). One stance leads to positivism, a lens through which a distinct line is drawn between our experience of the external (held to be reliable and measurable) and our experience of the internal (largely ignored). The opposing stance leads to constructivism, suggesting that all reality is the meaningful (though unreliable) product of internal experience and social construction. Pierre Bourdieu (1977) is perhaps one of the earliest authors who attempted to overcome this divide in social research. Bourdieu's concept of 'habitus' represents the framework of attitudes and dispositions through which we experience the world (similar to constructivism), but our habitus is itself the product of our social positioning, which assumes an external causal reality (a positivist position) (Bourdieu, 1977). Thus, Bourdieu develops a constructivist approach from a positivist starting point. Another bridge between these stances can be found in a realist philosophy of science. A notable contribution to this field has been Bhaskhar (1978). To account for the seemingly paradoxical assumptions held by positivism and constructivism, he expounded a 'layered' conception of reality, consisting of three layers: 'the empirical' (the experience of events), 'the actual' (all experiences and events), and 'the real' (the underlying causal mechanisms that give rise to experiences and events) (Bhaskar, 1978). Through this philosophy of layered understanding of how the world must be constituted for science to be possible (i.e. ontology), realism offers the potential to bridge and reconcile the aforementioned social science divide. For this reason, throughout this thesis, I have adopted a realist ontology.

Research on AIDS is an epitome of the necessity to move beyond dichotomised ontological stances. The HIV epidemic has been studied through parallel ontologies: through a positivistic logic as an infectious disease epidemic, with an external biophysiological expression that is independent of the internal human experience, and through a constructivist

logic as an 'epidemic of meanings', which are socially constructed and entirely dependent on the internal human experience and meaning making (Treichler, 1999). While the biophysiological understanding of HIV's lifecycle led to the introduction of antiretroviral therapy, the ascribed meanings and changing narratives about HIV simultaneously shape(d) the experience of living with HIV and the possibilities of engaging with antiretroviral therapy. Therefore, it becomes evident that scientific discoveries of biomedical treatments need to be conducted in parallel to research that interrogates subjective meanings, such as those that have historically been assigned to HIV and AIDS (see Box 1.2). For this reason, in the qualitative data collection phase of this thesis, I adopted a social constructivist lens to explore the subjective meaning making in the experience of living with HIV and engaging with antiretroviral therapy in Iran.

Box 1.2 Attributions to HIV and AIDS. Author's selection from (Treichler, 1999)

1. A modern plague.
2. A disease of the "4-H Club": homosexuals, heroin users, haemophiliacs, and Haitians.
3. The price paid for homosexuality, drug use, and promiscuity.
4. A massive human tragedy, demanding charity.
5. The crucible in which the field of immunology will be tested.
6. A creation of the state to legitimise surveillance over people's lives and sexual practices.
7. A capitalist plot to make new markets for pharmaceutical products.
8. An imperialist plot to destroy the Third World.
9. A sign that the end of the world is at hand.
10. An extra-terrestrial conspiracy to weaken the human immune system and make the earth more vulnerable for alien invasion.

Each of the selected attributions (presented in Box 1.2) played a significant role in the trajectory of the HIV epidemic, particularly prior to the advent of antiretroviral therapy (Treichler, 1999). In response, grassroots activism and critical research remain crucial to interrogate value-laden attributions and shift focused efforts on removing structural barriers

that hide behind narratives of blame, preventing timely action and diverting resources from reaching communities in need.

Interrogation of meanings and narratives leads to an epistemological question: could subjective examination produce knowledge that is transferable across space and time? When studying socially constructed realities, two hermeneutic levels are involved: the research participants' interpretation of their own social world (collected through data: qualitative interviews or quantitative surveys) and the researchers' interpretations of participants' interpretations (expressed through conceptualising, coding, and analysing the collected data). The two hermeneutic levels interact to *co-produce* knowledge (Furlong & Marsh, 2010). As such, the subjectivities of both researcher and participants come into play throughout the research process (Merton, 1972). Crucially, although we cannot fully know the world objectively through our own subjective interpretations and perceptions, we can learn about it through empirical methods (Pawson, 2013). Epistemology in realism therefore claims that it is possible to gain knowledge and understanding of social reality based on the interpretations and inferences we gather through our senses, however influenced these may be by our subjectivity (Bhaskar, 1978). For this reason, the socially constructed meanings that were accessed through the qualitative phase of this study, were subsequently analysed through a realist lens of inquiry to produce transferable findings on a possibly shared reality across space and time.

It is thus important to note that throughout this doctorate, I have been on a journey of learning and had to expand my own epistemological and ontological purviews. I started this research project having completed an undergraduate degree in biochemistry and graduate level education in biomedical sciences with methodological training in epidemiology and biostatistics. As a biochemist turned epidemiologist turned social scientist, I found it challenging to have to adhere to a single research paradigm, at either of the two polarised ends of the ontological and epistemological spectrum, considering the importance of both lenses in advancing knowledge that can improve the lives of people living with HIV. I engaged with social constructivism to conduct the qualitative phase of this study and interrogate the socially constructed meanings that impact the lives of people living with HIV in Iran. I participated in qualitative research training course offered by Oxford's Department of Education. In parallel, I further received training to familiarise myself with the scientific realism that was set forth

by Pawson and Tilley (1997) to evaluate social policies and interventions. Using Bhaskar's key concept of *generative mechanisms*, Pawson and Tilley (1997) propose that there is value in researchers looking for social mechanisms at the level of human reasoning and reactions. To further familiarise myself with realist methods, in the summer of 2018, I participated in the training course offered by the Centre for Advancement in Realist Evaluation and Synthesis, offered at the University of Liverpool. I hence applied a realist lens of inquiry to the data that were collected through the qualitative phase of this research and was further enabled to apply a 'full' realist lens, by starting with an initial programme theory to be refined, in a synthesis and evaluation that investigate *how, when, and in what context* mHealth programmes can improve HIV care for people who are receiving antiretroviral therapy.

1.5.5 Positionality and Place

A statement to detail how the researcher is located within the research project and in relation to the research participants, in addition to depicting the research place, can contextualise the research findings and thus enhance the confirmability and transferability of the knowledge that is produced (Elwood & Martin, 2000; Walsh, 2003). In this section, the ways in which the research place and my own positionality may have had an influence on this thesis will be summarised.

Figure 1.12 Study Site Photos. Imam Khomeini Hospital Complex (IKHC). One of the main teaching hospitals of Tehran University of Medical Sciences.

Figure 1.13 Main Collaborating Research Partner. Upper photo: Infectious Diseases Unit of IKHC; Lower photo: Iranian Research Center for HIV/AIDS (IRCHA) sign.

This study was conducted with the collaboration of the Iranian Research Centre for HIV/AIDS, which is linked to the infectious diseases unit of the Imam Khomeini Hospital Complex (IKHC), a large hospital complex that is one of the teaching hospitals of Tehran University of Medical Sciences (see Figures 1.12 and 1.13), based in the socio-demographically diverse city centre of Tehran. I forged a relationship with IRCHA following my participation in the call for research proposals, set out by TUMS in the Spring of 2017. Following pre-approval, I presented my research proposal at IRCHA and my proposed mHealth project for HIV treatment adherence was selected to be funded for the qualitative study, pilot trial, and realist evaluation. The research team was recruited from trained research professionals at IRCHA, the VCT, and the Positive Club. To help me manage this research project, I was fortunate to work with an effective and efficient team, familiar with the local context of HIV care, and trained in ethical practice of biomedical and health research. When I was away from Iran, I stayed in touch with the fieldwork team that comprised of: a local project manager who was a full-time hired research assistant at IRCHA; one research assistant who helped with transcription and coding of interview and focus group materials; two recruitment managers who were members of the peer group of people living with HIV and

hired at the Positive Club; a trained social worker who helped manage the mobile-messaging intervention; a trained outreach worker who helped with the planning, design, and recruitment of the project. Additionally, the overall research plan, funding allocation, and implementation was overseen by the director of IRCHA, an infectious disease specialist who provided evidence-based recommendations to the National AIDS Committee and was a core member of the Supervision of Service Implementation of Programmes (SIP) committee (see Figure 1.8).

The opportunity to conduct this research project and engage directly with the policy and programming context of Iran was new to me. I had left Iran at the age of eighteen to pursue higher education in the US and UK, spending most of my adult life as a 'global citizen'. I was born into the first post-revolutionary generation of Iran, but throughout my childhood and teenage years I had spent a considerable amount of time travelling between Iran and the West, given that both my parents were Western educated and maintained social and familial connections across the US and Europe. Thus, much of my sensibilities were formed through the prism (and privilege) of living in-between cultures, value systems, and worldviews, while simultaneously I remained ironically unfamiliar with the experiences and values of parts of the Iranian society. In Oxford, I took courses on the History of Contemporary Iran and the Anthropology of the Middle East, at the Department of Asian and Middle Eastern Studies.

From 2017 onwards, I spent a minimum of six months per year in Iran to manage the research project and data collection process. In visits that lasted from three weeks to six months, I not only engaged with the diverse views of Iranian society, I was also placed more proximately to the day-to-day life in Iran and the contexts of economic, social, and political problems that invariably interacted with the research process of this study. From 2018 to 2019, during the qualitative data collection phase of this project, when US's Maximum Pressure campaign (initiated by the unilateral withdrawal of the US from the JCPOA and reimposition of comprehensive financial sanctions against Iran, lasting through the COVID-19 pandemic and to the present) was enforced on Iran, I became acutely aware of how interlocking systems of oppression—both at the international and national levels—bear harm downwards, with social groups (such as people living with HIV) furthest from centres of socioeconomic and political power left worse-off. For instance, even though my parents, my family members, and I were all affected by the same forces of economic, social, and political pressures, the vantage

point through which I would experience the problems in Iran was always going to be from a position of an outsider, or someone who can choose to be an outsider at any moment. In my interactions with the local research team and research participants I was reminded of my privilege of having the experience and the opportunity to have a life inside and outside Iran. Thus, as an Iranian citizen *and* a global citizen, I became more aware of my positionality as an insider *and* an outsider.

To be placed as an insider or outsider can have advantages or disadvantages in terms of how truthfully and accurately experiences are shared and information is exchanged between research interviewers and research participants (Merton, 1972). While researchers are seldom placed fully inside or outside the participant group, the specific purpose of the study determines whether an insider or outsider positionality would strengthen or weaken the findings. In the current research project, I shared a culture and language with Iranians living with HIV and was thus viewed to possess a priori insider cultural knowledge. As a result, I could avoid a sense of disorientation or 'cultural shock' and could ask in-depth sociocultural questions, such as those related to the impact of relationship expectations and family traditions on individual wellbeing and by extension treatment adherence. However, I could also be exposed to a risk of confirmation bias by being overly sympathetic when discussing some aspects of the political, economic, and social experiences that I happened to share directly or indirectly with the participants. When discussing matters that related to more sensitive topics of sex and gender, I was provided with a trusted insider status by assuming that I would be familiar with the values and sensitivities of such discussions. Simultaneously, I may have missed the chance to hear about deeper beliefs and prevalent praxes that may have been assumed as too 'obvious' to disclose to an insider. An outsider would have been positioned such that information would be explicated in more detail by participants. Not being bound by shared customs and cultural codes, an outsider can more freely ask questions that may be considered as 'taboo' for insiders to ask. For instance, Iranian women predominantly maintain to have been exposed to HIV either via their (ex)husbands or accidentally through a 'needle stick' incident. As an insider Iranian woman, sensitive towards cultural norms regarding sex outside of marriage, I was unable to interrogate such statements. Had the topic of the study focused on transmission patterns or prevention contexts, such a pressure would have substantially influenced the research findings. But in light of this study's focus on treatment

adherence and engagement with care, my position as an insider didn't require me to delve into topics that were considered as 'taboo' culturally. Instead, my insider understanding of cultural norms and first-hand knowledge of political, social, and economic contexts, helped me to gain quicker access to deeper insights.

Figure 1.14 The Positive Club. Left: Positive Club Entry Right: Classes in the Positive Club. These cosy classes are where interviews and focus group discussions were conducted.

Importantly, my outsider position, particularly in relation to not sharing an HIV status with the participants, was mitigated through the location in which the interviews and focus group discussions (FGDs) took place. The research place is both the physical location, in which interviews take place, and the bounded space through which meanings unfold as power dynamics, social relations, and identities are played out (Gagnon et al., 2015). Such bounded spaces have been characterised as 'micro-geographies' through which social processes can operate differently, as these processes are socially constructed and not fixed within national or larger scale geographies (Elwood & Martin, 2000). All (but two) of the interviews and FGDs for this study took place within the Positive Club (see Figure 1.14), where a feeling of community, safety, support, and empowerment enabled patients to discuss and share their experience of living with HIV and engaging antiretroviral therapy. The two FGDs that took place within the IRCHA building, instead of the Positive Club, imbued a sense of formality to the meeting and the power relationships were pronounced as people living with HIV began to view the meeting as 'patients' giving feedback to research professionals or the staff. In contrast,

the Positive Club space was run *by* people living with HIV *for* people living with HIV. Cornered in a cosy spot in the open space campus of IKHC, the staff of the Positive Club were selected from people living with HIV who had received training for psychosocial support. Upon entry, people living with HIV would be greeted by a peer, offered tea, and encouraged to attend the classes and events of the Positive Club. The two peer members of this research team, who were living with HIV, were staff members of the PC and involved in the recruitment of study participants. On the day of FGDs and interviews the peer members would welcome participants to the PC (if it was their first visit) and make them feel comfortable. Such a warm reception balanced any power imbalances that existed between me as a researcher and the participants as they felt empowered by being in a space belonged to them, as *their* space, to voice *their* concerns, and share *their* stories.

Finally, it is important to consider the position I adopted through this research and its sociopolitical context and the impact of this position on sharing the research findings. I chose to engage in evidence-based and policy-relevant research in Iran from a position of believing in the possibility of progressive policies that can protect the health and wellbeing of marginalised Iranians. I was lucky to have, as a primary partner of this research, a female medical doctor and infectious disease specialist, Prof. Minoo Mohraz, who championed the cause of people living with HIV in Iran (Samarasekera, 2021), and introduced evidence-based impactful praxes, such as the introduction of the peer run Positive Clubs to provide psychosocial and treatment support to people living with HIV (United Nations Iran, 2016). Simultaneously, being aware of my position as an Iranian woman who spends her life in between Iran and the West, I was cautious at the outset to choose an area of research that would produce impact without being highly politicised. I did this by choosing to focus on treatment gaps rather than testing and prevention gaps, as the latter would have confronted a wider range of penal laws in terms of pre-marital and same sex relations. I soon began to learn that much of what I had presumed would be true was not correct, as much research and practice focused on caring for vulnerable men and women (such as men who have sex with men, and trans- and cis- male and female sex workers) (Izadi et al., 2023; Sharifi et al., 2018). I was moved by the sensitivity with which the staff at IRCHA (and policymakers at the National AIDS Committee and across the governmental organisations that were assessed by the Global Fund evaluation I conducted as part of an international team) discussed matters

that related to people living with HIV and those who were vulnerable and at risk of HIV because of drug use or sexual relations. Crucially, however, given that information shared about Iran can quickly become politicised, there exists pressures both from inside and outside the country that impacts the possibilities to share findings that challenge mainstream views. Inside the country, there is the real threat of progressive measures taken by the government being labelled as 'liberal', 'imperialist', or 'colonial' by the more conservative groups, thereby endangering the sustainability and continuity of vital programmes for vulnerable populations. Outside the country, there is a real challenge to share narratives that produce a positive outlook about Iran. Evidence that challenges the notion of a regressive state and highlights possibilities for progress is met with hostility, much of which I was exposed to when sharing my research findings, arguments, and viewpoints on social media. Thus, evidence that can shift programmes and policies, both domestically, such as HIV programmes, and internationally, such as sanctions policies, must be shared with sensitivity and a high standard of rigour and transparency to be saved from politicised attacks.

1.5.6 Ethical Considerations

There is an extensive body of local and international literature on ethical concerns in conducting research with vulnerable, stigmatised, and criminalised populations. These include the ongoing academic debate on informed consent and confidentiality (Dingwall et al., 2014), the ethical requirements of the local universities and research institutions involved in research design and implementation, and guidelines from international organizations, such as the WHO, on people living with HIV (WHO, 2014). These ethical considerations are especially salient in contexts where research participants are at risk of being criminalised. The British Society of Criminology has a code of ethics, addressing the specific considerations of confidentiality when studying criminalised behaviour (Finch, 2001). This Code seeks to address central issues that researchers may encounter and provides guidelines designed to promote good practice and high ethical standards, including the responsibility of the researcher towards research participants – especially in terms of confidentiality when researching criminalised activity (Finch, 2001). These guidelines were carefully considered in the planning phase of this research project.

The general ethical framework according to the most recent amendments of the Helsinki declaration has also informed the design of the intervention proposed in this study (WMA, 2013). These necessitate eight principles as requirements for the ethical justification of biomedical research with human participants: i) collaborative partnership, ii) social value, iii) scientific validity, iv) fair participant selection, v) favourable risk-benefit ratio, vi) independent review, vii) informed consent, and viii) respect for participants. For each principle, the framework specifies several benchmarks meant to indicate what its fulfilment requires in practice (Emanuel et al., 2008). All the principles are generally applicable to any sort of biomedical research with human participants. As this project aimed to improve engagement with and adherence to antiretroviral therapy, using mHealth strategies, it falls within the field of biomedical research. Thus, care was taken in the design of the study protocol to adhere to these guidelines and meet the eight necessities for ethical justification of conducting studies with human participants.

For the pilot trial, given that the goal is to develop and test the feasibility of an mHealth intervention that communicates regularly through mobile messaging to support people living with HIV in the engagement with treatment, a careful attempt was made to anticipate unintended harms, consulting guidelines specific to mHealth confidentiality concerns. With regard to mHealth, a distinction is made between 'privacy' and 'confidentiality'. 'Privacy can be defined in terms of having control over the extent, timing, and circumstances of sharing oneself' (physically, behaviourally, or intellectually) with others (Labrique et al., 2013). Confidentiality pertains to the 'treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission' (OHRP, 1993). Thus, the onus is on researchers to safeguard participant confidentiality. More details on specific steps taken on protecting privacy and confidentiality of mobile messaging used in this study is described in Chapter 4.

Ethical approval

Ethical approval was granted by the University of Oxford and Tehran University of Medical Sciences. Given the collaborative nature of this research, additional Institutional Review Board approval was granted by the Partner's Health Organisation in the US. Copies of ethical

approval forms are provided in Appendix A. Two rounds of ethical approval were obtained. The first round was for the initial qualitative phase of the study that was conducted in Tehran from September of 2018 to January of 2019. The second round of ethical approval was obtained in February of 2019 to begin the trial that is reported in DPhil paper III. In the summer of 2019, when the trial implementation had begun, I provided updates to the ethics review boards on the adaptations of the trial protocol. The results of the pilot trial and final qualitative phase are not reported within this thesis, as agreed as part of the confirmation of status examination. However, the results are currently being prepared for publication.

Informed Consent

This study sought informed consent from all participants, who were either directly invited by clinic staff members or voluntarily expressed interest in participation. Upon expression of interest in participation, a consent form was provided, explaining the purpose of the study and the format of participation, which was either through FGDs or semi-structured interviews. All interested candidates were reminded that participation in the study is voluntary, meaning that refusing invitation to participate or withdrawing interest at any stage will have no ramifications in terms of received services from, or the established relationship with, the VCT or the Positive Club.

All staff members conducting the recruitment and informed consent process were trained in the ethical treatment of human subjects and familiar with informed consent guidelines. Staff members were also trained in more advanced research topics such as protocol adherence, quality assurance, data management, and individual privacy. The consent process took place in Persian. All interviewers and intervention facilitators had previously worked with people living with HIV. I was the lead project manager for the research. Additionally, two Medical Doctors, who were hired at IRCHA, helped co-manage the project. In addition to the above-mentioned sources, I attended the Research Ethics Course at Oxford in 2015. I also carefully reviewed the Oxford's Central University Research Ethic Committee (CUREC) best practice guidelines, in addition to the ethical guidelines by Tehran University of Medical Sciences, to plan the informed consent process.

All eligible patients, who were receiving care from the Infectious Disease Unit at the study site, who were interested in participating in the study were referred to a local study team

member, by whom they were provided a detailed explanation of the study's purpose and requirements to obtain written informed consent prior to enrolling each patient. All participants had the opportunity to reflect on their desire to participate in the study and inform the research team within a week of the invitation to participate. All attempts were made to ensure that the research is a positive and participatory experience for all participants, and that all consent is both voluntary and informed.

The informed consent forms were originally written in English (provided in Appendix A), then translated into Persian to be shared with participants. Care was taken to avoid using technical terms and ensure that the language is understandable to lay audiences. Caution was applied to ensure that all participants should be capable of giving their own consent. The protocol included a plan for those whose literacy levels were not sufficient to receive verbal explanation of the forms in Persian. However, given high literacy rates in Iran, no such occasion arose. A written process was used due to multiple reasons: (a) reading and signing forms is not problematic for most of the potential participants; (b) the research purpose was explained as a written document in a more standardised and thorough manner; (c) patients could read the information provided at their own privacy; (d) patients could take as long as a week to confirm decision regarding participation. The written consent forms were adapted from the templates provided by TUMS and the CUREC website.

Confidentiality

The study was conducted with careful attention to confidentiality of all participants. All information disclosed during research (regardless or governmental or non-governmental approval or funding) benefits from full confidentiality. The FGDs and interviews took place in a private room in the Positive Club, where classes for people living with HIV are usually convened (see Figure 1.11 on right). Participants were given the choice to use a nickname during the interviews and FGD to ensure that confidentiality is protected. All data from the interviews and FGDs remained confidential. Interview transcripts were anonymised, and no identifying information was transcribed or kept. Given that this study took place within Imam Khomeini Hospital Complex (see Figures 1.12 and 1.13), the site provided a sense of safety to participants as they were aware of the doctor-patient confidentiality and generally experienced sensitive encounters in the peer-run Positive Club (see Figure 1.14).

Data Storage

FGDs and in-depth interviews were recorded with the consent of participants. The informed consent forms included participants' full names and signatures, but these were not collected by the administrator of the FGD or interviews. The audio recordings of participants' voices were transcribed. The transcription process deliberately did not transcribe any of the identifying information, in the event that any personal identifiers are disclosed. Only the gender and interview or FGD number were retained. As such, no information with personal identifiers was stored or accessible following transcription of the recordings. All data, both from qualitative interviews and quantitative surveys, are accessible to me as the primary investigator. The de-identified data was shared with co-investigators as needed only for analysis purposes.

Compensation

Participants who attended the interviews and FGDs were provided with a warm traditional chicken kabab meal with rice at the conclusion of the sessions. However, participants were reassured that should they choose to leave in the middle of the session, for any reason, they would still be able to take their lunch away and have it elsewhere. As an alternative to lunch, a gift-pass to a swimming pool club in Tehran's city centre was also offered. No financial rewards were given for participation as incentives can be particularly problematic by exerting a coercive appeal when targeting financially insecure individuals (Singer & Bossarte, 2006). The choice of reward was decided in consultation with peer supporters and research staff, who were aware of different compensation options, including lunch delivery choices near the hospital. Based on prior work, the research team advised that for qualitative studies, in which patients offer a significant portion of their time during the day, lunch appears to be the most desirable reward, even when compared to equivalent cash compensation.

Risks and referrals

Careful consideration was given to mitigate any foreseen adverse effects for participating in this study. Particularly given that the study site was the same location at which medications were collected, traveling to and from the study site was not expected to introduce new risks

in terms of the unintended disclosure of HIV status. Given the qualitative nature of the study and the extended opportunities for sharing information about themselves, participants could openly disclose information on their experience of intimate-partner violence, thoughts of suicide, possibilities of causing other types of self-harm or third-party harms, other adverse situations, and various mental health issues. In all cases, referrals were made to the clinic's licenced mental health and family counsellors, or psychiatrists if medical support was needed. At all times, patients were encouraged, but not forced, to be referred and seen by the appropriate service providers.

Researchers held the ethical responsibility and received necessary training to provide referral information to participants who needed support services, such as mental health care, substance use treatment, or other healthcare and social support services, without providing any sensitive information (e.g. drug use or sexual history) to third party, governmental, or non-governmental organisations.

1.6 Thesis Outline

This thesis has adopted a realist framework of inquiry to investigate how mHealth can improve HIV care outcomes. To do so, it will triangulate multiple research paradigms and methods, collect primary evidence from Iran, and assemble secondary global evidence. To produce a non-deterministic debate, the findings of this thesis are outlined across three domains that will recursively interact with the effectiveness, scale-up, and sustainability of mHealth for HIV care: the condition, the technology, and the value proposition.

In Chapter 2, I focus on contextualising the contexts in which people living with HIV in Iran engage with medical care and antiretroviral therapy. The chapter combines a social constructivist qualitative data collection phase with a realist framework of data analysis to produce a nuanced understanding of engagement with HIV care that is rooted in a shared reality. Thus, the findings may well have transferability to similar settings and provide the possibility of informing an evidence-based intervention that can work across space and time. This chapter is based on published work.

In Chapter 3, I focus on the affordances of mobile messaging and conceptualise how mHealth can offer provisions of care in such a way that the harsh contexts of living with HIV and engaging with antiretroviral therapy can be diluted in the Iranian setting. As in the

previous chapter, a social constructivist qualitative data collection phase is combined with a realist framework of data analysis to conceptualise how specific mHealth features and provisions can be situated within the socioecological pathways that were identified in the previous chapter to disrupt consistent engagement with antiretroviral therapy in Iran. This chapter is based on work that is accepted for publication.

In Chapter 4, I present HamRaah (meaning together-in-path in Persian), an evidence-based intervention that is suited, based on stakeholder views collected in the previous chapters, to the context of HIV care in Iran. This chapter is based on a published protocol for a pilot randomised controlled trial, feasibility, and acceptability study, with a nested realist evaluation, to examine the efficacy, acceptability, and programme theory of HamRaah. In this chapter, I further introduce the initial realist programme theory to be tested in a realist synthesis and the nested realist evaluation.

In Chapter 5, I systematically and iteratively assemble a secondary evidence base from various global settings to conduct a realist synthesis of evidence and produce a middle-range programme theory that explains the value of human supported two-way mHealth. The refined programme theory can further be tested across settings and will be used to inform the realist evaluation of HamRaah that will be shared as part of the findings that will follow this thesis. This chapter is based on work that is currently under review for publication.

In Chapter 6, I produce a contextualised discussion on the findings of the above chapters, by considering the three overarching domains of this thesis. I then discuss the relevant policy and practice implications for the Iranian and global contexts. I will also discuss the overall limitations and future research directions, before providing the concluding remarks.

This chapter is based on DPhil paper I, published as:

Ameli, V., et al. (2021). *'You just prefer to die early!': how socioecological context impedes treatment for people living with HIV in Iran.* BMJ Global Health.

2

DPhil Paper I: Qualitative Study

This chapter explores the socioecological context of living with HIV through lifelong antiretroviral therapy in Iran through its subjective and shared dimensions. This thesis is proposing an mHealth intervention for the specific context of engagement with HIV care and adherence to antiretroviral therapy in Iran. Though a valuable evidence base exists on the medical, behavioural, and psychosocial factors that are associated with sub-optimal adherence behaviour, these risk and protective factors are often explored in a decontextualised manner, thereby limiting explanatory and theoretical informativeness with regard to contexts that can be addressed by interventions. Here I apply a realist logic of analysis to qualitative data to understand how individuals react to their specific contexts via mechanisms that impede consistent engagement with HIV care and continued daily adherence to antiretroviral therapy.

2.0 Abstract

Despite the low-prevalence of HIV and broad provision of antiretroviral therapy, the Middle East and North Africa (MENA) remains the only region where new HIV infections and AIDS-related deaths are not declining. There is a dearth of evidence from MENA on antiretroviral therapy engagement. This qualitative study sought to identify the ways in which successful treatment is hindered in Iran. From September 2018 to January 2019, purposive sampling was used and twelve individual interviews and eight focus group discussions with 27 female and 31 male patients were conducted, in addition to five individual interviews with HIV care providers and one focus group discussion with eight care providers. Social constructivism augmented with realist-informed thematic analysis was used to understand *how* the socio-ecological context triggers cognitive and affective mechanisms that disrupt antiretroviral therapy. The use of Thematic Network Analysis resulted in the identification of three key cognitive and affective mechanisms that appear to shape treatment experience and are triggered via the socio-ecological context of HIV and changing economic conditions in Iran: denial in response to societal negative perceptions of HIV; fear in response to societal lack of awareness regarding HIV and misinformation; and despair in response to HIV-related stigma and enacted discrimination, economic insecurity, and social support. To my knowledge, this is the first study within MENA to identify pathways through which successful treatment is hindered. It appears that lack of societal awareness regarding HIV is specific to low prevalence settings, such as MENA countries, where negative perceptions, stigma, discrimination, and misinformation regarding HIV and its treatment produce denial, fear, and despair, acting as mechanisms that disrupt antiretroviral therapy. The experience of despair, in response to changing economic conditions and social support, further impacts treatment experience.

2.1 Introduction

The Middle East and North Africa (MENA) region is considered to be a 'black-hole' in terms of HIV/AIDS research (Abu-Raddad et al., 2010). Despite provision of antiretroviral therapy, new HIV infections continue to rise and AIDS-related deaths remain stagnantly high in most MENA countries, in contrast to the rest of the world (UNAIDS, 2021). Yet, there is a dearth of evidence from MENA countries on the lived experience of engaging with lifelong treatment (Alabaster, 2016; Dejong & Mortagy, 2013; Gökengin et al., 2016; Kamarulzaman, 2013). Of the few studies conducted within MENA, most focus on prevalence or biomedical aspects of the condition (Farrokhi et al., 2019; Moayed et al., 2019; Mohraz et al., 2018; Sadeghi et al., 2018), and studies of adherence focus on identifying key affected populations, such as people who use drugs and imprisoned individuals at risk of non-adherence (Khalili et al., 2012; Motazedian et al., 2018). Quantitative and biomedical studies promote understanding about the prevalence and risk profiles of non-adherence among key affected groups (Morowatisharifabad et al., n.d.; Seyed Alinaghi et al., 2016), and can increase knowledge on drug resistance profiles to antiretroviral therapy in different settings (Mohraz et al., 2018). Yet, qualitative studies are needed for identifying how and why engagement with and adherence to treatment decline, in addition to elucidating the pathways that lead from the socio-cultural, political, and economic contexts to individual reasonings and reactions that determine behaviour.

Studies from other regions provide evidence within the socio-ecological framework of multiple influences on lifelong antiretroviral use (Arrivillaga et al., 2011; E. M. Castro et al., 2015; Gourlay et al., 2013; Kaufman et al., 2014; Mukumbang et al., 2017; Yakob & Ncama, 2016). First, at a political level, health policies, incriminating laws, and public health priorities influence HIV risk behaviours (Berkman et al., 2005). Second, at a socio-structural level, poverty (Masanjala, 2007), HIV stigma (Katz et al., 2013; A. C. Tsai et al., 2013), violence victimisation (Cluver, Meinck, et al., 2018), and cultural norms, such as masculine stoicism (Skovdal et al., 2011), can act as barriers to consistent antiretroviral therapy. Third, at an institutional level, appropriate services, quality of care, competent staff, supportive health-workers, and sufficient resources contribute to engagement in care and adherence to treatment (Cluver, Pantelic, et al., 2018; Govindasamy et al., 2012). Fourth, at an interpersonal level, social support (Pecoraro et al., 2013), relationship intimacy, and personal satisfaction can

impact adherence behaviour (Rhodes & Cusick, 2000). Fifth, the aforementioned contextual levels, directly and indirectly, shape the situations in which individuals cope, experience emotions, use drugs, and engage with lifelong adherence (Bar-Lev, 2008; Friedland et al., 2010; J. C. Mills et al., 2019; Westergaard et al., 2013). Moreover, factors within a socio-ecological framework must be considered within the temporal junctures in which they meet; changes in political climate and policy directions could be a key contributor in shaping the coalescence of the influencing factors within individual lives.

This study was conducted using a social constructivist approach, augmented with a realist-informed analysis, to thematically investigate the pathways from the socio-ecological context to individual cognitive and affective mechanisms that impede treatment for people living with HIV in Tehran, Iran. The research question for this study was *how* individuals react to their context in ways that shape their adherence behaviours. The qualitative nature of the study allowed consideration of the impact of the time-period in which the study took place, including, for example, the increasing economic sanctions and inflation that exacerbated financial and psychological hardships. Augmenting the constructivist paradigm with a realist informed analysis enhanced the transferability of context-specific findings. Iran is the only country committed to UNAIDS Fast Track Targets in the MENA region (UNAIDS, 2020), and provides universal access to antiretroviral therapy, constituting a useful case-study for exploring the socio-ecological pathways that shape engagement with antiretroviral therapy.

2.2 Methods

2.2.1 Design and Setting

Qualitative methods are useful for situating behaviour within the wider social context and generating roadmaps for intervention design (C. Campbell & Cornish, 2010; Dalkin et al., 2015; Gupta et al., 2008; Seeley et al., 2012). This social constructivist qualitative study was augmented by realist-informed analytical thinking for a deeper understanding of *how* behaviours are produced via *context-specific* cognitive and affective *mechanisms* that cannot be measured quantitatively (Pope, 2000). Merging two research paradigms: social constructivism with realism, allowed the identification of cognitive and affective mechanisms as reactions to socio-ecological triggers that may be socially constructed, but remain rooted

in a shared reality, with transferable lessons to similar contexts (Bogna et al., 2020; Mir & Watson, 2001). Rather than seeking to generate standard characterisations of all members of a statistically representative sample, a social constructivist approach was used to answer the research question through an in-depth exploration of the diverse ways that antiretroviral users in this setting were responding to the socio-ecological context of living with HIV in Iran. A realist-informed thematic analysis was then applied to identify the mechanisms that appear to shape HIV treatment adherence and engagement within Iranian socioecological context. Thus, I was able to study *how* the understandings and actions of people living with HIV shape their engagement with and adherence to treatment, by exploring their collectively constructed representational realities, and their reactions to it, instead of surveying a list of individual and societal characteristics as de-contextualised properties of a closed social system. The identified mechanisms and context-specific findings of this study will inform a future mixed-methods trial and realist evaluation of an intervention to be empirically tested within this population. This study is part of an ongoing research project to understand and improve antiretroviral use of Iranians living with HIV. Recruitment for this study took place from September 2018 to January 2019.

The qualitative study draws on the perspectives of both recently diagnosed and more experienced active antiretroviral users, and their healthcare providers. The research method involved interviews and focus group discussions (FGDs), both of which allow researchers to explore areas of interest, albeit with important differences in terms of approach. For instance, individual interviews allow an in-depth exploration of personal and sensitive topics, while FGDs involve group interactions with the possibility to assess consensus and dissent within a trusted environment amongst peers (Denzin & Lincoln, 2011). The FGDs were conducted separately for men and women to explore any differences between genders in their reactions to contextual triggers and the impact on antiretroviral therapy engagement. The Positive Club, as the research place in which the interviews and FGDs took place (see Section 1.6.5), influenced the dynamics through which power relations, identities, and meanings unfolded.

The FGDs provided a sense of support and empowerment, through the ‘bounded space’ (Gagnon et al., 2015), which could be characterised as ‘micro-geographies’, through which social processes operated differently, representing how these processes are socially constructed and not fixed across locations within national or larger scale geographies (Elwood

& Martin, 2000). All (but two) of the FGDs took place within the Positive Club (see Figure 1.14), where a sense of 'peer support' was felt during the FGDs. A sense of peer support existed within the FGDs as feelings of community, safety, support, and empowerment enabled patients to share and intimately discuss their experience of living with HIV and engaging with antiretroviral therapy. The sense of 'peer support' was enhanced when the staff of the Positive Club, who were themselves members of the community of people living with HIV, welcomed the participants by highlighting their peer relationship. The FGDs themselves were then regarded as 'group classes'—an event *for the patients*, rather than one that was solely for the purpose of research. As such, the FGDs were very well-received and participants were open to sharing their experiences of living with HIV and engaging with antiretroviral therapy.

FGDs and interviews were recorded with the consent of participants, who chose their own nicknames to be used during the recording. Following transcription, the audio recorded files of participants' voices were deleted and no information with personal identifiers were stored or accessible.

Table 2.1 Participant Characteristics

Study Characteristics	Antiretroviral recipients	Healthcare Providers	Peer Supporters	Total
Research Participation Type				
Individual interview, no.	12	3	2	17
Women, no.	4	2	1	7
Men, no.	8	1	1	10
Focus group, total no. (no. of groups)	58 (8)	8 (1)	0	66
Women, no. (no. of groups)	27 (4)	4		31
Men, no. (no. of groups)	31 (4)	4		35
Total participants, no.	70	11	2	83
Mean age, y	38	58	41	
Women, no. (%)	31 (44%)	6		
Men, no. (%)	39 (55%)	5		

2.2.2 Sampling and Analysis

Purposive sampling was used to recruit participants with a range of experience in terms of adherence to antiretroviral therapy (Palinkas et al., 2015), based on information in clinic records of people living with HIV receiving antiretroviral therapy, using the following criteria: i) antiretroviral recipients diagnosed within the past year, ii) antiretroviral recipients diagnosed more than one year ago; iii) antiretroviral recipients who experienced disruptions in care and adherence, iv) antiretroviral recipients who had to change more than one treatment regimen due to drug resistance. For each of these criteria men and women were sampled separately from clinical records. Participants were phone-called by research staff, who were trained in informed consent process, and introduced to the research project. An overview of information included in the consent forms was provided with regards to the study purpose and design and details regarding the length, location, and general discussion points for the qualitative interviews. If interested, three dates were provided to choose for participation. A reminder phone-call was made one day prior to the scheduled date. On the day of the interview, participants were given informed consent sheets to read carefully before signing.

Twelve individual interviews and eight FGDs with a total of 27 female and 31 male patients were conducted. In addition, five individual interviews, with HIV care providers (two physicians, one counsellor, two peer supporters who were living with HIV), and one FGD, with a total of eight additional care providers (six physicians, one counsellor, one nurse), were conducted. Focus groups had an average of six participants, with the aim of creating a smaller and more intimate environment for conversations. Individual interviews averaged forty minutes and focus groups averaged 1.5 hours. Table 2.1 presents a summary of the characteristics of these participants.

Semi-structured topic guides focused on *what* the socio-ecological barriers and facilitators to antiretroviral therapy adherence are – and *how* and *why* they impact antiretroviral adherence and use. Interviews and FGDs were conducted by the lead researcher (VA), a native Persian-speaker, and audio-recorded with permission from the participants. These recordings were subsequently transcribed in Persian by VA and imported into MAXQDA, a qualitative analysis software package, for organizing and coding the text segments with descriptive headings. Two researchers (VA and LT) coded the data independently in Persian. The emerging codes were reviewed in intervals, after coding twenty

per cent of the transcripts, by discussing differences in coding to reach an agreement. Differences focused largely on different meanings being attributed to specific words rather than disagreements about the emerging themes, thereby requiring alignment of language more than the need to resolve disagreements about what the data meant. The agreed upon themes were then translated into English.

Thematic network analysis was employed to summarise the main themes within web-like networks that illustrated pathways from the specific socio-ecological context of living with HIV in Iran to individual cognitive and affective mechanisms that impact treatment uptake and adherence. Following the prescribed steps for thematic network analysis (Attride-Stirling, 2001), the transcribed texts were first coded with a basic code, informed by the socio-ecological framework of multi-level factors shaping antiretroviral therapy success; the basic codes were then clustered into higher order basic themes, identifying *how* the socio-ecological context produced specific cognitive and affective mechanisms of treatment uptake and adherence; the basic themes were then grouped by the identified contextual triggers into organising themes, which were then grouped by the cognitive and affective mechanisms into global themes. The outcome of this thematic network analysis is presented in Figure 2.1, highlighting the pathways that produce context-specific cognitive and affective mechanisms, via the main themes that address the research question and build the structure for the presentation of findings.

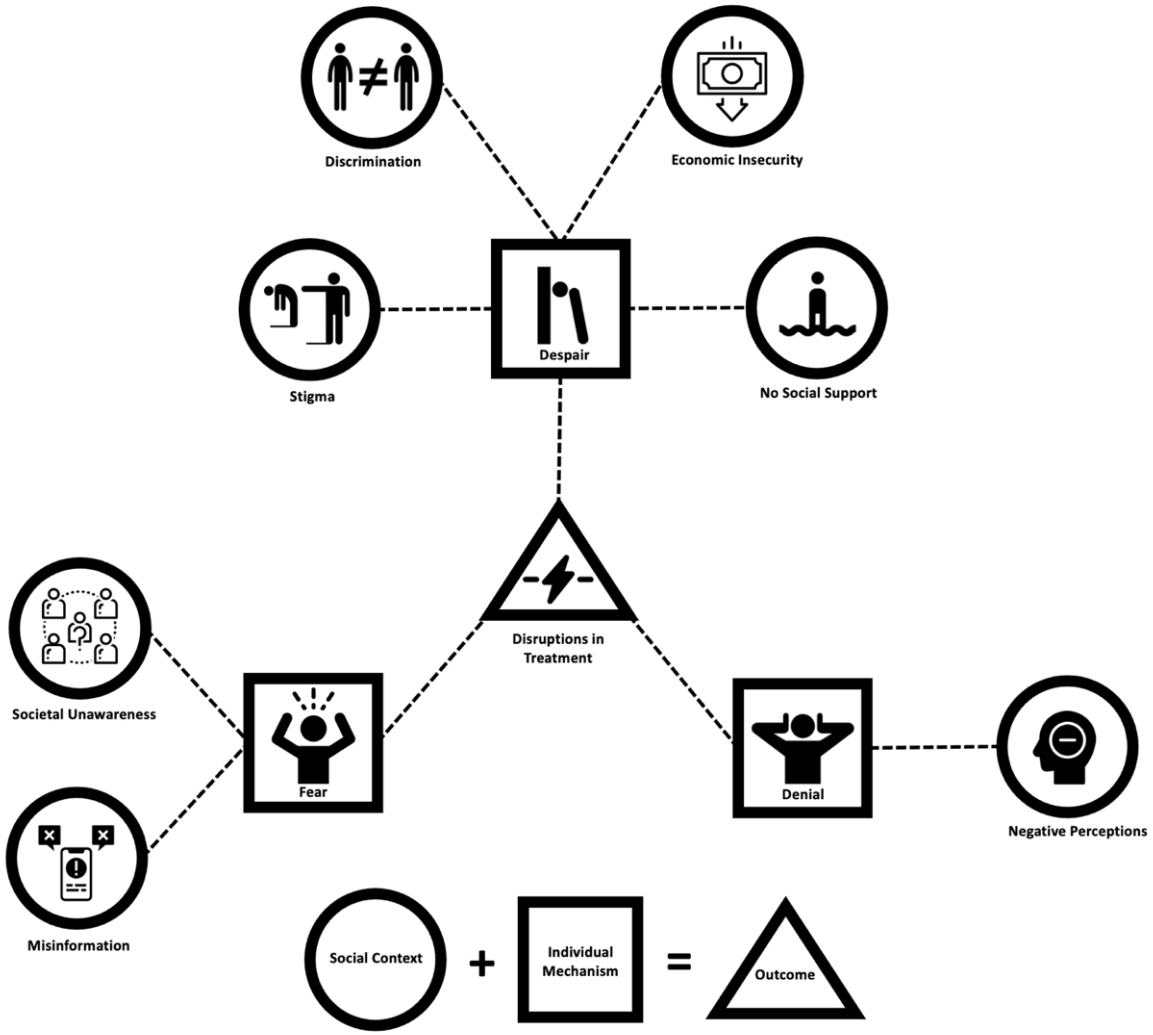

Figure 2.1 Socioecological Pathways of Treatment Disruption. Overview of results showing how socioecological contexts lead to individual reactions and reasonings that disrupt consistent antiretroviral therapy in Iran. This analysis is based on a realist-informed thematic network analysis. The socio-ecological contextual triggers represent the organising themes. The cognitive and affective mechanisms represent the global themes that disrupt antiretroviral therapy in Iran.

Table 2.2 Thematic Network Analysis of Basic, Organising, and Global Themes		
Global Themes *Mechanisms*	Organising Themes *Contextual triggers*	Basic Themes *How context triggers mechanisms*
Denial	Negative perceptions	Denial can be a coping mechanism to adjust to negative social perception of HIV. Staying in denial can delay treatment and encourage harmful drug use.
Fear	Lack of awareness	Fear appears to be caused by lack of societal awareness of HIV and antiretroviral therapy.
	Misinformation	Fear can be triggered as a result of misinformation.
Despair	Perceived stigma	Despair appears to be felt in response to perceived stigma against HIV status.
	Enacted discrimination	Newly diagnosed patients can experience stronger despair, which can cause depression. Despair can be an emotional response to acts of discrimination by the society. Discrimination by families and medical society can produce stronger despair.
	Economic insecurity	Despair can be an emotional response to economic insecurity.
	Social support	Despair appears to be felt when social support is lacking. Supportive family and services can moderate feelings of despair.

2.3 Results

The findings of this study identify cognitive and affective mechanisms that hinder adherence to antiretroviral therapy *situated within* the socio-ecological context of living with HIV in Iran, as opposed to decontextualised individual reasonings and reactions. The mechanisms specific to, and triggered within, the socioecological context of living with HIV in Iran appear to be: denial in response to societal negative perceptions of HIV; fear in response to societal lack of

awareness regarding HIV and misinformation, and despair in response to HIV-related stigma and enacted discrimination, economic insecurity, and lack of social support. Thematic pathways from socio-ecological contextual triggers to cognitive and affective mechanisms that disrupt antiretroviral therapy are depicted diagrammatically in Figure 2.1 and summarised in Table 2.2. The results section is presented in terms of the cognitive and affective mechanisms, within which are located further subsections based on socio-ecological contextual triggers. The mechanisms are presented in the order that they appear to be experienced as navigating through HIV care cascade after diagnosis: first experiencing denial and fear, followed by despair. For each cognitive and affective mechanism, a summary of gender differences is provided, as assessed by the extent to which each theme was emphasised among men versus women.

2.3.1 Denial as a Cognitive Mechanism

Denial was identified as a cognitive mechanism underpinning the rejection of the HIV diagnosis and need for treatment, motivated by the need to escape the negative societal perceptions regarding HIV. This mechanism was triggered in the initial stages of the HIV care cascade, exposing HIV diagnosed patients to an increased risk of harmful drug use due to the need to escape from the new reality of living with HIV. Denial appears to be the primary mechanism producing a lengthy gap between diagnosis and enrolment in care. As a coping mechanism, male interviewees commonly reported referring to denial and were more likely to use words such as *"not being in acceptance"* and *"being in denial"*.

I. Negative societal perceptions regarding HIV

A number of interviewees described the ways in which negative perceptions regarding HIV in the wider society triggered a state of denial following diagnosis. To avoid any association with the condition, some participants chose to not initiate or discontinue treatment.

The perception that people give is very negative. It's like it feels better to stay in denial even if you have it, to run away, but you don't realise that you are hurting yourself more. (Male patient – focus group 5)

The name of this disease is more negative than anything in our society. Because of it they blame you and embarrass you. It's not like cancer or anything else that you are the victim. (Male patient – interview 1)

Denial appeared to have hindered the decision to enrol in care in the first place, delaying the initiation of care until the point that CD4 levels were too low.

It took me exactly six years to come out of the denial stage. When I started treatment my CD4 count was 8, I couldn't walk, I couldn't breathe. I couldn't move. It's like you are in that denial stage in the beginning. Until you accept HIV, make other friends [who live with HIV], get treatment and get help. (Male patient – interview 7)

Using drugs, particularly trying new drugs and new routes of administration, were also described as a form of escape from the new reality of living with HIV, with significant long-term consequences for those who used more lethal types of drugs.

I had a friend who passed away. He went towards these new substances [methamphetamines] that are completely different from the traditional substances [opiates]. In one month, they [methamphetamines] do the harm of 10 years of [opiate] substance use. Before he exercised, he was in shape. But after his HIV diagnosis he just drowned himself in these substances [methamphetamine] and was soon gone. (Male patient – focus group 1)

2.3.2 Fear as an Affective Mechanism

Fear was identified as an affective mechanism in response to HIV treatment being perceived as daunting, and thereby avoided. As incorrect information is propagated through society, fear can spread easily among people living with HIV. More women, than men, cited fear as a mechanism of avoiding treatment.

I. *Lack of societal awareness regarding HIV*

Participants talked about a general lack of awareness of HIV in Iranian society due in part to the fact that HIV-related topics are not widely discussed in the society, thereby many people have never heard about HIV, still think of it as a death sentence, and lack knowledge with regards to the availability of treatment. The interviews indicated that existing knowledge

about HIV tended to be superficial, and that the condition itself was perceived to be stigmatising, leading to fear and a disinclination to seek treatment.

When I found out I have HIV I was shocked and afraid. I never even thought that in Iran anyone has HIV. I thought it only happens in other countries or to people who act transgressively. (Female patient – interview 4)

People are not even aware that now you can get treated and view [HIV] with fear. They don't see a difference between HIV and AIDS. You will be labelled [pejoratively] as 'AIDS-y'. This makes it scary to show up to appointments. You just prefer to stay away. (Male patient – interview 10)

II. *Misinformation*

Participants indicated that a range of issues related to medications could trigger fear and mistrust of antiretroviral therapy. Some described fear of long-term therapy affecting their ability to adapt to daily medication schedules.

I was really scared of these drugs [antiretrovirals]. I wasn't sure how sure I could be about how safe and useful they are. (Female – interview 5)

I really don't like medicines in general, so the thought that I have to take 60 pills every month was scary to me and it took me a long time to get used to this. (Female patient – focus group 8)

A peer counsellor recounted misinformation, false beliefs, and conspiracy theories, being disseminated amongst patients through waiting rooms and online chatrooms.

Some patients don't even believe in chemical medications. From the beginning, they go towards traditional medicine and say why should we take these drugs. They think they've been 'turned into lab mice'. This is their perspective. They also find scary information online and share with others in waiting rooms and chat groups. (Female peer counsellor – interview 1)

Concerns regarding treatment side-effects often appeared to be shared in ways that could lead to misinformation and trigger fear of treatment initiation in new patients.

When they speak about the side-effects of medications, they create such fear that new patients sometimes delay beginning treatment, or they won't start until they have become very

ill. Sometimes patients start to imagine they are experiencing side effects, for example saying that 'the drugs do not descend from their throat into their stomach'. (Female peer counsellor – interview 1)

2.3.3 Despair as an Affective Mechanism

Despair was identified as an affective mechanism that led to treatment adherence being perceived as meaningless and, subsequently, deprioritised. The societal context of HIV-related stigma, enacted discrimination against HIV status, and economic insecurity appeared to be the key contextual triggers for despair, sometimes causing depression. However, social support appeared to mitigate some of the despair that resulted from contextual adversities, while lack of support engendered more despair. Despair, as an underpinning motivator of disengagement from treatment was commonly referred to by female interviewees, especially in the context of family problems. Some women intentionally stopped adherence when they felt uncared for and depressed. Female respondents were more likely to use words such as *"wanting to give up on life"* and *"preferring to die early"*.

I. *HIV-related perceived stigma*

Participants described how from the onset of HIV diagnosis, the experience of HIV-related stigma and the feeling of being rejected by society, created a sense of despair, and in some cases depression, weakening the motivation to continue adherence with treatment.

This adherence to treatment requires motivation, hope. But a big problem that we have stems from the stigma [of HIV]. Sometimes the pressures from stigma and the attitude of the society are so strong that you just lose hope and want to disengage from the whole process of treatment. And it has happened to many of us. (Female patient – interview 2)

Indeed, the interview data suggests that stigma widely disrupts the social conditions in which people living with HIV interact with society and form relationships.

Stigma in this society is what makes everything in life more difficult for us, from medical treatment to the possibility of marriage. (Male patient – focus group 5)

The first year following diagnosis appeared to be the most sensitive period, in which the shock of being diagnosed with HIV combined with the experience of stigma contributed to the erosion of hope. Some participants appeared to have internalised the stigma in the early days, leading to isolation and depression, further diminishing adherence.

Unfortunately, in our society we have to live with this stigma, and in the beginning, you also believe this stigma yourself, so you are more depressed and live a hopeless life. (Female patient – focus group 4)

The early days were terrible. You know about stigma, but you do not expect to feel so much emotional pain because of it. You just retreat within yourself and this impacts your ability to function, let alone taking your treatment seriously. (Female patient – focus group 2)

II. *Enacted discrimination against HIV status*

Acts of discrimination against HIV were described to be present in all segments of the society and identified as a key trigger for despair.

When people discriminate against us [patients living with HIV] it's like the higher the education levels, the lower the 'sho'oor' (social intelligence), so you really lose hope. (Female – focus group 4)

My only problem is feeling depressed because people in the society do not accept us, they don't accept HIV, so I get hurt. (Female – focus group 2)

Many participants described being disowned by their families and whole communities when they discovered that they were living with HIV. Rejection by families appears to have forced some participants into homelessness, migration, and situations of severe adversity that hinder treatment adherence. This experience appeared to be more common among ethnic minorities and less common in Tehran.

When I found out I didn't tell anyone, but my brother found out, collected all my clothes, and threw me out of the house. A few weeks ago, I went for my uncle's funeral. The whole family asked my brother why he made me homeless. He easily said to my parents that I have HIV, and they all disowned me. (Male – Interview 3)

I was thrown out of the house and had to leave my community when they found out I am HIV positive. I ran away and came to Tehran and for 5 years I was sleeping in the streets,

under the bridges of this city. These things are more common among us [ethnic minorities]. (Male Patient – Focus group 1)

Interviewees also described acts of discrimination by medical practitioners, outside the circle of HIV experts. Nurses, dentists, and general practitioners were described as having a discriminatory attitude and as refusing medical and dental care to people living with HIV. This experience was described as intensifying despair, depression, and withdrawal from care.

When I go to the doctor unrelated to HIV, and they realise that I have HIV, their attitude changes. I have a glass of water and the doctor says to put the glass in the bin outside his office, or to not use the toilette in his office. Of course, this intensifies my depression. (Female patient – focus group 8)

In many cases the refusal to provide treatment to a patient occurred within the context of a breach of confidentiality within the hospital wards or clinics where they were receiving care that was unrelated to HIV.

I found out I have HIV when I was getting chemotherapy and was in my third session. The doctor told me to get tested for HIV and when I went back and told them I am positive they treated me with unbelievable avoidance. The nurses didn't even want to change my IV. They talked behind my back and told everyone in the ward that I have HIV. I just didn't go for my fourth session of chemotherapy. (Male patient – focus group 7)

An absence of dental care was described as impacting antiretroviral adherence in older patients who had not received necessary dental care and for whom food intake was compromised as a result, leading to nutritional problems that affected antiretroviral adherence.

So many dentists refused care to me, so I lose hope in them [dentists] and stop going for visits. For medication adherence, nutrition is most important, especially for older people like me. I now need to remove two of my teeth, but I can't go. (Female patient – focus group 6)

III. *Economic insecurity*

Financial insecurities are not a direct barrier to accessing treatment, given the provision of free and universal antiretroviral therapy in Iran. However, economic insecurity, caused by sanctions and inflation, appeared to have had a strong impact on the ability of people living with HIV to manage more generally, leading to feelings of despair, and in some cases suicidal

thoughts. One participant described not wanting to continue with life as a result of constant price increases.

Constant price increases bring you down [emotionally], so then you have no motivation to look after yourself. Adherence to treatment in reality is looking after yourself. (Female patient – focus group 8)

This year I just can't take the prices anymore. I've been thinking about giving up on this life. I just can't stop crying. It's getting harder every day and I can't continue this life anymore. (Female patient – focus group 8)

Sometimes the cost of living is so high that you feel like you are breaking under this life, everything becomes a challenge from waking up in the morning to taking your medications. (Male patient – Interview 6)

Participants noted that they would have stopped antiretroviral therapy if it were not free, but nutritional supplements prescribed by physicians were described as becoming increasingly unaffordable.

If they didn't give us the medicines for free, I would definitely not take [antiretroviral therapy]. Because for example right now doctor told me to take vitamin E and to take iron because I have 'Kist' (Cystitis). I try to buy it but sometimes when I don't have enough money I don't buy. Because right now all the prices have gone up. (Female patient interview 3)

One doctor described that economic hardship drives people to profit in the black-market by selling their medication on the streets as pre-exposure prophylaxis (PrEP).

We don't offer universal PrEP, so some patients who are in need go and sell their own medications as PrEP to others in the black market, so they end up not adhering properly. (Doctor – focus group with healthcare providers)

IV. *Social support*

The data also suggests that the existence or lack of social support can moderate despair. Participants described how the lack of family and social support made them feel 'uncared for' and was another trigger for despair and stopping treatment.

I don't have any support. In my family there is no one to help and support me to take my medicine. I have health problems and was in the emergency room, but it wasn't even important to them. I considered stopping the medicines all together. (Female patient – interview 11)

Feeling beset by family problems unrelated to HIV, led to one participant stopping treatment because she could no longer see the value in life.

For me what causes me to not take my medicine is problems in life. I have problems with my husband, I stop taking my medicine. I face problems with my family, my father and my mother, I can't take it at points, so I really lose hope in life, and I leave my medicine aside. It's like everything loses its importance for me. Living life loses its value. (Female patient – focus group 2)

The presence of social support was also perceived to be helpful in enabling some participants to cope better with adherence.

I am very lucky because my family is very supportive. They help me a lot and even called our relatives who live in America to get information for me from the Mayo Clinic [in the USA] and make sure I am getting the right care and that has been very reassuring for me. (Female patient – focus group 2)

The importance of having access to empowering classes, peer support clubs, harm reduction opportunities to quit drug use, and online support groups was highlighted by many participants. Interviewees who had taken advantage of such opportunities referred to developing a sense of self-love and an awareness of the need to take care of themselves, which they felt had protected against self-harm and non-adherence:

They teach us the antiretroviral therapy of life here. We used to even play music here, and these helped me come out of my depression. With time and counselling I realised that I am doing this [being on treatment] for myself. I have to love myself first, otherwise who will. (Male patient – interview 9)

I joined the Positive Club [Peer Support Club], they taught us a lot here. I started methadone, helped me get clean and come out of darkness and instead take care of myself. The classes taught us life-skills. I ended up even finding a job and going back into the society. (Male patient – focus group 5)

We help each other online, for example if a person runs out of medicine, we send it to them until they can go and get their pills. Our telegram groups have been helpful for us to look after each other. (Male patient – focus group 1)

Participants especially enjoyed the interaction with *'positives'* (a positive Persian term for living with HIV), and caring healthcare staff.

When I discovered the positive-club, I realised that I am not alone, and talking to other positives really gave me motivation to take care of myself. (Male patient – interview 1)

The staff here are really exceptional. Every one of them are very dear to me. Just knowing that they care gives us hope. It also helps that some of them are positives themselves and we share this pain together. (Female patient – focus group 2)

2.4 Discussion

This study aimed to identify pathways through which the socio-ecological context of living with HIV in Tehran, Iran, leads to cognitive and affective mechanisms that shape engagement with antiretroviral therapy. Previous studies from MENA, most of which from Iran, are largely comprised of quantitative surveys, producing lists of risk and protective factors for treatment adherence (Farrokhi et al., 2019; Khalili et al., 2012; Moayed et al., 2019; Mohraz et al., 2018; Morowatisharifabad et al., n.d.; Motazedian et al., 2018; Sadeghi et al., 2018; Seyed Alinaghi et al., 2016). The findings of this study suggest that the three key affective and cognitive mechanisms of denial, fear, and despair undermine successful and lifelong treatment. The realist-informed analysis details the ways in which denial and fear are triggered through a context of negative societal perceptions, lack of awareness regarding HIV, and widespread misinformation. While despair is described as occurring in response to experiencing HIV-related stigma, acts of discrimination, and living through economic insecurity, it is perceived to be moderated by social support. Importantly, a temporal effect was detected showing the impact of Iran's rapidly changing economic climate on the experience of despair and its influence on lifelong treatment.

Denial appears to be a cognitive mechanism that drives many away from treatment in an attempt to escape the negative societal perceptions regarding HIV, especially in the early

stages following diagnosis. Recognised as the first of five stages of grief, denial was similarly identified to be a coping mechanism following HIV diagnosis (Zeligman & Wood, 2017). However, participants in this study retrospectively reported unusually lengthy periods of being in denial and delaying treatment initiation, sometimes until they experienced AIDS-related illnesses and low CD4 counts, despite the availability of treatment at the time of diagnosis. While in denial, some participants began to experiment with new classes of drugs (e.g. Methamphetamines) or new routes of drug administration (e.g. increased injection), ultimately risking losing their life to harmful drug use.

More men than women described reacting through denial and avoidance, while more women described feelings of despair and depression. The former appears to act more as a barrier to enrolment and the latter to adherence. This potential difference between genders could be rooted in previously documented hegemonic notions of masculinity (Connell, 2005; Courtenay, 2000), whereby men view HIV as a threat to their manhood and dignity and are wary of any association with HIV (Skovdal et al., 2011). In the process of denying the diagnosis, they refuse treatment and may also prevent women and other members of their household from accessing treatment services (Skovdal et al., 2011). It was not within the scope of this study to explore how gender norms are defined within the Iranian context, or whether hegemonic notions of masculinity apply in the same way as findings from Zimbabwe in relation to HIV. I am highly cognisant of not commenting on gender roles in stereotypical orientalising ways (Said, 1978). Iranian society is undergoing highly rapid, dynamic, and complex changes with regards to gender norms and roles (Ferdows, 1983; Shahrokni, 2020). The past forty years has expanded access to higher education, especially for women, who now make up more than half of university students, and more than sixty per cent of science and technology students (Dobbs et al., 2016; Harris, 2017). Female participation in the workforce is rapidly increasing as influenced by an expanding service industry and by economic necessities of single-income households (Shahrokni, 2021), providing women more freedom and agency. Future research can further explore if and how the changing gender norms impact the success of antiretroviral therapy in Iran and the larger MENA region.

Fear also appears to be an affective mechanism that can hinder treatment. Lifelong adherence has been more easily achieved in contexts where there is an acceptance of HIV status (C. Campbell et al., 2011), allowing patients to fit medication schedules into their lives

without the impact of fear and stigma (Dahab et al., 2008). The findings of this study suggest that in contexts where HIV has a low prevalence and high stigma, such as the MENA region, lack of societal awareness regarding HIV and misinformation regarding treatment are key contributors to fear of antiretroviral therapy. While concerns about side effects and medical anxiety are valid and that they must be addressed, study participants reported having postponed treatment initiation due to the fear associated with attending appointments or resulting from intimidating information they received regarding antiretroviral therapy. This finding corroborates previous evidence suggesting that in low HIV-prevalence settings, where the wider society still lacks awareness and knowledge about the HIV epidemic, not only does the struggle for recognition still continue (Dejong & Mortagy, 2013), but daily adherence and lifelong engagement with treatment are sought in the face of much more powerful experiences of societal negative perceptions and incorrect knowledge regarding HIV (Genberg et al., 2009).

Despair was reported to be a key affective state in which people living with HIV reduce or intentionally stop adherence to treatment. Participants lose hope and the motivation for adherence when HIV-related stigma, enacted discrimination against HIV status, and economic insecurity seem overwhelming. The experience of HIV-related stigma and discrimination has been associated with reducing treatment success in previous studies (Katz et al., 2013; A. C. Tsai et al., 2013). Here, I have identified despair as a key construct within the pathway from the social context of stigma and discrimination to treatment engagement and lifelong adherence. This finding adds to a more recent body of evidence, highlighting despair as a new driver of morbidity and mortality (Shanahan et al., 2019).

Importantly, despair appears to manifest when economic stagnation dominates the lives of individuals (Case & Deaton, 2015, 2020). The phenomenon of ‘deaths of despair’ was first identified in the United States, suggesting that social and economic immobility produce morbidity and mortality through despair, demanding public health attention (Case & Deaton, 2015, 2020). Following the 2018 re-imposition of sanctions on Iran, the Iranian Rial lost half of its value during this study’s data collection period, with continued devaluation and steep inflation rates to the present time. Many participants expressed loss of hope and suicidal thoughts in response to the continuously increasing economic pressures they felt and their decreasing ability to manage financially. This finding suggests new causes of morbidity and mortality linked to despair that is driven in a climate of economic insecurity, sanctions, and

inflation. It appears that for Iranians living with HIV, despair caused by economic insecurity can undermine motivation for adherence, drive intentional disengagement with care, and lead to suicidal thoughts. While global health studies often ignore the health impacts of different economic realities, the findings of the current study, suggests the need for further investigation into despair-driven adverse health events within the context of such realities, particularly for vulnerable groups such as people living with HIV.

Moreover, this study sheds light on the importance of people's behaviours and responses within the context of their lives as lived through time (Beckmann, 2012). For instance, in Iran, the drive to harmful drug use must be understood within a context in which people lose hope, or rather stay in denial, in the face of HIV-related stigma, discrimination, and misinformation, sometimes resulting from low awareness at a societal level. The HIV epidemic is highly dynamic in terms of transmission routes, the populations affected, and the resources available at any given social and economic time-point. Drug use patterns in Iran have changed substantially over time, from an older generation that smoked opium to a younger generation that injects heroin, and a recent increase in methamphetamine use across all ages and socio-economic groups (Ghiabi, 2019). These transitions have been linked to drastic political and economic changes, from the aftermath of an eight-year war to over three decades of sanctions, inflation, un(der)-employment, with chronic mental health consequences (Behrouzan, 2016), thereby revealing the impact of temporal junctures in which politics and economics can have a significant direct and indirect impact on health outcomes.

The findings of this study also show that in the face of adversities linked to living with HIV, social support plays a key role in enhancing or reducing hope. Perceived lack of support, especially in terms of unsupportive family members, appears to fuel despair and disrupt adherence, with some participants reporting intentionally stopping daily adherence or disengaging from treatment as a result of not feeling cared for. In contrast, competent healthcare providers and peers can make a positive impact on helping people living with HIV overcome difficulties in making sense of their experiences and negotiating support. Many antiretroviral users indicated the rewarding and positive relationships with healthcare staff and peer supporters that were viewed as enabling them to gain optimal benefits from the healthcare system. Access to caring support appears to dilute the experiences of stigma and discrimination from the wider society. Participants especially enjoyed the interaction with

peers living with HIV, through which a feeling of 'us' – the *'positives'* in Persian – and the uninformed and hostile 'others' enables an empowering distinction. Online and offline support networks in which patients give and receive supportive information appear to be particularly valued.

The findings from this study have informed an intervention for improving engagement with and adherence to antiretroviral therapy for people living with HIV in Iran. Rather than simply orienting the intervention to the outcome of improving adherence, the findings here are used to develop a personalised mobile health intervention that is oriented to Iran's particular socio-ecological context, tailored to individual cognitive and affective states, and attuned to the socio-political and economic climate of the time (Beckmann, 2012). While public awareness campaigns are chiefly needed to change the attitude of Iranian society towards HIV, personalised mobile health strategies will help people living with HIV to benefit more widely from available care and mitigate the experiences of 'deadly stigma' (Alabaster, 2016).

2.4.1 Strengths and Limitations

This qualitative study provided participants with an opportunity to discuss *their* perceptions of Iran's HIV context and define *their* responses to that context, thereby giving voice to a population living within the hidden context of the HIV epidemic in Iran. This enabled me to capture the nuances of experience in terms of living with HIV within this particular socio-ecological context and thereby to identify the cognitive and affective states that can shape antiretroviral use. Moreover, the coding and analysis was conducted in Persian by two independent researchers, who are native speakers of the language. This approach ensured that the essence of language, used by participants, was not lost within the analysis of the emerging themes. Participation in this study was voluntary with recruitment from an HIV/AIDS clinic, and the sample may have been biased toward more motivated patients, who were able to overcome and report retrospectively on multiple barriers to lifelong treatment, including (but not limited to) stigma, transportation costs, and opportunity costs. However, in accordance with principles of social constructivist research (Flyvbjerg, 2001), rather than seeking to generate characterizations of all members of a statistically representative sample, an in-depth

exploration of a small sample was undertaken to identify the diverse ways that the lived experience of people living with HIV influences their reasoning and reactions in terms of their relationship with antiretroviral therapy.

Importantly, this study began with a social constructive approach in the data collection stage and shifted to a realist approach in the data analysis stage. Using this combined approach introduced strengths and limitations. First, the depth of findings was enhanced by collecting data through a social constructivist approach, where interviews were conducted openly. As opposed to starting from a realist approach, where pre-identified theories or hypotheses are tested and refined, the social constructivist approach enabled me to understand participants' subjective experience of engaging with antiretroviral therapy, without imposing previous assumptions and hypotheses in the interview process. Second, using a realist-informed data analysis, through which realist concepts such as 'mechanisms' were used, produced findings that can be transferable to similar contexts, using the realist ontological lens (J. Greenhalgh & Manzano, 2021). However, a limitation is that the findings cannot be interpreted in 'full' constructivist or realist terms and the configurations are limited in nuance and refinement.

2.5 Conclusion

The findings of this study suggest that engagement with and adherence to antiretroviral therapy are disrupted when people living with HIV respond to Iran's socio-ecological context through the cognitive and affective states of denial, fear, and despair. Therefore, in addition to the availability of free antiretroviral therapy, more awareness about HIV is needed to prevent the rejection of treatment caused by denial and fear, and to provide hope and motivation for lifelong engagement with antiretroviral therapy. The low prevalence of HIV in Iran has stymied societal awareness and knowledge regarding HIV and antiretroviral therapy. Moreover, the profound experiences of despair, in response to harsh economic conditions, jeopardise hope and motivation for continued adherence to daily treatment. These findings support recent calls for the study of global health to not be decoupled from that of international power politics (Benatar, 2016), and emphasises the importance of understanding the nuances of experience that impact health decisions within the social, economic, and structural contexts of living with HIV (C. Campbell & Cornish, 2010; A. Castro & Farmer, 2005; G. R. Gupta et al., 2008).

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3

DPhil Paper II: Qualitative Study

This chapter considers the mobile health (mHealth) affordances and provisions that can interact with the contexts of HIV care into which mHealth is introduced. This thesis has focused on employing mHealth approaches to enhance the contexts in which people living with HIV in Iran engage with antiretroviral therapy. To introduce a feature as simple as mobile messaging into the lives of people experiencing a long-term condition, such as HIV, there needs to be a conceptual alignment between the messaging provisions and the contexts into which these provisions are added and may influence. This chapter builds on the treatment disrupting socioecological pathways that were identified in the previous chapter to conceptualise how mHealth affordances can reduce disengagement from care. By applying a realist logic of analysis, the socially constructed views of people living with HIV and their providers are used to conceptualise how mHealth, when using mobile messaging, might influence the contexts of engaging with HIV care in Iran.

3.0 Abstract

Mobile health (mHealth) interventions are increasingly used to address the challenges of living with HIV and engaging with antiretroviral therapy. A wealth of evidence supports the efficacy of mHealth in supporting living with HIV. Yet, there is a dearth of evidence on how mHealth improves outcomes, which features are effective, and why these work in a particular setting. This study uses stakeholder views, including patients, providers, peer supporters, counsellors, and programme directors, to conceptualise how specific mHealth features could interact with contexts of living with HIV and mechanisms that shape engagement with treatment. The study is part of an ongoing research project on engagement with HIV care in Iran. I draw on the perspectives of recently diagnosed and more treatment experienced patients and their providers, using purposive sampling, conducting 9 focus group discussions with a total of 66 participants, in addition to 17 interviews. The findings suggest that mHealth designs that feature provider connection, proactive care, privacy and personalisation are expected to dilute the harsh contexts of living with HIV. I build on previously identified socioecological pathways that disrupt antiretroviral therapy in Iran and find that mHealth can enhance the relation between the health-system and patients. These findings suggest that personalised mHealth features and provisions can partially mitigate the compounded impacts of harsh socioecological pathways that impede treatment success in Iran. This social constructivist study was augmented with realist-informed analysis and could have transferability to similar contexts that trigger similar mechanisms of treatment disruption.

3.1 Introduction

The World Health Organization (WHO) has endorsed the use of mobile phones for supporting people living with HIV through tailored and differentiated models of care delivery (WHO, 2016), highlighting the potential of mobile health (mHealth) for health system strengthening (WHO, 2019). In recent years, mobile messaging has been the key mHealth feature used in interventions to deliver a combination of reminders, support, and information to improve treatment linkage, retention, and adherence (Haberer et al., 2017; Sabin et al., 2018; Ware et al., 2016). A range of different designs and provisions can be offered. For instance, reminders

can be scheduled (e.g. weekly, daily, or according to appointment and/or dosing schedule) (Christopoulos et al., 2014; Mbuagbaw, Mursleen, Lytvyn, Smieja, Dolovich, & Thabane, 2015; Sidney et al., 2012), or triggered (e.g. by missed appointment and/or doses captured through electronic drug monitoring) (Haberer et al., 2016; Sabin et al., 2015); information can be passively received (e.g. according to a pre-defined health promotion strategy) (Glasner-Edwards et al., 2016; Haberer et al., 2017), or proactively requested (e.g. according to individual patient questions) (Chiang et al., 2018; Van der Kop et al., 2012); support can be provided via human resources (e.g. peers, clinicians, and counsellors) (Amankwaa et al., 2018; Bassett et al., 2016; Lester et al., 2010), or leveraged via technological resources (e.g. automated systems and digital applications) (Nittas et al., 2020; Sabin et al., 2010; Westergaard et al., 2017). Perhaps most importantly, patients can be either passive recipients or active partakers depending on the use of one- or two-way messaging, respectively. The appeal of mobile messaging programmes is that they are affordable, easy to use, offered through a variety of platforms (such as basic SMS, WhatsApp, iMessage, and other applications), and can provide a personalised array of support components (J. I. Campbell & Haberer, 2015). Importantly, any combination of components must be carefully chosen to match the context into which an intervention is being implemented.

The simplicity, flexibility, and adaptability of mobile messaging provide a powerfully dynamic programmatic tool that can address multiple barriers to treatment; however, this flexibility adds a layer of complexity to the standardization of mobile messaging intervention designs. Moreover, just as with most technological interventions, mobile messaging programmes can recursively change (and be changed by) the very social setting and relations into which they are introduced (Abimbola et al., 2019; Greenhalgh et al., 2021; Pawson et al., 2005). Dynamic interactions, material exchanges, and nascent connections enabled by mobile messaging between patients and providers can change the relational contexts in which people living with HIV engage with treatment. Nevertheless, these changes remain understudied within the larger body of experimental mHealth research that are predominantly underpinned by technological determinism, which assumes technology X will have impact Y that is measurable (Greenhalgh et al., 2011; Greenhalgh & Swinglehurst, 2011). This research orientation and its deterministic suppositions largely produce studies that evaluate the impact of mobile messaging on a set of pre-defined outcomes. As a result, a wealth of evidence

supports the efficacy of mobile messaging in improving adherence to antiretroviral therapy, but a dearth of evidence can demonstrate how mobile messaging changes the contexts of treatment delivery, and why it is suited to a particular context of living with HIV. Randomised controlled trials can evaluate the efficacy of programmes, but real-world effectiveness of complex interventions needs to also consider the interactive contextual effects.

To evaluate complex interventions, Pawson and Tilley (1997) proposed the scientific realist method, arguing that researchers must look for social mechanisms at the level of human reasoning and reactions (Pawson & Tilley, 1997), building on the key concept of *generative mechanisms* set forth by Bhaskar in *A Realist Theory of Science* (Bhaskar, 1978). In realist research and evaluation, interventions are not conceptualised as causing outcomes *themselves*, rather people's reactions to what interventions offer can cause outcomes (Dalkin et al., 2015). For instance, an mHealth programme may provide useful information and a new connection that makes people *feel cared for*, so that they better engage with their treatment and care. Their subjective reasoning, followed by a decision to act or not, will depend on the context. As such, an mHealth programme is designed to change the context in such a way to induce the desired mechanism(s) and in turn generate the intended outcome(s). Such data is best collected qualitatively to enable researchers to engage with the reasoning of participants (which is interpretive and socially constructed). Using this approach, this study was conducted to conceptualise how an mHealth programme can change the contexts of living with HIV in Iran.

3.2 Methods

3.2.1 Design and Setting

The study is part of a three-staged, ongoing research project to understand and improve use of antiretroviral therapy by Iranians living with HIV. In *the first stage*, I investigated the socioecological contexts of living with HIV in Iran and the mechanisms that disrupt engagement with treatment . The current study comprises *the second stage* of the larger project and aims to conceptualise *how* an mHealth approach may be used to change the contexts of engagement with antiretroviral therapy in Iran, and to optimise an mHealth design that suits these contexts, based on stakeholder views. In *the final stage* of the larger research project, I hope to evaluate the effectiveness of the mHealth intervention that is conceptualised here in

terms of reducing disruptions to treatment as part of a randomised controlled pilot and a nested realist evaluation.

A social constructivist approach was used to explore subjective participant reasonings and inform the design of an evidence-based mHealth intervention for the contexts of living with HIV in Iran. The social constructivist approach aimed to answer the research question through an in-depth exploration of the subjective ways stakeholders in this setting interpreted the role of a mobile connection in changing the contexts of HIV treatment and relational aspects to care. A realist-informed analytical framework was then used to help hypothesise how the intervention design might change the contexts of HIV care and treatment in Iran (presented in the previous chapter, Figure 2.1). Within the realist research paradigm, mechanisms and contexts interact to produce outcomes, and the relationship is expressed as: Context + Mechanism → Outcome (Pawson, 2013; Pawson & Tilley, 1997). Thus, when introducing interventions, it is important to recognise which aspects of a context are changed by the intervention, and how that change, in turn, alters mechanisms and resulting outcomes. By combining a social constructivist data collection phase with a realist-informed data analysis phase, the findings on the shared realities produced here are accessed via the socially constructed understandings and interpretations of interviewed stakeholders, while the realist-informed lens provided additional concepts (i.e. context and mechanisms) to further unpack the empirical data to produce an understanding of when and how possible mHealth design features may be useful.

The research questions for the current study were: i) what are user preferences with regards to features of an mHealth intervention that uses mobile messaging? And ii) how might these features of an mHealth intervention impact antiretroviral use within the contexts of living with HIV in Iran? I draw on the perspectives of both recently diagnosed and more experienced antiretroviral users, their care providers, counsellors, peer supporters, and programme directors to explore their preferences and views regarding how a mobile connection can address some of the psychosocial and ecological factors (such as those depicted in the previous chapter, Figure 2.1) that disrupt antiretroviral use in Iran.

3.2.3 Data Analysis

The overall recruitment strategy, sampling, coding, and analysis are reported in the previous chapter (section 2.2.2). For the purposes of this study, the developed themes on key mHealth features, to be used in the delivered intervention, were discussed between the local research directors, research assistant, a peer supporter, a person living with HIV, and a psychosocial support provider. These themes were translated into English and informed the mHealth intervention that was developed for the context of Iran, named HamRaah (in Persian meaning together-in-path), the pilot trial, and the nested realist intervention, which were conducted in collaboration with international research directors. The protocol for this trial and intervention is published elsewhere (reference withheld to maintain anonymity).

Thematic network analysis was used to summarise the main themes that were developed from user preferences on mHealth design features and their views on how these features *could* have an effect in the contexts of engagement with antiretroviral therapy in Iran. Following the prescribed steps for thematic network analysis (Attride-Stirling, 2001), the transcribed texts were first coded with a basic code and then clustered into higher order themes. The basic themes identify the useful mHealth provisions and relational changes to care (such as informational, support, motivational, patient initiative and agency) as basic themes. The basic themes were then grouped into organising themes by the identified design features (provider connection, proactive care, privacy and personalisation) that comprise the sub-sections of the results section. Once the thematic analysis was completed, a realist-informed analysis of the themes was conducted. The purpose of the additional analysis was to explore whether using the realist concept of context-mechanism-outcome configurations might help conceptualise how the mHealth intervention features might contribute to the contexts of living with HIV in Iran. These results were used to inform a mobile messaging intervention (named HamRaah, meaning 'together-in-path' in Persian) that is suited for the Iranian context, the protocol for which is presented in chapter 4.

3.3 Results

The findings of this study suggest that mHealth interventions can change the relationship of people living with HIV with the health system in terms of information, support, motivation, and options to take the initiative for engaging with treatment, via three overarching design features of: i) provider connection, ii) proactive care, and iii) privacy and personalization (presented in Figure 3.1). This section presents the three proposed mHealth design features and how these produce their effects. A modified conceptual pathway is then presented that conceptualises how these design features of the intervention can influence the previously identified socioecological contexts of living with HIV in Iran.

3.3.1 Provider Connection

The ability to communicate with providers more readily through mobile messaging was identified by participants as an essential design element of mHealth that was perceived to be useful, rather than cumbersome, in the contexts of living with HIV in Iran. Emphasis was placed on the ability to directly message a provider who can offer reliable information and support. Some participants suggested that such support can counteract feelings of despair and dilute the harsh realities of living with HIV in Iran:

The benefit of texting with a provider is that you can be connected to someone who can give you useful support and maybe a backing when you are faced with the harshness coming from society and the difficulties of everyday life with HIV. The utility of mobile messaging can be a connection to support that can dilute the harshness of life. [Male patient – focus group 7]

When given the choice between receiving one- or two-way messages, participants chose the latter because it provided them with the option of communicating with someone. They highlighted the value of a personalised approach that is open-ended and can accommodate unique patient needs. One physician described how having healthcare staff help patients with their unique needs had been useful in her private clinic.

One-way text-messages without the option to respond feels very mechanised and without having the chance for an open conversation these messages will become monotonous and lose their effect. [Male patient – focus group 5]

Our patients could really benefit from a personalised approach, because each of them have unique needs and so they would need unique support. But we provide this kind of support to my patients in the private clinic, and we see that each person's needs are completely different, and that having one person who helps them through this process makes a big difference. [Doctor – focus group healthcare providers]

One of the elements emphasised regarding the value of the mobile messaging was its role in providing patients with a reminder about the support available, more than a specific reminder about taking their medication:

Reminders for taking pills are good, but I guess they depend on the person. For me, I prefer to get more support. [Female patient – focus group 4]

This helps because we will know that there is some support on the other line that comes to you every week. It can make a world of difference and really gives hope. Reminders [to take medicine] will act just like an alarm. If you are in a hopeless place no alarm can help you. [Male patient – focus group 3]

Some participants referred to the importance of having access to a person providing trust-worthy information, especially when there is significant misinformation:

Although we can ask things on the internet or telegram, this way [direct mobile messaging with the provider] we know who is responding. This is a good way to get information that we can trust. [Male patient – interview 9]

Sometimes you really need to ask a question, especially in the beginning when there is so much confusion and contradictory information. We have the hotline but having one person

who you know will answer your questions every week is very useful. [Female patient – focus group 4]

Overall, participants appeared to value having a two-way connection to providers for the possibility of receiving material support and needed information. As opposed to receiving one-way information or reminders, they prioritised having the option to ask individual questions and seek support as they saw fit and as problems arose that impacted their ability to adhere to treatment.

3.3.2 Proactive Care

The interview data also suggests that participants would value the proactive demonstration of care (i.e. by checking up on them) on the part of the clinic. It was suggested that this would help them to feel cared for, reminded them to value themselves, and was a source of motivation in terms of staying on track with their treatment:

For me I go through these waves of time that I hate myself. I isolate myself in a corner and lose motivation for continuing life tasks. At that moment I can feel uplifted if I get a message. It could give me motivation to keep going and continue my treatment too. [Male patient – focus group 7]

One participant described how the proactive check-up initiated by the clinic felt like a service that was delivered to their home:

This is great because it is like having a home-clinic once a week. Instead of you having to go all the way there they come to you and take the initiative to make sure you are doing okay. [Male patient – focus group 5]

Another interviewee stressed that the caring that is demonstrated by the weekly texting motivates them to value themselves:

As patients we become very depressed and isolated sometimes. We retreat within ourselves sometimes. But someone reaching out to us can give happiness. It's like someone is looking after us even though we are not caring for ourselves. It makes you think that if someone else values you this much, why are you not valuing yourself, why are you neglecting your treatment. [Female patient – interview 2]

On the other hand, patients and peer supporters living with HIV described how a mobile messaging connection can provide patients with a pathway for taking the initiative, thus having more agency, to ask questions when they need help:

Having someone to text your problems to encourages you to think about your problems and take the initiative of contacting the clinic as it's much easier through texting. [Female patient – focus group 4]

I think regular mobile messaging by itself can make patients better at acting and taking initiative for getting the medication and staying on track. [Peer supporter]

Overall, the participants appeared to value receiving messages from the clinic, in addition to being able to respond to the messages. Such follow-up demonstrated care and helped reinforce an internal sense of self-worth and self-care, which in turn enhanced motivation for treatment and care, and enhanced agency and initiative on the part of the patient.

3.3.3 Privacy and Personalisation

I asked stakeholders about the features of the mobile messaging intervention that they found to be important in terms of its acceptability in their daily lives and the minimization of harms, such as unintended disclosure of HIV status. High levels of privacy, low frequency of text-messages and a personalised approach were emphasised by most stakeholders, because such features were perceived to help patients to trust the communication channels, thereby encouraging them to take more initiatives in terms of seeking care and treatment.

I would be interested in getting this kind of messaging support, but then again it is important to keep it confidential and not mention HIV, because for me other than my wife no one else in the family knows that I have HIV. [Male patient – focus group 7]

As long as it is discrete, I do like to get the text-messages for support, but I prefer not getting direct references to HIV. I think receiving a check-up message once a week is sufficient to give help. [Female patient – focus group 4]

Healthcare providers emphasised the value of a programme that would increase contact with patients who are not typically aware of the resources available within the healthcare setting and described the value of a tailored personalised approach over a uniform, and unidirectional approach.

Different patients have different needs and rather than deciding on patient's behalf it would be more useful to let patients tell us their needs so we can guide and direct them accordingly. [Counsellor – interview 1]

In Iran we do have a lot of services available, by far more than other countries in our region we provide harm reduction, peer support, social support, and access to free counselling. The problem we have is that a lot of patients aren't aware of these services. If you have a programme that reaches patients who are not using the resources, especially in the first year of their diagnosis when they are not familiar with the system, that can change their treatment outlook completely. [Doctor – interview 2]

The overarching importance of maintaining patient privacy and keeping message contents discrete was evident through all discussions. Further, the significance of having personalised communication that addressed individual needs of patients appeared as a key opportunity for providing information and support to more patients, by enabling them to take advantage of the already existing but under-utilised support services. Such a personalised approach was perceived to improve patient agency to take initiatives towards an improved treatment outlook and better trajectory of retention in care.

3.3.4 Conceptual Model

In this section, the findings of the previous chapter are used as a backdrop for the additional realist-analysis that was done to hypothesise how the proposed mHealth design features will introduce relational changes within the contexts of living with HIV to reduce the negative outcomes and experiences. Details about where specific mHealth features can produce potential relational changes are illustrated in blue within Figure 3.1.

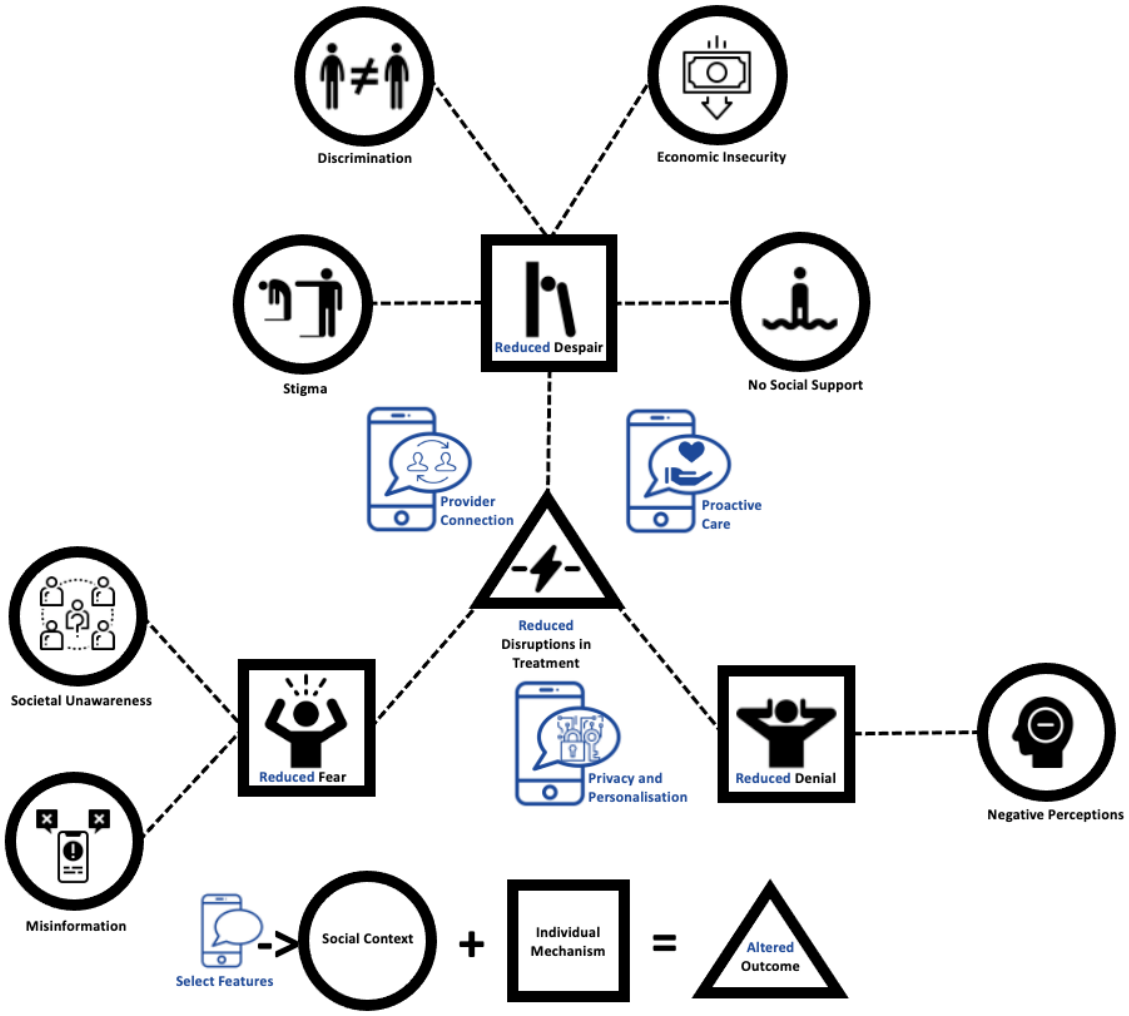

Figure 3.1 Two-way mHealth Features (blue), Introduced into the Contexts of Living with HIV in Iran. This figure shows the conceptualised model of how specific mHealth features can be placed within the socioecological contexts of living with HIV and engaging with antiretroviral therapy in Iran.

Participants viewed the most useful aspect of mHealth to be relational by connecting them to providers and improving access to support, especially within the contexts of feeling despair and lacking social support. Misinformation regarding HIV in Iran was shown to trigger fear, which acted as a mechanism driving patients away from treatment and the health system in general. Therefore, having access to information and support from trusted providers who offer proactive care, and the opportunity to ask questions through a private and personalised communication channel could counteract fear as a mechanism that disengages and drives patients away from treatment. Societal stigma against HIV in Iran appears to lead to internalised stigma and a self-defeating feeling of despair, which acts as a mechanism that reduces the motivation to continue treatment. Participants explained that when clinics demonstrate proactive care, the check-in messages acted as an 'antidote' to internalised stigma, reinstating feelings of self-worth and motivation for engagement with treatment and adherence to daily medications. Denial in response to negative perception of HIV in Iran appears to act as a mechanism that keeps patients away from existing resources. By providing private and personalised communication links, patients can learn about and access health system resources more seamlessly, have more agency to seek support, and be more informed to take the initiatives needed to engage with treatment, overcoming the state of denial less challengingly.

3.4 Discussion

The findings of this study delineate the potentially useful features of mHealth that can change how people living with HIV relate to treatment and care in Iran—namely by offering provider connection, proactive care, and privacy and personalization in communication. These mHealth features could support Iranians living with HIV to stay engaged with antiretroviral therapy, especially early-on after diagnosis, addressing Iran's significant gap in treatment retention. It is also possible that this realist informed analysis has developed knowledge that may be of value in other similar settings, such as where HIV is highly stigmatised and affects marginalised populations, thus remaining hidden from public attention and absent in public debates. Iran sits at the border of two UNAIDS designated regions: the Middle East and North Africa, and Asia and the Pacific. The hidden HIV epidemic shares characteristics with

countries in both regions, in which the prevalence of HIV is low, but new HIV infections and AIDS-related mortality are high because the enactment and internalization of stigma are high, undermining engagement with antiretroviral therapy, despite free and universal access (UNAIDS, 2022). Therefore, approaches specific to such settings are needed to address the gap between treatment supply and demand, by focusing on the barriers to treatment uptake and adherence through providing services that improve continuity of care, and promote mental and physical wellbeing of marginalised populations and people living with HIV (Byng et al., 2023; Hajebi et al., 2022; Rasoolinajad et al., 2018).

Being connected to a provider is hypothesised to be the most valued aspect of mHealth and expected to improve access to information and support. Proactive demonstration of care offered through regular text-message check-ins is expected to provide motivation for self-care and continuing treatment. Privacy and personalisation in communication is expected to facilitate access to existing HIV care and support services. These findings resonate with previous evidence on mHealth interventions that use two-way messaging, showing that this approach can improve adherence to treatment, particularly for newly diagnosed patients (Gross et al., 2019; Lester et al., 2010). Importantly, here I conceptualise *how* these outcomes can be impacted through specific mHealth features, using stakeholder views in the seldom-studied setting of living with HIV in Iran. Previously, I reported that the socioecological contexts of living with HIV in Iran is characterised by stigma and discrimination, negative perceptions, misinformation, and low awareness regarding HIV, amidst economic insecurity that is fuelled by financial sanctions and economic inflation (reference omitted for anonymity, 2021). The findings here suggest that select mHealth features and personalised provisions can partially minimise the confluence of the detrimental socioecological impacts on treatment outcomes by enhancing information, support, motivation, and initiative for treatment.

Globally, WelTel Kenya was the first study to provide weekly text-message check-ins to people living with HIV who were initiating treatment (Lester et al., 2010). Other quantitative studies have shown that mobile messaging could be effective in promoting adherence, monitoring, and viral load suppression, the outcomes that have most frequently been examined using experimental methods (Badawy et al., 2017; Devi et al., 2015; Hall et al., 2015). Previous qualitative studies have shown that mobile messaging can reduce feelings of loneliness and isolation, while enhancing feelings of being supported by the health system

(Sabin et al., 2018; Venables et al., 2019; Ware et al., 2016). I have also seen in other settings that mHealth designs, and mobile messaging interventions in particular, can increase support, not just by making people living with HIV feel cared for and supported, but also by linking patients to under-utilised existing support services, including counselling and mental health support, and accessing harm reduction, medical support or other existing resources when needed. However, few studies have provided detail with regard to the role of context in the potential causal pathways that may explain the impact of mobile messaging on adherence behaviour (Glasziou et al., 2014; Nittas et al., 2020; Sutcliffe et al., 2015).

Methodologically, as the body of effectiveness studies on mHealth grows (Lee & Valerius, 2020; Marcolino et al., 2018), it is important to bear in mind that mHealth does not work in a uniform way for all participants and in all settings, thereby bearing means-based results potentially misleading. Mobile messaging is a simple yet flexible and dynamic communication tool, one that can change the social relations and the contexts into which it is introduced. Moreover, reception towards mobile messaging varies depending on the burden of use across countries. In Iran, SMS use is adopted for a wide variety of purposes, from public alerts, to banking and advertisements, but stakeholders in this study indicated there is more trust in WhatsApp and Telegram messaging when it comes to private communication options. Thus, it is important to qualitatively investigate and understand what critical features of mHealth are needed for any given context, and how these features could change patient-provider relations and the contexts in which programmes will be implemented. Such approaches can be conducted through frameworks that study the recursive relationship of technology interventions with contexts (Abimbola et al., 2019; Aranda-Jan et al., 2014; James et al., 2021). The realist-informed lens in this study provided additional concepts (i.e. context and mechanisms) to further unpack the empirical data and produce transferable findings. Concretely, merging two research paradigms: social constructivism with realism, allowed conceptualizing intervention effects based on reasoning that may be socially constructed, but refers to a shared reality and an understanding of causation (i.e. through mechanism), which may produce transferable lessons for similar contexts (Bogna et al., 2020).

Stakeholders in this study described how a two-way private and personalised communication, proactive care, and provider connection could increase information, support, motivation, and patient initiative, that could ultimately contribute to improved engagement

with care and treatment. These findings echo the constructs highlighted by the widely applied Information, Motivation, and Behavioural skills (IMB) model, which posits that HIV services are successful at the level of individuals when providing information regarding HIV, motivation to practice, and necessary behavioural skills (Fisher & Fisher, 2000). The IMB model is often used as a guide to identify the content of interventions, by specifying specific informational, motivational, and skills factors that are needed in each setting (Aliabadi et al., 2015). However, the model has often been viewed as simplistic for dynamic behavioural contexts, requiring attention to multiple aspects of context that influences individual decisions and behaviours (Rivet Amico, 2011). In line with these critical perspectives, the findings of this study suggest that instead of identifying intervention content that can be delivered uniformly across a population or within a setting, selecting specific mHealth design features––that by their very nature are more personalised—can be more responsive to the informational, motivational, and behavioural exigencies across socioecological settings and structural systems. Future research is now needed to study the ways in which mobile phones can change the contexts of relating to treatment, care, and providers. Through a realist lens the research focus on the efficacy of specific interventions can be expanded to answer more questions on when, how, and why mHealth with its various provisions can be incorporated in scale and sustained (J. Greenhalgh & Manzano, 2021). Investigating how certain mechanisms are triggered within specific contexts can unpack causal pathways and produce reusable concepts that can enhance the design and implementation of future interventions.

3.4.1 Strengths and Limitations

Augmenting the constructivist paradigm with a realist informed conceptualisation enhanced understanding of the value and locations where specific design features have their impacts and potentially produced transferable context-specific findings. A key strength of this study was the co-conceptualisation of *how* mHealth can be useful with and for people with lived experience of (dis)engagement with antiretroviral therapy in Iran. Further, the strength of these findings are enhanced because of engagement with the socially constructed realities of living with HIV in Iran, engaging and interacting with stakeholder views, while producing transferable findings for a shared reality in which an mHealth intervention can be implemented and empirically tested. Thus, the strength of adding the realist analysis to the

social constructivist study is that while engaging with subjective realities, the produced findings can be transferable to similar settings through the realist ontological lens (J. Greenhalgh & Manzano, 2021). The conceptualised mHealth intervention here can be useful where there is a need for increasing treatment demand and continuity, and where treatment supply is not a barrier to successful treatment, but profound stigma, discrimination and low awareness regarding HIV continue to pose challenges to treatment success. However, a key limitation of this study is that it is only hypothesis generating, in which I attempted to theorise and understand the impacts of specific proposed mHealth design features on living with HIV in Iran, or similar contexts. By conducting the study through a social constructivist lens, I acknowledge the subjective nature of the knowledge produced, and possibilities for the role of the interviewer to have influenced the findings through their interactions and conversations with the participants.

3.6 Conclusion

This study used local stakeholder interviews to conceptualise how selecting specific mHealth features of offering provider connection, proactive care, and privacy and personalization in communication could mitigate disruptions in treatment within identified adversarial contexts of living with HIV in Iran. Importantly, this study is hypothesis generating, in that I attempted to conceptualise and understand the impacts of specific proposed mHealth design features on living with HIV in Iran. The data on the shared realities discussed were accessed via the socially constructed understandings of interviewed stakeholders. The realist concepts of ‘context’ and ‘mechanism’ enabled unpacking the collected data. Thus, the strength of this study’s findings lies in the contextualised conceptualization, based on stakeholder views, of the role that mHealth could play to prevent treatment disruption in similar settings where universal antiretroviral therapy supply is offered.

This chapter presents DPhil paper III, published as:

*'*Ameli, V., et al. (2021). *'Tailored mHealth intervention for improving treatment adherence for people living with HIV in Iran (HamRaah): protocol for a feasibility study and randomised pilot trial with a nested realist evaluation.'* BMJ Open.

4

DPhil Paper III: Protocol

This chapter proposes a mobile-messaging intervention to be tested in terms of efficacy, feasibility, and acceptability in Iran. HamRaah, meaning together-in-path in Persian, is introduced to enhance retention in care and adherence to treatment among Iranians living with HIV. In line with patient perspectives and provider priorities, this intervention was proposed to be delivered for the newly diagnosed, to curtail the identified impacts of denial, fear, and despair. To conceptualise HamRaah as a complex intervention, it necessitates to go beyond asking whether HamRaah will achieve its intended outcomes, to asking a broader range of questions in terms of theorising how it works in relation to the contexts into which it is introduced. As such, this protocol includes a nested-realist intervention. To this end, an initial programme theory that is based on stakeholder views, expert advice, and theoretical knowledge is unveiled in this chapter as a steppingstone for theorising how human-supported mHealth can change the contexts in which lifelong care and treatment are engaged with.

4.0 Abstract

Middle East and North Africa (MENA) has a rising rate of new HIV infections and AIDS-related mortality. Consistent adherence to antiretroviral therapy (ART) leads to viral suppression, preventing HIV transmission and treatment failure. Mobile health (mHealth) interventions can improve antiretroviral therapy adherence by providing tailored support and directing patients to existing healthcare services. HamRaah (Persian for 'together-in-path') is the first mHealth-based intervention in a MENA country and is designed to improve adherence through two-way mobile messaging for people recently diagnosed with HIV in Tehran, Iran. The objectives of this pilot RCT are to examine the feasibility, acceptability, and preliminary effectiveness of HamRaah, and to develop an explanatory theory for any observed effects through a nested realist evaluation. A feasibility study and two-arm pilot randomised controlled trial of HamRaah, with an embedded realist evaluation will be conducted. Participants will be randomised 1:1 to HamRaah or routine care for a six-month intervention. The initial effectiveness of HamRaah will be assessed through the primary outcome of self-reported antiretroviral therapy adherence and several secondary outcomes: retention in care, CD4 count, and viral suppression. A theory-driven realist evaluation framework will be used to develop an explanatory theory regarding what works, for whom, how, and in what context. The study received ethical clearance from Tehran University of Medical Sciences Ethics Committee and Oxford Tropical Research Ethics Committee. The trial is registered with the Iranian Registry of Clinical Trials (ID: IRCT20100601004076N23). People living with HIV in Tehran and key country stakeholders in HIV policy and programming have been involved in the development of HamRaah and this pilot trial. Participants will provide informed consent prior to study enrolment. The results will be disseminated to all stakeholders and presented in peer-reviewed journal publications and conferences.

4.1 Introduction

Consistent adherence to antiretroviral therapy promotes viral suppression and maximises the benefits of treatment-as-prevention (Cohen et al., 2011). Conversely, non-adherence is a major contributor to poor viral suppression (Boender et al., 2015), ultimately leading to treatment failure (Conway, 2007), and increasing total morbidity and mortality (Hogg et al., 2002; Siegrist et al., 1994). Over the past two decades of antiretroviral therapy expansion, a variety of adherence interventions have been tested and shown to be effective and sustainable in both high- and low-resource settings (Haberer et al., 2017; Kanters et al., 2017). Interventions that build on existing healthcare infrastructure and leverage available resources to support people living with HIV can be particularly useful (WHO, 2019a). Rather than devoting additional resources for conventional programmes, connecting patients digitally to existing programmes can potentially support antiretroviral therapy adherence with increased personalisation and scale at a lower cost (Chiasson et al., 2010; Noar, 2011; Noar et al., 2009).

HIV differentially affects key population groups, such as people who inject drugs, sex workers and their clients, men who have sex with men, transgendered individuals, and the general population. This heterogeneity of the HIV epidemic has propelled a paradigm shift, calling for differentiated care models to manage HIV (Grimsrud et al., 2016; WHO, 2016). Moreover, in dealing with highly vulnerable segments of the population, experts caution against transporting interventions across groups, regions, and countries, and recommend interventions that fit regional, national, and local contexts (Beckmann, 2012; Rhodes et al., 2005). This concern is especially salient with regards to settings where high levels of HIV-related stigma and discrimination call for programmes to respect privacy concerns (Dejong & Mortagy, 2013; Santos et al., 2017). Digital interventions offer the potential solution for increased personalisation and privacy, and can deliver remote and differentiated HIV care, provided that patients have personal access to mobile phones, and that providers can ensure data security. There is, however, a paucity of evidence on the effectiveness, and acceptability of interventions in settings where HIV prevalence is low, but stigmatisation is high.

In response, and for the first time in a MENA country, this study aims to examine the feasibility, acceptability, and preliminary effectiveness of an mHealth intervention in Tehran, Iran, with an emphasis on the role of context to discover how, for whom, and why the intervention works (or not), using a nested realist approach (Pawson & Tilley, 1997). The rate

of new HIV infections in Iran has declined by 12% since 2010 (UNAIDS, 2020). This improvement could be attributable to the healthcare infrastructure, which provides access to methadone replacement therapy, needle exchange programmes, free and universal access to antiretroviral therapy at the point of diagnosis, and peer-run adherence clubs to support people living with HIV throughout every province in the country. This combination of services provides the optimal setting for an mHealth intervention that leverages existing healthcare capacities. By 2018, Iranians had been assigned over 169.5 million SIM cards, of which 88 million were actively in use for a population of 81.8 million (CommsMEA, 2018), thus making text-messaging a widely accessible form of communication. Smartphone use has also rapidly increased over the past three years, and the country was 11th in the world in terms of smartphone penetration rate in 2019 (Newzoo, 2019). Thus, mHealth interventions that offer remote support, safely and effectively, could be a promising approach to manage HIV care.

4.1.1 Intervention Rationale

Two-way communication approaches appear to have important benefits for improving antiretroviral therapy adherence and achieving viral suppression. WelTelKenya was the first study supporting antiretroviral therapy-initiating patients through weekly text-message check-ins and in a similar study in Uganda (Pop-Eleches et al., 2011), weekly, but not daily, communication improved adherence. Meta-analyses corroborate that two-way and weekly messaging interventions appear more effective and less burdensome than daily one-way reminders (Amankwaa et al., 2018; Finitsis et al., 2014). Moreover, recent studies show that mobile messaging may not be effective for patients starting second-line therapy as a result of non-adherence (Gross et al., 2019), suggesting that mHealth interventions may be more effective when implemented at the onset of antiretroviral therapy to promote better habit formation (Ware et al., 2016), leading to improved long-term outcomes, although the long-term effectiveness has not been studied beyond a year. Further, by providing an efficient and personalised means of connecting patients to needed care before they reach a critical clinical stage, either from non-adherence or untreated co-morbidities, interventions may reduce mortality and save costs for the health system (Grimsrud et al., 2016).

HamRaah (Persian for *'together-in-path'*) is a two-way mHealth intervention for recently diagnosed people living with HIV in Tehran, Iran (for intervention protocol see Figure 4.1). An initial qualitative study was conducted to understand Iran's HIV care structures, the socioecological pathways that disrupt consistent adherence, and stakeholder perceptions in terms of the acceptability and usefulness of an mHealth intervention. These qualitative findings were presented in chapters 2 and 3. Stakeholders emphasised that mHealth would be most useful within the first year following diagnosis, when navigation of the HIV care system and access to available resources is still unfamiliar. Iran provides universal and free access to antiretroviral therapy through a de-centralised model of health delivery across thirty-one provinces via the universities of medical sciences' hospitals, providing uniform HIV services, such as Voluntary Counselling and Treatment (VCT) centres and Positive Clubs that offer psychosocial support to people living with HIV. Thus, an mHealth programme that provides personalised messaging with providers (for messaging protocol see Figure 4.2) and builds on existing resources can proactively support patients and improve HIV care.

4.1.2 Aims and Objectives

The current pilot study's overarching aims are to examine HamRaah's: i) trial feasibility and intervention acceptability, ii) initial effectiveness, and iii) explanatory programme theory. The specific objectives are as follows:

1. Assess the feasibility of recruitment, randomization, allocation concealment, and blinding procedures for outcome assessment;
2. Determine the acceptability of HamRaah intervention by participants and fidelity to protocol by counsellor;
3. Determine preliminary effects of the pilot intervention on the primary outcome of adherence to antiretroviral therapy;
4. Conduct a nested realist evaluation to refine an explanatory programme theory with enriched evidence on what works, for whom, how, and in what circumstances;
5. Triangulate realist, qualitative, and quantitative findings in a sequential approach to investigate mediating relationships.

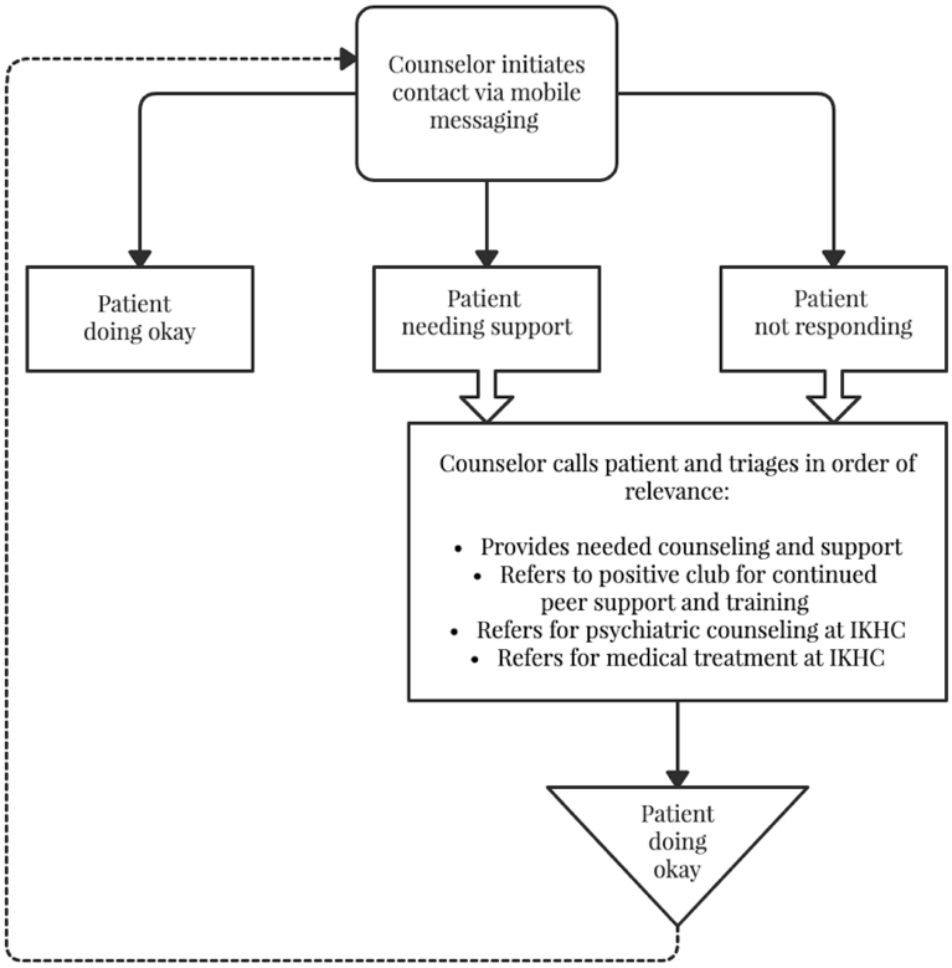

Figure 4.1 HamRaah Intervention Protocol, showing how patients will be proactively followed up and connected to providers at the Imam Khomeini Hospital Complex (IKHC).

4.2 Methods and Analysis

4.2.1 Overview of Study Design

The feasibility and acceptability study relate to procedural uncertainties of the trial and the acceptability of HamRaah. These aspects will be examined via quantitative and qualitative data, collected throughout the implementation process and at the conclusion of the trial through checklists, spreadsheets, focus group discussions and interviews. The perspectives of HamRaah participants, counsellor, and project staff will be collected to answer the feasibility and acceptability questions that could inform a future definitive trial.

The HamRaah pilot consists of:

Arm 1: routine care + HamRaah

Arm 2: routine care

Participants will be assigned through permutated even-number blocks to be randomised in a 1:1 ratio to Arm 1 (depicted in Figure 4.1) or Arm 2 (explained below). The intervention period is six months for each participant in Arm 1, with equivalent follow up for participants in Arm 2. The initial effectiveness of HamRaah will be assessed through self-reported antiretroviral therapy adherence, as a primary outcome, and retention in routine clinical care, immune reconstitution, and viral suppression, as secondary outcomes.

The nested realist evaluation will be informed by HamRaah participants through mechanistic thinking, which aims to develop an explanatory theory of *how* and *why* HamRaah may work (or not). The individual reasoning and reactions to the context, and interventions introduced within it, form the roots of mechanisms that may or may not be 'triggered' (Pawson, 2006). Contexts and mechanisms are perceived as working together to produce outcomes, and interventions are thought to alter the context by introducing new resources, thereby providing a new path for individual reasoning and reaction, expressed as: C+M (Reasoning) → O (Dalkin et al., 2015). Thus, the focus of the nested realist intervention will be to recognise which aspects of the study context are changed through HamRaah, and how this change could alter participants' reasoning, trigger a new mechanism, and produce an observed outcome, explained in a refined theory.

4.2.2 Routine Care

Routine care offered at the VCT centres consists of an initial general counselling session at the time of diagnosis. Medication pick-up is initially set at a monthly interval, and as patients collect medications regularly, and appear to be adhering well, the window for collection is extended to every two months. However, as a result of the COVID-19 pandemic and recent WHO guidelines, the medication collection periods have been extended to every three to six months.

Counselling on adherence is offered to patients who miss monthly visits or report problems with medication adherence, viral suppression, or treatment resistance. As part of the routine care, a mandatory check-up with an infectious disease specialist is also offered every three months for patients with clinical signs of non-adherence or signs of irregular medication pick up. The Positive Club offers additional counselling and support, on referral, for people living with HIV who are facing adherence or psychosocial difficulties. The intervention group will also receive these routine services, in addition to the HamRaah intervention, which includes independent counsellors to prevent risk of contamination.

4.2.3 HamRaah Intervention

HamRaah is a weekly mobile messaging intervention, based on the WelTel model (Lester et al., 2010), which serves as a counsellor-initiated check-in with recently diagnosed people living with HIV to assess adherence and physical and mental wellbeing in the past week. Figure 4.2 is a pictorial representation of the weekly messaging protocol.

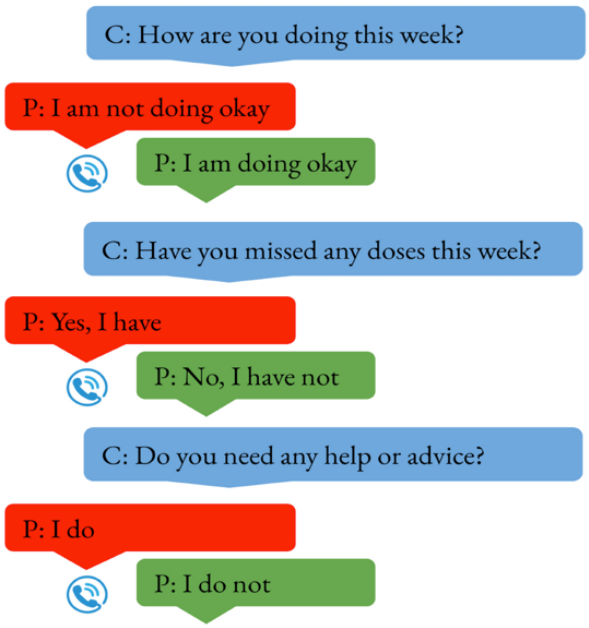

Figure 4.2 HamRaah Mobile Messaging Protocol, showing how patients will be proactively checked-in on via mobile messages, and when they will receive a phone call (depicted via a phone symbol).

HamRaah recipients will be contacted on a weekly basis by a counsellor. The counsellor specifically asks patients how many (if any) days they missed their doses, and what (if any) problems they may be facing. If contacted patients do not respond to the messages, or report back on missing doses or facing challenges, a follow-up contact by live phone call will be made to assess the patient's current needs. When contact is triggered, the counsellor will enquire about the problems the patient may be facing, or the reasons for missing doses. The counsellor will be selected from the pool of locally trained social workers or psychologists, to ensure people living with HIV are treated sensitively and professionally on the phone. The intervention is not meant to provide therapy or psychological counselling, but rather identify patients who may need a one-time over-the-phone support and those who need to be referred for long-term therapy. If long-term support is needed, the counsellor, familiar with IKHC resources, will refer the patient according and tailored to their needs to further services. Thus, HamRaah can boost access to available healthcare capacities. At the first instance, patients could be linked to the free of charge peer-run Positive Club, which provides educational, motivational, and skill-building classes, and where both peers and trained psychologists operate a variety of weekly classes to help patients address barriers to adherence through problem solving and encouraging good habit formation. Patients who are facing mental health challenges will be encouraged to accept a psychotherapy referral to address any emotional needs. In cases where medical counselling and clinical treatment are necessary, appropriate referrals are offered.

Whilst HamRaah aims to promote adherence to treatment as primary outcome, it simultaneously aims to streamline the process through which newly diagnosed patients get connected to available health services that can meet their needs in a timely window before critical care becomes necessary. The weekly check-in schedule could also prevent prolonged gaps in adherence that increase the risk of viral rebound.

4.2.4 Research Population

Newly identified people living with HIV, enrolled under care at the VCT centre, will be eligible to participate if they meet the following criteria: 1) are aged 18 years or above; 2) are treatment naïve, defined as starting antiretroviral therapy within the six months; 3) own or

have access to a mobile phone; 4) are able to operate a cell phone to communicate using mobile-messaging (help by a partner is sufficient for patients with reading and/or writing difficulties); 5) consent to be contacted through mobile communication to receive HIV- and antiretroviral therapy-related information. Figure 4.3 depicts the selection and flow of participants through the study.

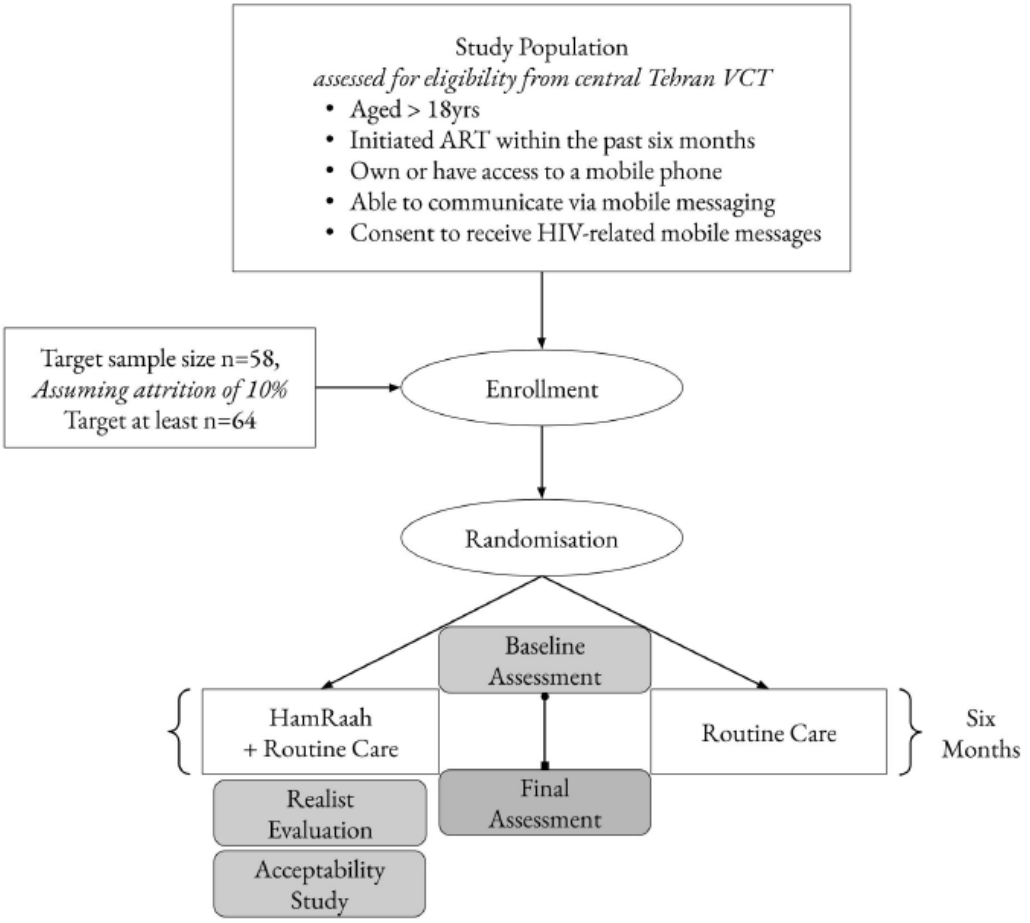

Figure 2.3 Study Population Flow Diagram

4.2.5 Sample Size

This study is designed as a pilot. The target sample size of 58 is based on the number needed to detect a 20% improvement in the primary outcome of mean adherence, which will be measured as a continuous variable based on the number of missed doses. These calculations were estimated using PS software by Vanderbilt University, and assumed a 75% baseline

estimate of adherence, based on clinician estimations from pharmacy refill data, with 90% power and a two-sided alpha of 0.05; I also allowed for 10% attrition. However, the clinical significance of any observed improvement will depend on the baseline level of adherence, and as such smaller effects, observed within the range of 5-10%, would also be suggestive of impact to be assessed in a fully powered study.

4.2.6 Participant Recruitment

Study recruitment began in August of 2019 and has faced delays due to the COVID-19 pandemic. Participants are identified from the list of HIV patients, who are diagnosed within the past six months and meet eligibility criteria. The IRCHA, where the research team is based, is located within the same hospital complex. All staff members conducting the recruitment and informed consent process are recruited from IRCHA, trained in the ethical treatment of human participants, and familiar with informed consent guidelines. To maximise recruitment, two approaches will be used:

i. Direct, which involves obtaining contact information of the recently diagnosed patients and contacting them via telephone to invite them to participate. patients who show initial interest on the phone will be asked to visit IRCHA to receive further information about the trial and provide informed consent.
ii. Indirect, which involves a brief introduction during individual clinic visits. patients who show initial interest will be asked to visit IRCHA and meet with a staff member of the research team to receive further information and provide informed consent.

4.2.7 Randomisation and Blinding

Randomisation procedures follows a permutated block technique, which occurs after baseline data collection. R software is utilised by a researcher in Oxford to produce a set of randomly generated assignments through permutated even-number block sizes that will randomise in a 1:1 ratio to HamRaah or routine care. A study team member in Tehran allocates participants to intervention and comparison groups based on the order of completing the informed consent forms, and the pre-determined assignments received from the researcher in Oxford. This

process reduces the potential for allocation bias through correct sequence generation. Researchers will notify each participant individually about his/her allocation.

Given the nature of the mHealth HamRaah intervention, participants in this study cannot be blinded. The intervention facilitator, who is the counsellor delivering the weekly messages, can also not be blinded to the participant group assignment. Similarly, researchers conducting the nested realist evaluation will be aware of participant assignments. To mitigate against interviewer bias, participants will be encouraged to complete the questionnaires online. In cases where participants ask to be assisted in completing the questionnaires, a concerted effort will be made to minimise interviewer bias by keeping the research assistants responsible for interviewing and outcome assessment blinded to the group allocations of the participants. Any incident of unblinding of the assessors will be recorded and the interviewer's knowledge regarding group assignment will be documented.

4.2.8 Data Collection

Quantitative data for efficacy outcomes will be collected at baseline and at the end of the six-month intervention. Participants can choose to complete and submit the forms within the privacy of their homes on their mobile phones, tablets, or computers. For those who need assistance in completing the survey, research assistants will arrange an appointment to guide them through the process using a computer at IRCHA. Should a participant prefer to stay at home, the research assistant will provide guidance over the phone. For participants who prefer not to fill in online questionnaires, a paper questionnaire option will also be available.

Qualitative data, for the realist evaluation and for the acceptability study, will draw on the perspectives of HamRaah participants, lead counsellor, and other providers for care to participants referred from HamRaah. The research method will involve interviews and focus group discussions, both of which allow researchers to explore areas of interest, albeit with important differences in terms of approach. Recruitment for focus groups and individual interviews will continue until theoretical saturation is reached, or until all who received six months of HamRaah have been interviewed.

4.2.9 Outcome Measures

Feasibility outcomes

Feasibility outcomes of interest relate to methodological and procedural uncertainties. Table 4.1 lists the measurements that will be used to assess recruitment, randomisation, retention, fidelity to the delivery of the intervention, and engagement with the intervention.

Table 4.1 Feasibility Outcome Measurements (Kruse et al., 2019)

Variables	Measure	Mode of Administration	Weekly	Monthly	24 weeks
Recruitment (Kruse et al., 2019)	Number of subjects enrolled per month	Spreadsheet *		√	
	Number of recruitment calls made per enrolee	Spreadsheet *		√	
	Proportion of new patients successfully reached	Spreadsheet *		√	
	Proportion of new patients enrolled and randomised	Spreadsheet *		√	
Randomisation	Balance achieved across two arms	Analysis †			√
Retention	Proportion of participants with complete study data	Spreadsheet *			√
Intervention fidelity	Adherence to per protocol delivery of text-messages	Checklist ‡	√		
	Follow-up with patients per protocol	Checklist ‡	√		
	Provision of counselling when needed	Checklist ‡	√		
	Arranging referrals when needed	Checklist ‡	√		
Intervention Engagement	Participant response rate within a 48-hour window	Checklist ‡	√		
	Number of times participants initiate messaging	Checklist ‡	√		
	Time of active participation in the study	Checklist ‡			√

Mode of Administration:

* Track-sheet: Project leader will enter all data into tracking sheets

† Analysis: Post-intervention analysis of sociodemographic and clinical data across study groups

‡ Check-list: The intervention facilitator and research assistants will have checklists

Primary outcome: *Adherence to antiretroviral therapy*

The primary outcome of the pilot trial is adherence to daily antiretroviral therapy, which will be measured as a continuous variable of self-reported adherence using the Wilson 3-item self-report scale on adherence (Wilson et al., 2016). The scale will measure the number of missed doses in the past thirty days. Given that variations in viral suppression rates require a longer time and a larger sample size, for the current pilot the decision was made to use self-reported adherence as a primary outcome. Notably, the Wilson 3-item self-report scale on adherence has been validated against electronic drug monitors and viral suppression, showing good psychometric characteristics and good construct validity (Wilson et al., 2016, 2020).

Secondary outcomes: *Retention in care*

Retention in care will be measured as visit constancy for monthly (or bi-monthly) appointments. Evidence suggests that there is no gold standard tool to measure retention in care and selection of approach must be tailored to context (Mugavero et al., 2012). Larger windows for pick up are generally reserved for adherent patients; however, in the current context of the COVID-19 pandemic, medications are either being delivered to patients, or given for a longer period of time. As such, measuring the percentage of expected visits that were attended, within a one-week window, accommodates the variability in scheduling as a result of personal or COVID-related reasons.

Clinical measures

The clinical measures of immune reconstitution (CD4>500/ μL) and viral suppression (mRNA<200 copies/μL) will be assessed through change of CD4 cell counts from baseline; however, it is unlikely to observe an effect, given the short duration of the trial. Viral load tests are not included in the free national antiretroviral programme and are offered in this trial as a benefit of participation at the conclusion of the trial; consequently, virologic suppression is measured at a single time-point.

Psychosocial measures

Psychosocial measures, treatment barriers, and demographic factors are measured through the questionnaires listed in Table 4.2. These measurements will inform the study as they could be impacted by the intervention, or act as a mediator or moderator. The study is not powered to detect definitive effect sizes, but any change in direction would likely inform the future definitive trial.

Table 4.2 Trial Outcome Measurements

Outcome Measures		Baseline	6 Months
Adherence to antiretroviral therapy	Wilson 3-item self-report scale on adherence (Wilson et al., 2016c)		√
Retention in care	Missed visits and monthly visit constancy (Mugavero et al., 2012)		√
† Viral load	Virologic suppression (<200 copies/μL) (WHO, 2013)		√
CD4 cell count	Immune reconstitution, (>500/ μL) (WHO, 2013)		√
Depression	Patient Health Questionnaire-9 (PHQ-9) (Nolan et al., 2018)	√	√
Anxiety	Hospital Anxiety and Depression Scale (HADs-A) (Julian, 2011; Reda, 2011)	√	√
Social support	Multidimensional Scale Perceived Social Support *(MSPSS)* (Zimet et al., 1990)	√	√
Stigma and disclosure	The Berger stigma scale shortened and validated (Reinius et al., 2017)	√	√
Coping	Coping responses (Mohanraj et al., 2015)	√	√
Drug use	WHO – ASSIST (Humeniuk et al., 2008)	√	√
Beliefs	Concerns and beliefs on antiretroviral therapy necessity (Horne et al., 2004)	√	√
Barriers	Structural barriers to clinic attendance for antiretroviral therapy patients (Coetzee & Kagee, 2013)	√	√
Demographic factors	Age, gender, education, marital status, housing, household-size, employment, income, and poverty. These items are picked from Iranian Ministry of Health's demographic questionnaire.	√	√

4.2.10 Data Analysis

To assess the feasibility of the trial, a descriptive data analysis approach will be undertaken. Participant flow will be summarised, reporting the proportion of recently diagnosed people living with HIV who were eligible to participate from the list of those who are new patients under the care of the VCT centre, and those of which who were reached, screened, enrolled, and randomised, respectively. Following randomisation, the rate of retention of participants will be used to assess potential for bias and the representativeness of the final analytic sample. Baseline characteristics will be compared between participants and eligible patients who did not participate utilizing clinic files, using Cochran Mantel–Haenszel χ^2 tests for categorical variables and Student's *t* tests for continuous variables. Comparisons will also be made between intervention vs. comparison participants to assess randomisation, and between those who completed the intervention vs. those lost to follow up. A descriptive analysis of the outcome measures for intervention fidelity, intervention engagement and acceptability will be summarised. All analyses will be conducted using the R programming software.

The pilot trial will be reported using CONSORT guidelines on standards of reporting randomised trials. All randomised participants will be included in analyses. I will perform both intention-to-treat (ITT) and per-protocol analyses. Given the pilot nature of this study, all analyses will be non-confirmatory. To generate preliminary data on the efficacy of HamRaah, univariate logistic and linear regression models will be used for dichotomous (retention and viral suppression) and continuous (adherence and CD4 Cell count) outcomes respectively. For the main dichotomous outcome (% $\geq$ 95% adherence after the six-month intervention), risk differences and 95% confidence intervals will be calculated. Achieving undetectable viral load will be similarly treated as a dichotomous outcome. Estimates of effect sizes for the differences between HamRaah and comparison groups will be used to perform calculations of sample sizes needed for a future definitive RCT. To examine interrelationships among adherence and other psychosocial measures, bivariate Pearson correlations will also be explored. Given the limited statistical power, subgroup analyses will be exploratory only.

The acceptability study aims to focus on participant perceptions regarding the cultural and logistic appropriateness of HamRaah, and the burden of the intervention. The research question will aim to answer whether HamRaah fits the personal, cultural, and social contexts

of recently diagnosed HIV patients, and whether the intervention was useful in ways that may have not been captured via the quantitative measures.

4.2.11 Nested Realist Evaluation

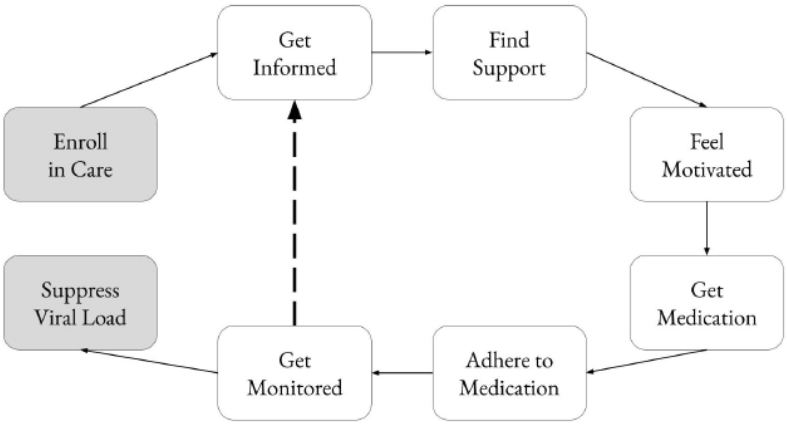

Figure 4.4 Initial Programme Theory, showing steps taken in lifetime antiretroviral therapy.

The nested realist evaluation will use a theory-driven approach and aims to examine why, how, for whom, and in what context HamRaah works. The process will be informed by the Initial Programme Theory (IPT), which was developed in the prior qualitative study (figure 4.4). The theory highlights the steps taken in the lifetime of antiretroviral therapy and will be the guide to examine how (if at all) HamRaah will change the contexts of steps taken in lifetime antiretroviral therapy and diagnose intervention mechanism(s) for future trials. The realist evaluation and acceptability study will both be embedded into the intervention arm of the trial, and qualitative interviews and focus group discussions will begin following participants' completion of the intervention. All qualitative data will be managed through MAXQDA. The IPT will first be refined in a realist synthesis of secondary global evidence (the findings of which are presented in the chapter 5 of this thesis). The synthesis will be followed by the nested realist evaluation by testing the refined programme theory developed within the realist synthesis, which is comprised of a range of context-mechanism-outcome configurations (CMOc). Realist evaluations are theory-driven. As such, each domain of the programme theory (Figure 5.2) will be tested as a hypothesis through interviews with patients

who have participated in the intervention arm of this pilot RCT. The eight CMOCs developed will be used as an interview guide. This will contribute to illuminating the underpinning programme theory of HamRaah its interactive relationship with context and the mechanisms that can be transferable to similar settings. The results will inform future investigations of such mHealth interventions.

4.2.12 Patient and Public Involvement

Decisions regarding the intervention, such as two-way versus one-way, and frequency of, messaging, were made in consultation with people living with HIV and the healthcare team in the qualitative phase to ensure that the intervention is low burden, suited to context, and a good fit for individual patient needs. Similarly, decisions regarding trial conduct were made in consultation with patients. These decisions included offering free viral load tests as a benefit of participation, optionality on which messaging application to receive HamRaah, and both online and offline means of completing the questionnaires. Moreover, research assistants, leading the recruitment, enrolment, and interviewing of participants are members of the HIV community. Per the research plan, the results of the trial will be disseminated in a report format to all participants via mobile messaging, in the spirit of HamRaah.

4.4 Ethics and Dissemination

4.4.1 Ethical considerations

The HIV epidemic in Iran is concentrated among people who use drugs, sex workers, and men who have sex with men. In Iran, research conducted with such populations and approved by local ethics committee benefits from full confidentiality. Access to medical care is not restricted for these populations who are protected by doctor-patient confidentiality. However, special care and consideration needs to be applied in order to protect patient confidentiality. Specifically, with regard to this mobile-messaging intervention, it is important to highlight the inability to control the privacy of text messages. Messages may be read by persons other than the intended recipient, can easily be forwarded, and could remain resident on unsecured devices for the lifetime of the technology. Text messages containing reminders to take

medications, for example, could result in unintended disclosure of a medical condition even without specifying any details. To address this issue, following consultation with the local institution, it was decided that the study would exclude participants who do not consent to receiving HIV-related communication on their phones due to concerns regarding unintended disclosure. As such, the risk of such disclosure will be minimised for study purposes. Moreover, potential psychosocial harms will be investigated to arrange counselling services as needed. Finally, the following steps will be taken to further minimise these risks:

i. No direct mention of HIV will be included in the initial message. Only if patient initiates direct questions on HIV, would the counsellor follow up with providing HIV-specific information.
ii. Messaging intervention can be delivered through SMS, or through participants' preferred choice of WhatsApp, Telegram or Signal, which are fully encrypted. Participants will choose a nickname to be used for chatting with the counsellor.
iii. To safeguard patient privacy, the option is given to choose a pin, which they will share with the staff upon initiation of conversation to ensure that counsellor is not in contact with a third party.
iv. Participants can choose to discontinue participation at any point, and the study team will be responsible to ensure no harm is inflicted on the study population as a result of their participation in the trial.

No financial rewards will be given for participation to avoid coercive appeal for participation. A warm meal will be provided in appreciation of participation upon presenting for final assessment, focus groups, and interviews. In light of the COVID-19 pandemic, arrangements can be made to offer a meal-card for a food delivery service.

4.4.3 Data Transfer and Storage

Study data are collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Partners Health Care. REDCap is a secure, SSL encrypted, web-based software platform designed to support data capture for research studies. The survey link is a singular URL to the survey, which does not track IP addresses, e-mail

addresses, or any other identifying information. No identifiable questions will be included in the survey items. The data will be stored in the secure servers of REDCap, and the anonymised data will be exported to the research group in the chosen file format. All data, both from qualitative interviews and quantitative surveys, will be accessible to the primary investigator, who will share de-identified data with co-investigators as needed only for analysis purposes.

4.4.4 Dissemination

The results will be disseminated at several levels, including people living with HIV, peer supporters, practitioners, researchers, healthcare organisations, and policy and programme stakeholders. Annual reports to Tehran University oof Medical Sciences research committee will be provided, in addition to presentations at the Iranian Research Center for HIV/AIDS for local stakeholders and representatives from the HIV community in Tehran. Dissemination will also include peer-reviewed journal publications and presentations at national and international conferences. It is also hoped that the results of the trial will be disseminated in a report format to all participants via mobile messaging, in the spirit of HamRaah.

4.4.5 Strengths and Limitations

This pilot RCT of mHealth for adherence to antiretroviral therapy is the first of its kind in Iran and in a MENA country. It addresses an important evidence gap with regards to the feasibility, acceptability, and potential for impact of a tailored mHealth approach within care settings that universal treatment is provided but stigmatisation of HIV is keeping people away from treatment and consistent engagement with care. The study triangulates quantitative, qualitative, and realist methods to produce complimentary evidence and a nuanced understanding of how HamRaah interacts with the contexts of HIV care in Iran to trigger mechanisms that produce observed outcomes. Patients and public stakeholders were consulted in the design of HamRaah and its trial planning and implementation. However, in terms of efficacy this pilot trial is designed to provide a preliminary estimate of effect size and will have insufficient statistical power to detect differences in outcomes between groups. The intervention period will be relatively short, limiting the capacity to show long-term effects that might accumulate over time. The realist evaluation will be limited to the intervention arm to investigate how context interacts with the intervention, but as a result the evaluation will be limited in size.

4.5 Conclusion

This study is the first to explore the potential of mHealth to improve antiretroviral therapy adherence in a MENA country. Iran offers universal access to antiretroviral therapy and a robust healthcare infrastructure, thus providing the ideal setting for a digital intervention to support existing healthcare resources. Digital health cannot substitute for the fundamental components of health systems, such as the workforce, financing, and access to medical care. However, guidelines by WHO (WHO, 2019a) recommend that digital health should complement and enhance health system functions through mechanisms such as accelerated exchange of information and directing patients to existing services. Given the known relationship between adherence to antiretroviral therapy and viral load suppression (Genberg et al., 2012), the results will further shed light on the potential of mHealth to suppress viral load within the first year of HIV diagnosis. The results of this study will provide important information with respect to feasibility and acceptability of mHealth within the HIV care structure of Iran. Findings could inform the implementation of a larger definitive trial, which could apply a multi-city design. The embedded realist evaluation will shed light on the mechanism of the intervention; how, for whom, in what context, and why the programme is effective.

This chapter presents DPhil paper IV, under review as:

Ameli, V., et al. (2024). *'The Added Value of Human supported digital health in HIV Care.* npj Digital Medicine

5

DPhil Paper IV: Realist Synthesis

The current literature has largely ignored the human-supported versus machine-based designs when offering interactive and 'two-way' mHealth for HIV care. In this chapter, I systematically and iteratively assemble a secondary evidence base from various global settings to produce an explanatory theory to answer how, when, why, and in what context human supported mHealth adds value to HIV care, at the micro level, from the perspective of people living with HIV. I synthesise the secondary evidence to refine the initial programme theory that was developed in the previous chapter based on stakeholder views, expert advice, and theoretical knowledge. A set of refined and collated context-mechanism-outcome configurations are produced in an explanatory middle-range programme theory that can be tested (refined, confirmed, or refuted) in future studies of human-supported mHealth. The findings of this chapter are particularly timely given the potential shift towards care that is provided by chatbots that are driven by generative artificial intelligence, instead of humans.

5.0 Abstract

Mobile phones can be used to offer HIV care in various ways. Mobile Health (mHealth) approaches that use mobile messaging connect patients either to human providers, or to technologies. This realist synthesis was conducted to contextualise how human supported mHealth can improve HIV care through mobile messaging. Evidence across multiple disciplines was assembled via systematic and iterative searching processes. The data were synthesised according to realist principles. The findings suggest that a therapeutic relationship emerges when mHealth proactively engages patients, through tailored, flexible, open, and ongoing messaging, with providers who are responsive to patient needs. Building a therapeutic relationship can enhance trust and patients' ability to share concerns, in turn enhancing providers' ability to offer holistic care. I provide recommendations on when and how to use human support and when and how to emulate aspects of a therapeutic relationship in interactive digital health.

5.1 Introduction

Given the increasing use across social groups of mobile phones, mobile health (mHealth) strategies are being increasingly employed to deliver support and make services less 'hard-to-reach' for multiple patient groups, including people living with HIV (S. B. Lee & Valerius, 2020; Mills & Lester, 2019; Nittas et al., 2020). Based on existing evidence with regard to mobile-messaging interventions, the World Health Organisation (WHO) recommends the use of two-way messaging interventions to promote engagement with the HIV care continuum (WHO, 2015), from diagnosis to treatment linkage, initiation, retention, adherence, and ultimately viral suppression (see Figure 1.9). As a platform, mHealth can offer a range of services such as remote monitoring, support, counselling, and data-collection, utilising a variety of features, including mobile-messaging, video-calling, smartphone applications, and biosensors (Marcolino et al., 2018). While mHealth can be high-tech, options such as mobile messaging that are relatively simple, low-cost, and easy-to-use are particularly suited to supporting the provision of long-term care for those who face challenges in reaching or engaging with traditional health services (Haberer et al., 2017).

Importantly, two-way messaging interventions either connect patients to a human (a healthcare provider or peer supporter) or alternatively to a technological response (an automated system that can be personalised) (Haberer et al., 2017; Hardy et al., 2011; Lester et al., 2010; Mbuagbaw et al., 2012), including artificial intelligence (AI) platforms and chatbots (Fadhil, 2023; Peng et al., 2022; You et al., 2020). Both designs introduce regular check-ins and active-follow-up initiated by the health system, but the former produces patient-provider human interactions (Lester et al., 2010), while the latter could generate automated (Gross et al., 2019; Nordberg et al., 2023) or interactive responses operated by AI chatbots (Fadhil, 2023; Peng et al., 2022; You et al., 2020). Further, upon taking the medication dosage, each approach may involve optional (Mbuagbaw et al., 2012) or required (Hardy et al., 2011) responses from patients. Yet, systematic reviews and meta-syntheses have largely disregarded these important differences in the design of two-way messaging interventions, with the implication that overall two-way messaging has been found to be an effective strategy to promote adherence behaviour (Taylor et al., 2019; WHO, 2015a) but with little consideration for the potential differential impacts that could stem from the operational mode of the messaging (i.e. human supported or technology-based). However, two-way interventions are more complex when they are human-supported as they involve patients' and providers' decisions, reasoning, responses, and (re)actions. Therefore, it is essential to disentangle the contribution of different design features and investigate the differential impact of human support and patient-provider interactions (or lack thereof) on engagement with the HIIV care continuum (see Figure 1.9), in terms of retention in care and adherence to treatment.

This paper investigates what value (if any) is added to HIV care when a *human* provider (as opposed to a technological response) proactively sends and responds to patients via mobile messaging platforms. To answer this question, a realist synthesis was conducted with the aim of exploring *how, why, for whom, and in what context* mHealth that offers two-way mobile messaging with human providers may support retention in HIV care and adherence to treatment. The specific review questions below seek to produce a nuanced understanding of what contextual aspects of the intervention are important in triggering the specific mechanisms that may in turn generate different outcomes. Based on this explanatory evidence synthesis, I provide recommendations to inform the design and evaluation of *interactive* mHealth and digital health services. Henceforth, given the focus of this paper on

two-way mobile messaging, any reference to mobile messaging is specifically referring to two-way messaging. Importantly, the term mobile messaging is inclusive of app communication, such as WhatsApp and iMessage, in addition to SMS communication.

5.1.1 Review Questions

- In what contexts (if any) could mHealth provide better HIV care by offering mobile messaging between patients and *human* providers?
- What mechanisms might be initiated within the context of mHealth that offers mobile messaging with *human* providers to promote retention in HIV care and adherence to treatment?
- What are the outcomes produced by the context and mechanisms triggered via mHealth messaging with *human* providers for people in HIV care?

5.2 Methods

To unpack the underlying processes by which human-supported mHealth programmes produce improved outcomes in terms of retention in care and adherence to treatment, a realist approach was used because this provides the opportunity to develop explanatory insights by using a broader spectrum of evidence in a configurational, as opposed to summative, synthesis. Specifically, realist synthesis can unpack the black box of interventions that involve human reasoning, decisions, and (re)actions (Pawson & Tilley, 2014). Rooted in a realist philosophy of science, this approach aims to study social reality indirectly through contextual, interpretive, unmeasured (qualitative) and measured (quantitative) evidence. As a theory-driven approach with an explanatory purpose, realist synthesis aims to uncover how context interacts with causal mechanisms to produce specific outcomes (Duddy & Wong, 2023). Rather than summating the evidence on what works, evidence is configured to provide an explanation of what works, in what context, how, why, and for whom (Pawson et al., 2005).

This realist synthesis was conducted using the five stages outlined by Pawson (2006) with the aim of refining an initial programme theory that explains how mHealth designs using patient-provider mobile messaging can be useful in the context of lifelong treatment for HIV.

The synthesis is reported according to The Realist and Meta-narrative Evidence Synthesis: Evolving Standards (RAMESES) (Wong, 2017). The synthesis is an iterative process of evidence gathering, data analysis, and programme theory enrichment to reach a refined set of configurations that capture the interactions between the context and mechanisms that produce specific outcomes. The stages of the synthesis are briefly outlined in Table 5.1 below and in detail in Table B1 of Appendix B.

Table 5.1 Summary of Realist Synthesis Methodology	
Stage 1: Developing the initial programme theory (IPT)	The IPT summarises the initial understanding of how a programme works. The IPT for this synthesis (see Figure 4.4) was underpinned by patient perspectives, expert advice, brainstorming, and identified theories in the literature. The scope of the synthesis was narrowed through the IPT in two major ways: a) narrowing the focus to aspects of lifetime treatment that can be modified by mHealth, and b) limiting it to the causal explanations on how mHealth affects care *for* people living with HIV, setting aside the question of how mHealth can change the larger health system.
Stage 2: Searching for evidence	The search for evidence aimed to assemble a body of relevant data with explanatory power to refine the IPT. A broad range of sources were searched and literature across multiple disciplines was considered. Additional documents were identified via supplementary search methods such as citation tracking and expert advice. Later searches identified relevant substantive theory to act as a theoretical lens through which to understand the overall findings. Overview of the main search is provided in Table B4. Full details of the main search and supplemental search strategies are provided in Appendix B Tables B5 and B6.
Stage 3: Selecting and appraising documents	Documents were included when providing evidence on two-way mHealth to support treatment adherence and engagement with care by connecting patients to providers for interactive communication. Studies of two-way messaging were excluded when they did not involve human support. Full text articles were further screened for relevance (whether some part[s] of the document contributed insight) and rigour (whether the data used was

	credible). The theoretical literature was selected when providing insights on the refinement of programme theory and recommendations for designing interactive digital health interventions.
Stage 4: Extracting and organising data	The documents were read and coded in MAXQDA. Contributing documents were organised within three layers: *the primary core* included primary studies on human supported mHealth for HIV care; *the topical core* included studies and key reviews that provided insights on the contexts and mechanisms of human supported digital health for HIV care; *the theoretical core* included studies that provided a theoretical lens through which to understand the overall findings of the synthesis. Characteristics of selected documents are provided in within Appendix B, Table B3.
Stage 5: Synthesising the evidence	The coded data extracts were configured to produce explanations of the relationship between context, mechanism, and outcomes, which form the building blocks of the refined programme theory. The iterative process of synthesis continued until theoretical saturation was reached, at which point many of the overlapping context-mechanism-outcome configurations (CMOCs) were collated. To mitigate subjectivity in the analysis, the reasoning behind the analytic stage of developing CMOCs and refining the programme theory was discussed in various rounds between two authors (VA and GW). VA is a doctoral student, who is investigating the possibilities of mHealth for HIV care, and GW a clinically active family physician (general practitioner). Two collaborators (JH and LS), who provided feedback on the findings and refined programme theory, are content experts with experience in designing and conducting several key trials of mHealth for HIV care. JH is also a practicing infectious diseases specialist.

5.3 Results

A total of 77 documents, including primary studies, key reviews, theoretical literature, and commentaries, contributed to this review, of which 61 documents were identified through the main search strategy and an additional 16 documents were identified through additional searches. The document flow chart is presented in Figure 5.1. A core group of 15 empirical studies examined various aspects of mobile messaging with providers for adults living with HIV. An additional 46 documents, including key reviews, relevant primary studies, and commentaries contributed more data to the synthesis. Further insight was derived from a total of 16 documents, comprised of theoretical literature and relevant empirical studies, that were identified through iterative searching and citation snowballing. Overall, the documents comprised of six randomised controlled trials, two quasi-experimental studies, four qualitative studies, three conversation analyses, one mixed-method study, one theoretical evaluation of an intervention protocol, two protocols, one pilot trial, one cost-effectiveness analysis, one gender analysis, thirteen systematic reviews, five overviews of evidence, one realist review, eight narrative reviews, and eight commentaries. The additional theoretical literature and relevant empirical studies included two books, one qualitative study, six empirical studies, and seven literature reviews. Full details of the included documents are provided in Appendix B, Table B7.

The finalised refined programme theory developed from the realist synthesis is underpinned by seven CMOCs, which are briefly summarised and organised by the four outcome domains of the refined programme theory (see Figure 5.2), highlighting the added value of human interactions through mHealth check-ins between patients and providers. These seven overarching CMOCs help to explain how, when, why, to what extent, and for whom living with HIV can be influenced by regular mobile messaging between patients and providers. The data suggests that mHealth communication with providers can offer a range of benefits in the context of living with HIV, that are underpinned by the building of a therapeutic relationship that enables continuous care. This finding is consistent with Mol's work on diabetes and the logic of care for lifelong treatments (Mol, 2008). In the following sections, the findings are presented in a narrative format, structured around the four outcome domains that emerge from the interactions between the context provided by mHealth and mechanisms triggered as a result. Details about the CMOCs may be found in Appendix B, Table B8.

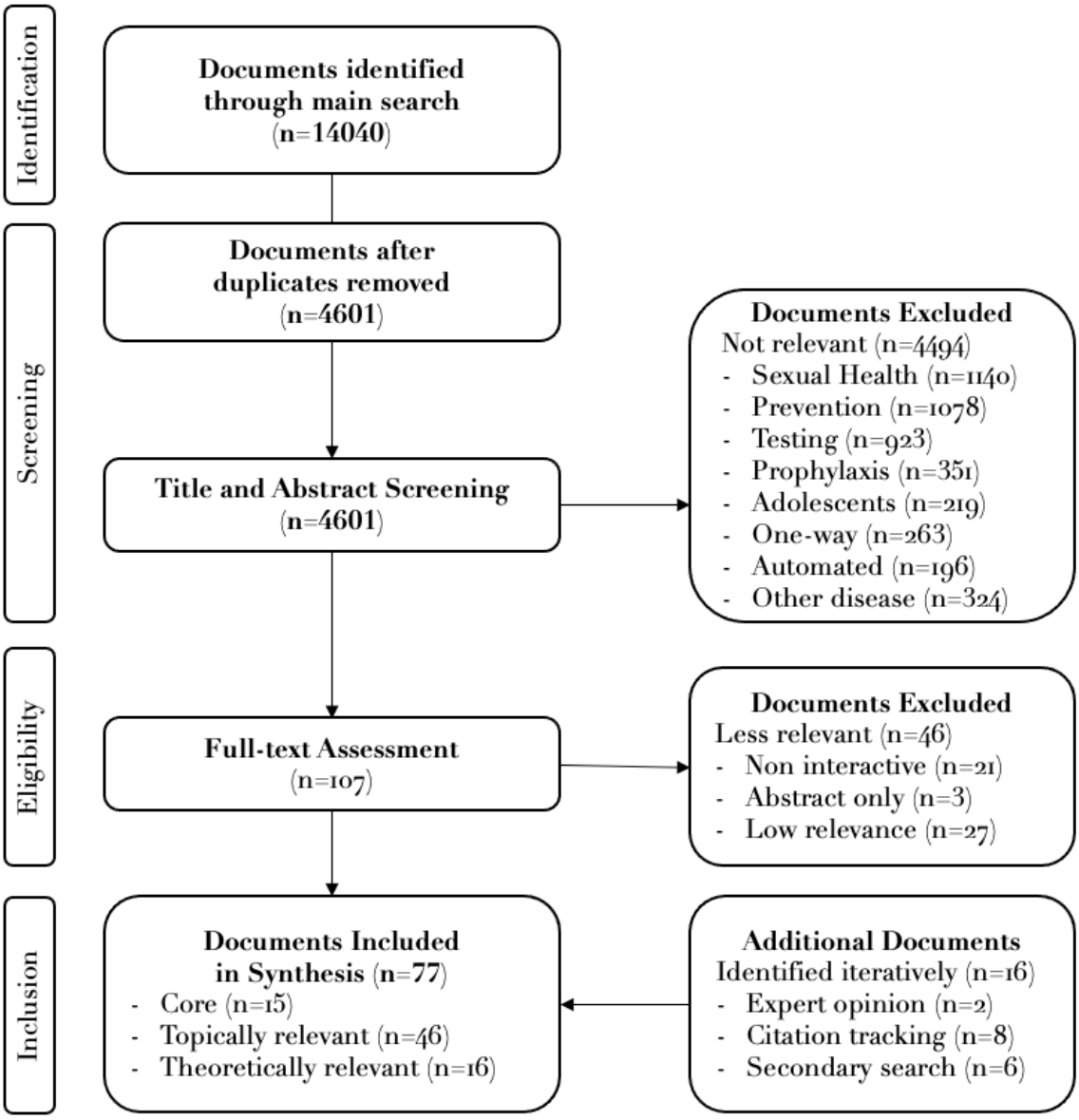

Figure 5.1 Document Flow Chart

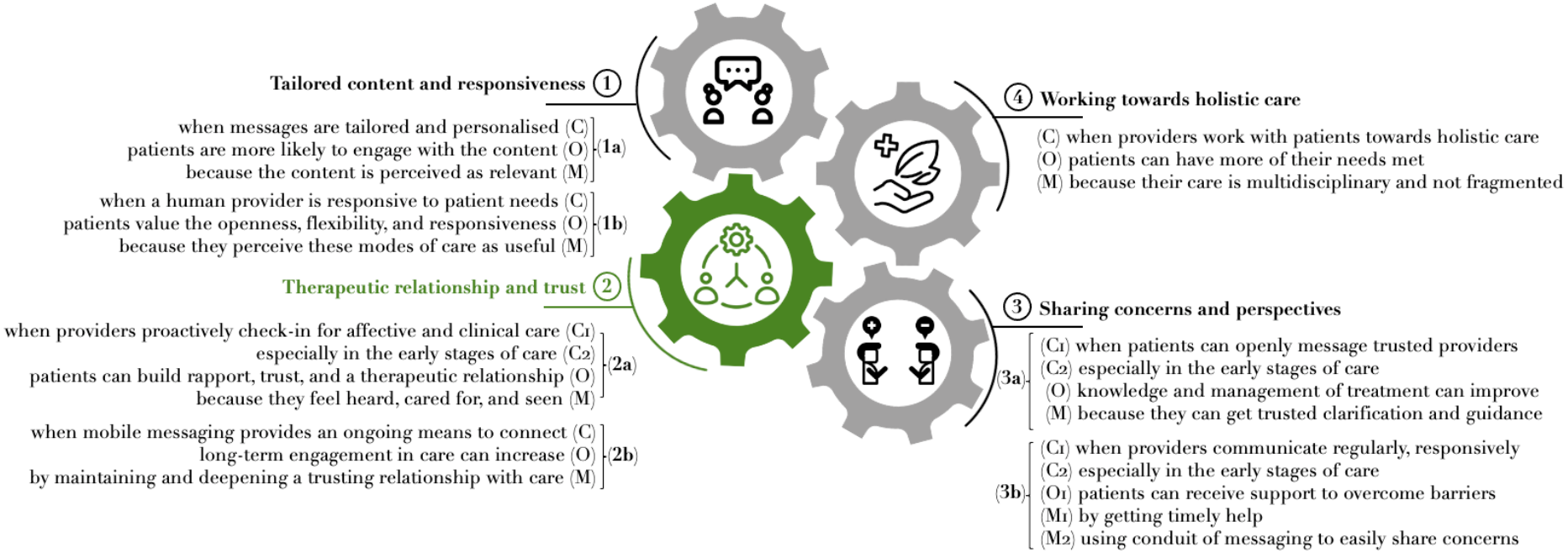

Figure 5.2 Realist Programme Theory. This figure is a summary of the final programme theory that is assembled through a configuration of data as Contexts (C), Mechanisms (M), and Outcomes (O). The figure illustrates the interconnectedness of the four domains (wheels) that hinge on the building of therapeutic relationship (green) between patients and providers. The detailed analysis and data illustrations that underpin these four domains and seven CMOCs are outlined in Appendix B Table B8.

5.3.1 Tailored Content and Responsiveness

Our findings suggest that personalised models of mHealth for people living with HIV can improve perceptions about the relevance of the content, and add value through perceived openness, flexibility, and responsiveness of the service. This may reflect the fact that mHealth intervention designs with a more personalised and tailored approach can engage different individuals with different needs (i.e. reflecting the diversity of groups who live with HIV and the complexity of lifelong antiretroviral therapy adherence for each group). Providing tailored content through a personalised language enhances engagement and interaction with patients, because patients find the content to be individually relevant to them (CMOC-1a). Beyond personalisation, having a human provider to regularly check-in via mobile messaging was reported to be a useful, worthwhile, and trustworthy aspect of the intervention (Rana et al., 2016), providing a sense of having a 'lifeline' (Bardosh et al., 2017). Patients then used this lifeline to discuss complex personal, emotional, and psychosocial issues that form the barriers to engagement in care and adherence to treatment (i.e. in terms of the stigma and discrimination that is faced in the context of living with HIV).

When messaging with a human provider, patients perceive their communication as useful as a result of being unbounded and responsive towards their specific needs and intended goals (CMOC-1b). Perceived responsiveness can predict patient satisfaction and contribute to subjective health status (Reis et al., 2008). Being responsive to patient needs appears to help patients build trust and engage more with the intervention and their treatment. Importantly, being connected to a responsive provider, who is known and identifiable, elevates the perceived value and credibility of the intervention (Müssener, 2021).

5.3.2 Therapeutic Relationship and Trust

When providers use mobile messaging to proactively check-in on patients (Chi & Stringer, 2010), especially in the early stages of care (Bayona et al., 2017), patients feel cared for and can raise their clinical and non-clinical concerns with providers. If providers are willing to be proactive and attentive to concerns raised by patients, the platform can also be used to discuss the affective aspects of living with HIV and engaging with care (Bardosh et al., 2017). In turn, patients are able to build trust and rapport with providers over time, leading to a therapeutic

relationship in which providers can provide affective communication, and patients can share their problems while feeling heard, cared for, and seen (CMOC-2a) (Müssener, 2021). When patients have established relationships with their healthcare providers, continued mobile messaging can help them maintain the existing relationship (Smillie et al., 2014).When patients lack support and pre-existing relationships with their healthcare providers, the platform can help them build one and remain connected to care (Mwai, 2015). Over time, ongoing communication can maintain and deepen the therapeutic relationship, which can enhance engagement in care (CMOC-2b).

Proactive and affective care, which focuses on socioemotional needs of patients, can protect against a sense of being neglected (Mol, 2008), and can enhance trust in the therapeutic relationship, between patients, their providers, and the healthcare system. The extent to which providers are open to affective care can be distinguished through conversation analysis, assessing the proportion of 'cure talk' versus 'care talk'. The former focuses on instrumental needs and tasks, such as diagnosis and medical treatment. The latter focuses on the psychosocial needs and forms the basis of building a therapeutic relationship (Greenhalgh & Heath, 2010; Roter & Larson, 2002). Acknowledging socioemotional needs when prescribing treatment plans can help patients be more accepting of treatment goals, because they can trust that providers and the healthcare system are offering services with their best interests at heart. Indeed, patients are more likely to be dissatisfied and change their provider when they do not feel listened to (Federman et al., 2001), while across settings, perceived trust has been shown to be an important predictor of care satisfaction (Reis et al., 2008). Building a long-term therapeutic relationship with trusted providers can be a valuable resource to enhance how patients relate to healthcare services as they feel understood, accepted, and supported by their providers (Reis et al., 2008). Digital health and mHealth approaches will equally benefit from maintaining a human touch, emphasising the value of continuous and long-term therapeutic relationships, while simultaneously utilising digital features that can enhance frequency, ease, and efficiency of patient-provider communication (Tremain et al., 2020; Verhoeks et al., 2019).

5.3.3 Sharing Concerns and Perspectives

Our findings suggest that when patients need to openly share their questions and concerns with providers, especially in the early stages of care, they can access a trusted source to receive timely clarification with regards to ambiguities and misinformation, and clinical guidance regarding concerns and complex treatment tasks; this enables them to become equipped in coping with their condition and adhere to medications more easily (CMOC-3a) (Bayona et al., 2017). Moreover, managing HIV is facilitated for populations who face barriers in reaching brick and mortar health services (Marcolino et al., 2018). As such, in accordance with good practice, patients are not left 'to their own devices' (Mol, 2008), when they have open and direct access to clinical care at times when they face ambiguities relating to treatment and care.

Moreover, these findings indicate that mHealth and mobile messaging platforms facilitate convenient and frequent sharing and exchange of information in multimedia forms. Flexible, versatile, and unbounded sharing of experiences and perspectives can benefit clinical decisions: clinicians can receive multimedia and photographic information, and patients can share detailed information on the side-effects they experience in real-time or as needed, depending on how frequently they are able to contact providers (Bayona et al., 2017). The timeliness, convenience and versatility of mobile messaging's conduit for knowledge and perspective sharing between patients and providers can significantly broaden the possibilities of addressing challenges faced by patients to better care for and live with HIV (CMOC-3b). For patients, having a trusted human source of information, someone who is accessible easily and directly, and with whom they have built a relationship, can be highly impactful. For providers, having access to timely updates and perspectives from patients and their experiences can improve tailoring of care for more patients. Overall, the capacity for mobile messaging to be a convenient, frequent, reliable, flexible, fast, and versatile conduit can be instrumental in exchanging knowledge, concerns, and perspectives to provide good and timely care (Müssener, 2021).

5.3.4 Working Towards Holistic Care

People living with HIV often face a multitude of psychosocial issues that interfere with and inhibit adherence to treatment. Opportunities for patients and providers to work and strategise together can help overcome some of these barriers, but this requires providers to be willing and able to counsel patients and find appropriate solutions to psychosocial and behavioural challenges, making appropriate referrals and keeping track of multidisciplinary needs of patients (M. C. M. Murray et al., 2015). Multidisciplinary care, in which the caregiving team works together with patients to meet more of patients' needs, reduces fragmentation of care and enhances retention. By eliciting and bolstering problem-solving and constructive interactions with mHealth providers, patients can solve their immediate problems collectively with providers, and providers can more readily make holistic and multidisciplinary care available to patients with complex needs (CMOC-4). Working towards holistic care and shared goals represents a shift towards patient-centred practice and appears to be more affective as a result of the active demonstration of care (Mol, 2008).

5.4 Discussion

5.4.1 Summary of Findings

Overall, the data included in this synthesis suggests that the convenient and versatile conduit of mobile messaging can proactively engage patients, through tailored, flexible, open, and ongoing mobile messaging, with providers who are responsive to patient needs, thereby providing a therapeutic relationship. The building of a therapeutic relationship can in turn enhance trust and increase the patients' ability to share concerns. Furthermore, the ability of providers to offer holistic care is enhanced through the use of this technology to connect users with multidisciplinary sources of support. Importantly, these findings show that in order to realise these benefits, three overarching contexts need to be present: mHealth should facilitate communication that is tailored and open; with providers who are willing and able to regularly be attentive and responsive to patient shared needs; and patients who are enabled to trust providers for sharing their concerns. The presence of these three contexts enables a patient-provider therapeutic relationship that can act as an overarching mechanism in facilitating improved outcomes.

This synthesis focussed on answering the question: what value (if any) is added to HIV care when a *human* provider (as opposed to a technological response) proactively sends and responds to patients via mobile messaging platforms. This study's findings suggest that forming a relationship with providers adds value that can be transformative in the care, treatment, and ultimately lives of people with HIV. This finding is consistent with the wider psychotherapy literature, which also recognises the contribution of the client-therapist relationship as being core to the healing process. Moreover, this synthesis finds that the key aspects of the emerging therapeutic relationship are consistent with Mol's work on *logic of care* for lifelong diabetes treatment (Mol, 2008), which provides a useful framework to examine how mHealth can impact upon patient relationships with providers and the larger healthcare systems, in terms of: openness, continuity, flexibility, reflexivity, unboundedness, and holisticness of care.

Patients may need care for multiple long-term conditions; instead of addressing these conditions separately, holistic care considers the 'whole person' and distinct individual needs, addressing the combined impact of co-morbidities, psychosocial, and lifestyle factors in the lives of diverse groups living with HIV (Jongbloed et al., 2015). Across clinical settings, differences in consultation styles relates to the extent to which psychosocial problems are addressed when diagnosing medical conditions. Empirical evidence shows that different countries, cultures, and health systems may provide a different degree of psychosocial consultation as part of routine medical treatments (Deveugele et al., 2004). Relative to most clinical care, HIV care has generally strived to be more sensitive and responsive to psychosocial needs, but differences in care culture and contexts should be considered when designing digital interventions with provider support. The extent of provider willingness and ability to strategise with patients for enhancing multidisciplinary care will be an important context that will interact with the intervention design to produce different outcomes.

Finally, the findings of this study signify the interconnectedness of the key outcomes. First, engagement is improved by offering tailored content and connecting with responsive providers. Second, a therapeutic relationship can develop when patients can trust and feel cared for by providers. Third, the conduit of messaging is used in a way to facilitate the sharing of concerns and perspectives, through various multimedia forms, between patients and providers who have developed a trusting, responsive, and therapeutic relationship. Fourth, the relationship built, and the opportunities created for more

interactions, can empower patients and providers to strategise together and address treatment needs holistically and through multidisciplinary care. As such, each domain of the programme theory deepens the therapeutic relationship over time, improving the conditions through which patients engage with antiretroviral therapy. Such interconnectedness resonates previous findings on the 'ripple effects' of trust built in partnerships through community-based research, between researchers and community stakeholders (Jagosh et al., 2015). The model that I developed comprises a set of interconnected middle-range theories, with rippling effects, that can be tested (i.e. refined, confirmed, or refuted) through future research. It provides possible explanations in terms of the interaction of contexts and mechanisms, that in turn influence the patient-provider relationship, in terms of trust, support, care, and life of patients.

5.4.2 Contribution to Existing Literature

Evidence from mobile-messaging studies, designed as one-way versus two-way, have contributed to guidelines developed by the WHO for treatment adherence support strategies (WHO, 2015a). Indeed, several systematic reviews and meta-analyses have examined the efficacy of bidirectional and unidirectional messaging interventions, emphasising the salience of directionality, flexibility, tailoring, and appropriate frequency of messaging, but ignoring the intervention's mode of operation (i.e. human supported or purely technology-based) (Amankwaa et al., 2018; Finitsis et al., 2014). The findings of the current review extend existing knowledge with regard to the processes by which human support make vital contributions to intervention outcomes via human reasonings and (re)actions.

Notably, prior studies have found that unidirectional and technology-based approaches can also elicit feelings of being 'cared for' by the health-system (Ware et al., 2016), especially when these are tailored to specific patient needs (Dillingham et al., 2018). As such, there is an ongoing debate on whether adding 'warmer', 'caring', and more 'human' touches to technology-based approaches, such as chatbots that are operated by generative AI, can induce some aspects of a therapeutic relationship, such as engagement, trust, and responsiveness (Müssener, 2021; Tremain et al., 2020; Verhoeks et al., 2019). The findings add to this debate, by highlighting key aspects of a therapeutic relationship in human-supported mHealth that could be emulated (even if partially) to improve engagement with digital health.

The therapeutic relationship construct has been applied to various settings where relationships are important, including classrooms, hospitals, and even reformative prison settings (A. Horvath, 2000). Originally constructed within psychotherapy literature, Rogers first theorised, and later empirically demonstrated, that the therapeutic relationship *itself* can be transformative by providing the three main constructs of unconditional positive regard, empathy, and congruence (C. Rogers, 1951). Balint applied this therapeutic relationship modality to medical care, suggesting that some patients benefit from 'the doctor as the drug', emphasising the relational connection of patients to practitioners (Balint, 1955). Bordin later highlighted that the *strength* of the therapeutic relationship, regardless of treatment modalities and therapeutic approaches, can determine treatment outcomes (Bordin, 1979). Remarkably, recent empirical studies on the mechanisms of the placebo effect highlight the significance of the relationship with providers, in addition to the rituals of treatment and care, in producing the placebo effect, thereby individuals cannot give themselves a placebo 'treatment' (Kaptchuk et al., 2008). The findings can be better understood within this theoretical backdrop, suggesting that *relational connection* appears to be the key driver of engagement with digital health interventions, while highlighting the importance of trust, openness, and responsiveness that shape the therapeutic relationship (or working alliance) and add value in the context of living with HIV and adhering to lifelong antiretroviral therapy.

5.4.3 Recommendation for Practice

The uptake of technologies in healthcare is rising at an unprecedented speed following the COVID-19 pandemic, and it would as such be timely to examine exactly what human supported digital interventions can offer that unsupported digital solutions cannot. Importantly, two-way communication strategies that involve (often unacknowledged) provider support, have been shown to lead to burnout, especially among female providers (Mano & Morgan, 2022; Rittenberg et al., 2022). Thus, it is vital to consider when to use human-supported digital health, and what relational aspects of such interventions, such as trust, responsiveness, and flexibility, can be carefully emulated in the design of purely technology-based interventions. To this end, I applied the review findings to develop a checklist of recommendations (see Box 5.1).

Box 5.1 Checklist to Support Designing Interactive Digital Health Programmes

I. To enhance usefulness, consider:
1. Working towards a logic of care, through:
    a. Openness
    b. Continuity
    c. Responsiveness
    d. Personalisation
2. Building a therapeutic relationship,
    a. Empathic engagement
    b. Enhanced trust

II. To enhance ease of use, consider:
3. Facilitating communication and interaction, through:
    a. Flexibility and speed
    b. Simple communication
    c. Multimedia platforms

III. To enhance compatibility, consider:
4. Tailored content
5. Holistic care

To articulate the recommendations, I used the main constructs of the Technology Acceptance Model (i.e. perceived usefulness and perceived ease of use), but also maintain the additional and original construct of compatibility from the Diffusion of Innovations Theory (Davis, 1989; Rogers et al., 2014). The findings of this synthesis suggest that the perceived usefulness of mobile messaging with human providers lies in the existence of a therapeutic relationship and endorsing a logic of care. Perceptions of ease of use lie in the proactiveness and convenience of interactions. The perceived compatibility appears to relate to the tailoring of content and caring holistically. Through applying these constructs, the aforementioned checklist to support decision making in the design of interactive digital health, which may have transferability to non-HIV care, was developed (see Box 1).

5.4.4 Strengths and Limitations

This is the first realist synthesis of evidence to explore the added benefits of having human support and interactions in mHealth interventions. A key strength of this realist synthesis is the incorporation of a range of evidence from diverse sources. In contrast to summative reviews of evidence, in which typically only one type of evidence is used, the configurational orientation of the realist synthesis relies on the interpretation of evidence and theoretical

literature across disciplines. As a result, the findings and recommendations may be transferable to other non-HIV care settings, where therapeutic relationships are important. While there are considerable differences with regards to HIV care from that of diabetes for example (e.g. by making provider trust essential in the context of HIV-related enacted and self-stigma), similar aspects of a therapeutic relationship elicited here are instrumental in other care contexts (e.g. to a different extent for diabetes care which may involve self-blame and shame in terms of dietary and lifestyle habits) (Mol, 2008).

Importantly, given the interpretive nature of a realist synthesis, researcher background and perspectives may have influenced the direction of the iterative process of developing a programme theory. To mitigate this, I discussed my decisions at key stages of the review process with my supervisor, a clinically active family physician (general practitioner) (GW). Moreover, the predominant use of randomised controlled designs to assess the primary and secondary outcomes of mHealth technologies, also meant that information on the contexts and mechanisms of interventions was sparse. To compensate, I drew on a wider range of perspectives to inform the interpretations of the data during analyses. Two collaborators (JH and LS) were content experts, with experience designing and conducting several key randomised controlled trials of mobile-messaging interventions on adherence to medication and provided feedback and advice on the findings and programme theory (JH is also a practicing Infectious Disease specialist). However, due to financial constraints, it was not possible to recruit a larger expert advisory group for the entire duration of the study. In a future study, I will further refine the programme theory through a realist evaluation of a human supported messaging intervention between providers and patients (Ameli et al., 2021), which would be the first realist evaluation of a messaging intervention.

5.4.5 Implications for Future Research

The programme theory conceptualised in this synthesis can form a steppingstone in the future design and evaluation of interactive digital interventions for retention in care and lifelong treatment: first, there is a need to improve engagement by tailoring content and responsiveness to patient needs; second, to assess how the strength of the therapeutic relationship can be increased and the further impact on building patient trust; third, increasing the opportunities

for sharing concerns, experiences, perspectives, and information in multimedia forms and evaluating stakeholder perceptions about this; and fourth, by working towards holistic care. It would be beneficial to further examine the relational contribution of human support in digital health interventions, by opening the 'black box' of the therapeutic relationship that exists within the 'black box' of the digital intervention itself. An important research question that remains critical is how and when to include human support, considering that human resources are limited across health systems, and when to use technological responses, considering the aspects of a therapeutic relationship that can be induced via technology-based designs.

5.5 Conclusion

This study has presented the first realist synthesis of evidence to unpack the value of human-supported mHealth in the contexts of HIV care and engagement with antiretroviral therapy. The synthesis has produced a middle-range theory, with seven configurations of contexts, mechanisms, and outcomes that are categorised within four overarching and interactive domains. These domains that highlight the added value of connecting patients and providers through an interactive mobile messaging programme include: (1) the ability to offer tailored content and responsiveness; (2) the building of a therapeutic relationship and trust; (3) the sharing of concerns and perspectives; and (4) the possibility of working towards holistic care. Crucially, in light of healthcare staff and resource shortages across various global settings and given the emerging possibilities to offer care via interactive technological features (e.g. by taking advantage of generative AI, such as ChatGPT) it is highly relevant to consider whether, when, how, for whom, and in what contexts similar therapeutic relationships can be developed. To this end, using the findings of this synthesis I have developed a checklist to support decision makers when designing interactive digital health interventions for HIV care and conditions that require long-term treatment.

We have the tools for prevention, diagnosis, and care. What we lack is an equity plan linked to a delivery system.

— Paul Farmer & Louise Ivers

6

Discussion

6.0 Contribution

Living with HIV is a chronic condition that entails lifelong engagement with medical care and adherence to antiretroviral therapy. Mobile phones have enabled new modes of caring for people living with HIV. High quality evidence is needed to produce a more nuanced understanding of how remote care, offered via mobile phones, can interact with the contexts of living with HIV in ways that can improve lifelong engagement with antiretroviral therapy. To enhance the adoption, scale-up, and sustainability of mHealth interventions, a wide range of evidence is needed (Greenhalgh et al., 2017). Yet, public health research into how mobile phones can enhance HIV care and adherence to treatment are distinctively short-term and narrowly focused. Further, research is predominantly conducted in settings that either have high resources or a high prevalence of HIV and as such different priorities for HIV care in policymaking. The effect sizes produced through such research, demonstrating the positive impact of mHealth in terms of improved daily adherence and viral suppression rates, fail to inform stakeholders on how various mHealth approaches can fit the wider contexts into which they must be adopted. As a result, there is a wide gap between research output and practice input.

Translation of research findings into practice in the area of mHealth and HIV care is highly stagnant—as illustrated by numerous randomised controlled trials and over 50 competing meta-analyses and systematic reviews with regard to the design and efficacy of mHealth interventions in improving adherence behaviour or enhancing HIV care. Yet, the field remains popular as a large amount of research money, time, and effort are invested to support trials of mHealth for adherence behaviour and HIV care. To date, these investments have not engendered much clarity in terms of when, how, for whom, and in what context mHealth can improve HIV care and treatment outcomes. After a decade of investigation, academics are still researching the efficacy of various designs, while practitioners have rarely adopted and scaled-up these programmes beyond the research trial periods. Such academic research produces findings with high internal validity at the expense of external validity and limited impact on policy and practice, thereby resonating with the challenges faced in other areas of policy-relevant evidence-based research (Cairney, 2016; Pearson & Coomber, 2010). Moving forward from these narrow debates demands a research approach that produces an in-depth understanding of how a complex intervention or phenomenon unravels, in addition to addressing 'what works.'

In the introduction to this thesis, I highlighted the challenge of complexity that underpins the plight of digital health interventions to repeatedly reincarnate through deterministic research paradigms. As such, to explore the role of context and its interactive relationship with mHealth, throughout this thesis I adopted a realist lens of inquiry and drew on diverse sources and types of evidence (Wong et al., 2013). The knowledge produced in this thesis is aimed at enabling researchers and practitioners to configure interactive mHealth programmes across contexts in a way that triggers desired mechanisms that in turn generate intended outcomes. The standalone papers presented in this thesis are part of a larger research project that conceptualises interactive mHealth as a complex intervention for HIV care in various global settings and uses a range of evidence to investigate the efficacy, effectiveness, acceptability, and feasibility of mHealth interventions to enhance HIV care in Iran. In this discussion, I will use the first three domains of the NASSS framework to thematically summarise the main findings of the standalone papers that were presented in previous chapters, before discussing overall limitations, further research, and policy implications.

6.1 Overview of Findings

The overarching aim of this thesis was to understand how mHealth can change the contexts in which HIV care is engaged with, using primary data from Iran and secondary evidence from a range of global settings. To structure the findings of this thesis in a way that allows a broad discussion about the interactive role of mHealth interventions in the contexts of HIV care, the findings are presented thematically, as follows:

1) *The condition*: DPhil paper I contextualised (dis)engagement from HIV care and lifelong treatment by studying the socioecological context of living with HIV in Iran.
2) *The technology*: DPhil papers II and III conceptualised and proposed how mHealth features change the contexts of HIV care and engagement with treatment in Iran.
3) *The value proposition:* DPhil paper IV conceptualised an evidence-based and theory-informed programme theory that underpins two-way provider-supported mHealth for HIV care.

6.1.1 The Condition

The experience of living with HIV is strongly influenced by sociocultural factors that introduce multiple layers of complexity into the contexts of lifelong engagement with treatment. DPhil paper I advanced a more nuanced understanding of (dis)engagement from antiretroviral therapy in Iran. Previous studies mostly consisted of decontextualised quantitative surveys of risk and protective factors for treatment adherence. My findings advanced what is already known by shedding light on the pathways from socioecological context to individual level reasonings and (re)actions that result in disruptions of daily treatment and disengagement from HIV care. These pathways were found to be thematically driven through the individual-level affective and cognitive responses of *denial, fear, and despair.* The pathways specific to the socioecological context of living with HIV in Iran appear to be denial in response to societal negative perceptions of HIV, fear in response to societal lack of awareness regarding HIV and misinformation, despair in response to HIV-related stigma and enacted discrimination, economic insecurity, and lack of social support. Temporal changes in economic and political conditions, such as intensified financial sanctions that led

to higher levels of economic insecurity, price inflations, and a cost-of-living crisis further intensified feelings of despair, negatively interacting with the motivation for self-care and treatment continuity. Thus, interventions that aim to prevent disengagement from HIV care in Iran, must counter the triggered reactions of fear, denial, and despair. To do so, they must intervene in the multi-layered socio-ecological and temporal forces that trigger these reactions and shape the experience of living with HIV in Iran.

In settings such as Iran, where societal stigmatisation of HIV can trigger a very strong sense of internalised shame and stigma (UNAIDS, 2022), an HIV diagnosis can lead to a grief response. The findings of this thesis suggest that grief for the newly diagnosed was triggered through the process of engaging with lifelong antiretroviral therapy that was accompanied with a sense of bereavement over the loss of one's former self and having to accept a new identity. As a result, denial appeared to act as a primary coping mechanism to reject the new identity of living with HIV, thus rejecting treatment initiation until HIV becomes symptomatic. But even after treatment initiation, living with HIV and adhering to daily and lifelong treatment can include a sense of loss that is associated with the new reality of living with a chronic illness. The sense of bereavement over the loss of self that follows a chronic illness experience has been previously referred to as '*chronic sorrow*' (Roos, 2013; Weingarten, 2012). In Iran, such chronic sorrow, when combined with economic pressures and daily encounters of enacted stigma, discrimination, and family disapproval, appears to pronounce feelings of despair, leading to isolation, disengagement from care, and suicidal thoughts. This finding corroborates previous evidence of heightened despair in response to precarious economic conditions and transitions into poverty, which can erode motivation for selfcare and lead to addictive and suicidal behaviour, characterised as 'deaths of despair'(Case & Deaton, 2015, 2020). As previously seen, coping with HIV and lifelong antiretroviral therapy, when experienced within periods of precarity and vulnerability, can be characterised by pronounced and oscillating experiences of grief, that can be conceptualised through the stage theory of grief (Kübler-Ross, 1969).

Crucially, the underlying patterns of reacting to and coping with HIV are context-specific and can vary as patients navigate across the HIV continuum of care (Gardner, 2011). The findings of my research show that the patterns of reacting to lifelong and daily adherence to antiretroviral therapy through denial, fear, and despair, differed among three groups: people

who were newly diagnosed with HIV, those who were living with HIV for over a year, and those who had multiple episodes of disengagement from care. These findings aligned with previous studies that cited denial as a primary reason for delayed *entrance* into medical care, as the newly diagnosed chose to not take up medical treatment to avoid and escape from their diagnosis (Jenness et al., 2012). Therefore, denial appears to be a strong cognitive reaction in the early period following diagnosis, during which phase it is crucial to keep people engaged in care and attempt to make the process of treatment initiation seamless, informative, and empowering.

Additionally, in the initial period following an HIV diagnosis, fear appears to have a strong presence, triggered by misinformation regarding antiretroviral therapy and concerns regarding a new medicalised life. Previous studies show that fear can be overcome through active, informative, and strengthened provisions of care (C. Campbell et al., 2011). Thus, interventions that produce care contexts that can lessen misinformation, reduce negative perceptions regarding HIV, and provide more clarity regarding antiretroviral therapy can diminish fear. While denial and fear constitute strong initial reactions to an HIV diagnosis, the findings here corroborate previous evidence that shows feelings of despair or a sense of chronic sorrow appear to have a more constant presence amongst those who were living with HIV for over a year, thus requiring long-term care and cyclical phases of support (Brion et al., 2013). It is therefore important to categorise and tailor interventions to the specific needs of patients that are newly diagnosed and those who have longer trajectories of (dis)engaging with antiretroviral therapy, given the different psychosocial needs of each group.

6.1.2 The Technology

Mobile messaging is a simple mHealth feature, available on all mobile phones, that requires minimal advanced knowledge for usage. Simultaneously, it can be used dynamically, leading to new configurations of patients and providers. For instance, when mobile messaging is used as an active communication channel between patients and providers, information and support can be delivered remotely, while symptoms and concerns can be reported as they are experienced in real-time. DPhil paper II conceptualised *how* mobile messaging can protect against (dis)engagement from antiretroviral therapy in Iran. When adopted for communication

between patients and providers, simple messaging can introduce new care structures, through which patients and providers exchange information and care. This thesis unpicked the potentially useful features and provisions of mobile messaging, when used for two-way communication between patients and providers, to be comprised of three key opportunities: provider connection, proactive care, and privacy and personalization in communication. When such provisions are introduced within health systems, existing resources can be retrieved more seamlessly, and patients can access providers more effortlessly. I used stakeholder views to ensure that the mobile messaging intervention that is based on evidence from other global settings will suit the priorities of patients and providers in Iran. Participants viewed the most useful aspect of mHealth to be relational by connecting them to providers and improving access to information and support. Further, participants explained that the proactive demonstration of care, as expressed through weekly check-in messages, could boost motivation for engagement with treatment and adherence to daily medications. Finally, the privacy and personalisation offered by mobile messaging was viewed by patients to provide a trusted and reliable connection to providers and health system resources.

The findings of this study were built on the contexts that lead to (dis)engagement with antiretroviral therapy in Iran as the focus group discussions and interviews included questions that addressed both the aspects of *the condition* and *the technology.* As such, stakeholders in this study envisioned *how* a two-way private and personalised communication, proactive care, and provider connection could dilute the harsh contexts that trigger fear, denial, and despair. An emphasis was made by stakeholders to focus intervention resources on the newly diagnosed, to keep them retained in care by countering reactions that are triggered by early-stage denial, fear, and despair. By enhancing access to trusted information and support, and by boosting patient motivation and initiative, the simple feature of mobile messaging with providers was conceptualised to be useful. These findings resonated with the constructs highlighted by the widely applied Information, Motivation, and Behavioural skills (IMB) model, positing that HIV-related behaviour can be influenced through enhancing individual-level information, motivation, and behavioural skills (Fisher & Fisher, 2000). In accordance, digital health interventions often apply the IMB model to identify intervention content (Aliabadi et al., 2015), despite valid criticisms that such application of the IMB model in technological interventions are too simplistic and decontextualised (Rivet Amico, 2011).

Instead of identifying intervention content, the findings here identified specific mHealth design features, including the key role of *human support* through provider connection, that offers proactive, personalised, and safe care that can enhance access to information and boost motivational and behavioural aspects of patient journeys.

Using stakeholder views and the conceptualisation of mHealth features for the context of HIV care in Iran, and the need to retain the newly diagnosed with HIV on treatment, I proposed a finalised adapted intervention, named HamRaah, meaning “together-in-path" in Persian. The protocol comprised of a pilot trial, a feasibility and acceptability study, in addition to a nested realist evaluation. DPhil paper III presents this protocol and the core process of HamRaah, shedding light on the role that will be played by human providers, as opposed to an automated system. To conceptualise HamRaah as a complex intervention and go beyond answering whether the intervention works in terms of achieving its outcomes, a full realist arm was proposed to be conducted in parallel to the trial. To this end, an initial programme theory (IPT) was developed by combining stakeholder views and qualitative findings from Iran, in addition to insights from the IMB model and critical expert advice. The IPT provided a starting point for the realist synthesis of evidence and enabled viewing mHealth recursively when considering *how* the contexts of lifetime antiretroviral therapy could be amenable to change via mobile messaging between patients and providers.

6.1.3 The Value Proposition

The value proposition that can inform decision makers and patients on whether (or not) to adopt and scale-up a technological intervention will be determined though the tangible ways in which the contexts of care will be influenced. Nonetheless, public health research predominantly examines the efficacy of mHealth interventions in terms of improved HIV care outcomes, treatment adherence, and viral suppression rates. There is a need for evidence that can shed light on other tangible benefits that can make mHealth useful to engage with in the daily contexts of engaging with HIV care. DPhil Paper IV is a realist synthesis that provides nuanced answers on the added value of mHealth that offers two-way mobile messaging with human providers. This synthesis was conducted from the perspective of people living with HIV, and not through the lens of the providers who offered proactive care through regular

check-in mobile messages. The findings of this synthesis can be summarised in terms of *when, how, why, for whom, and in what context* mHealth is useful by outlining the explanatory configurations of context, mechanism, and outcome. These configurations were developed as part of a programme theory that consists of four overarching and interconnected domains: tailored content and responsiveness, therapeutic relationship and trust, sharing concerns and perspectives, and working towards holistic care.

First, when mobile messages offer a tailored content and use a personalised language, patients are more likely to engage with the intervention content, because they perceive the content to be individually relevant to them. Further, when mHealth offers communication with a human provider (as opposed to an automated system) who is responsive to patients' expressed needs, patients value the openness, flexibility, and responsiveness of interactions offered by the intervention, because they perceive these modes of care as useful. Second, when providers are willing to use mHealth to proactively check-in for affective and clinical care, patients can build rapport, trust, and a therapeutic relationship with providers, because they feel heard, cared for, and seen. Over time, when mobile messaging provides the means to connect and maintain an ongoing therapeutic relationship, long-term engagement in care can be enhanced, because patients can maintain and deepen their trusting relationship with providers and the wider health system. Third, when patients can openly message their questions to their trusted providers, especially in the early stages of care, their knowledge and management of treatment can improve, because they can get trusted clarification and clinical guidance. When providers regularly and responsively communicate with patients, patients are more able to get the support and help needed to overcome challenges and barriers that arise, because they can get timely help and advice, and use the conduit of messaging to share concerns more easily in various forms. Fourth, when providers are willing and able to counsel patients and work towards holistic care, patients can have more of their needs met, because their care is multidisciplinary and not fragmented. These configurations of the overall programme theory can each be tested further research.

Through my findings, I infer that the foundation of the above contexts, through which mHealth can contribute value, is the formation of a therapeutic relationship between patients and providers. In other words, for technological interventions to add value when taking advantage of the capacities of the professional health workforce, the contribution of the human

relationship appears to be vital, if somewhat unsurprising. This synthesis finds that by building and assessing the strength and existence of the therapeutic relationship within digital interventions and acknowledging the often-unrecognised role of the human provider in mobile messaging interventions, we can enrich our understanding of the usefulness of interactive mHealth when supporting patients. The modern understandings of the therapeutic relationship and working alliance, which have evolved with the evolution of psychotherapeutic praxis (A. Horvath, 2000), are useful to consider in terms of contribution to human supported digital interventions, while they could potentially enrich aspects of unsupported digital interventions with more human touches that can be characterised as 'warm', or more informatively as 'care that fits' the emotional and clinical needs of patients (Pols, 2012). When considering primary care settings, Greenhalgh (2010) distinguishes between distinct objective aspects to a therapeutic relationship that can be measured systematically through validated instruments (Greenhalgh & Heath, 2010a), and the more subjective aspects that can recursively shape care can and contribute value within multiple realms (Greenhalgh & Heath, 2010b). Emerging research is investigating the extent to which the formation of a *digital therapeutic alliance* is possible (Tong F et al., 2022).

To inform the design of interactive digital health interventions, I drew on the logic of care as introduced by Mol (2008). Conceptualised within diabetes care settings, Mol (2008) views treatment of and life with diabetes as indivisible, just as living with HIV and lifelong treatment are undividable. The logic of care is juxtaposed against the logic of choice, which is characterised by objective, detached, and disjointed caring (Mol, 2008). For instance, the logic of choice would designate an mHealth intervention with a defined set of features based on known needs of patients and evidence-based support strategies. In contrast, the logic of care would design a more expansive intervention, contingent on the unpredictable nature of an illness and the changing needs and contexts of a life with HIV, beyond the linear pathobiology of the disease itself. Given that adherence to treatment is influenced by the daily lives and socio-emotional challenges faced by patients, any intervention that attempts to only use the logic of choice to improve treatment adherence would provide an incomplete understanding of the 'whole person' living with HIV.

To this end, I provide a set of recommendations for designing interactive mHealth interventions that can engage people living with long-term conditions. At an early stage of the

realist synthesis, I found that Davis's Technology Acceptance Model (TAM) was useful in explaining the fit and acceptance of mHealth interventions and other technological innovations in healthcare settings (Davis, 1989; Holloway et al., 2017). This theory is adapted from Roger's Diffusion of Innovations theory (E. M. Rogers et al., 2014). To articulate the recommendations, I use the main constructs of TAM (i.e. *perceived usefulness* and *perceived ease of use*), but also maintain the additional and original construct of *compatibility* from the Diffusion of Innovations Theory. My findings suggest that the perceived usefulness of mobile messaging with human providers lies in the existence of caring elements (such as openness, responsiveness, and continuity) and strength of a therapeutic relationship (such as enhanced trust and empathy). Perceptions of ease of use lies in simple and fast communication through multimedia platforms (such as WhatsApp and iMessage that allow multimedia sharing) of mobile messaging for sharing questions and concerns in timely and versatile forms. The perceived compatibility appears to relate to how well the intervention content and design address the specific and individual needs of patients, which can be enhanced through tailoring of the intervention content and provision of holistic care.

6.2 Overview of Limitations

It is important to recognise some of the overall limitations of this research project before discussing next steps. While key limitations were discussed as part of each standalone paper, I would like to refocus attention on the overall thesis and research scope. To manage the scope of information that can be covered by this research project in Iran, and to limit the breadth of focus in the refinement of the programme theory, two deliberate attempts were made: a) narrowing the focus to aspects of living with HIV and lifetime treatment that can be modified by mobile messaging, and b) limiting it to the causal explanations on how mobile messaging affects care *for* people living with HIV, setting aside the question of how the intervention alters the larger health system and demands redirection of scarce health resources. These key decisions allowed me to gain an in-depth understanding of the value of mHealth at the micro level, from the perspective of people living with HIV, at the expense of not gaining an insight into the perspective of providers and necessities of the wider health system. However, technological interventions that are introduced within healthcare settings usually need to be

adopted by at least two groups of users: patients and providers. To enhance adoption, scale-up, and sustainability of mHealth for HIV care, their usefulness, ease of use, and compatibility must be considered from the perspectives of multiple adopters, including people living with HIV, their providers, and the wider health system (Greenhalgh & Abimbola, 2019). This thesis adopted a realist framework of inquiry to understand how mHealth interacts with multiple levels of contexts in which it is implemented. Yet, a key question that remains unanswered is the value of such an mHealth approach relative to the resources required to deliver it. These resources include the time and availability of trained healthcare workforce, and the financial and technological means, that are necessary to deliver a two-way digital intervention and sustain it over the long-term. Further, other research methods could have enhanced the scope of my findings. For instance, using ethnographic observations could have enabled a more nuanced understanding of the healthcare setting and the patient-provider interactions. Sociomaterial analysis would have enabled a more nuanced understanding of the role of mobile phones and messaging, such as different platforms used and differences in comfort levels with using mobile phones. It would be important to take advantage of such methods in future steps, especially during implementation and possible scale-up.

Methodologically, the research approach adopted through this research project evolved over time. At the outset of this doctorate, I had thought of mHealth as a simple biomedical intervention, as opposed to a complex social intervention. Perhaps this was not surprising, considering my training and background in epidemiology and biostatistics. However, as I progressively viewed mHealth interventions as complex, I was enabled to adopt a range of methods to go beyond answering an efficacy question, consider the interaction of mHealth with its context, and diagnose the programme theory that underpins the impacts of mHealth. I used the social constructivist paradigm to answer the research question through an in-depth exploration of the diverse ways stakeholders in this setting viewed HIV care in Iran and the role of a mobile connection in changing the context of relating to HIV care. Gradually, I gained familiarity and training to conduct realist research, but I only adopted a realist lens after the completion of qualitative data collection in Iran, thus DPhil papers I and II were conducted at the crossroads of a social constructivist and realist research paradigms.

While the combined research lens used in this thesis strengthened the findings (as discussed in section 2.4.1), it is important to acknowledge that a ‘full’ realist approach may

have produced a more nuanced middle-range theory in papers I and II. At the point of analysis, the realist-informed lens provided distinct concepts (i.e. contexts and mechanisms) to further unpack the empirical data collected to produce an understanding of when, how, why and for whom disengagement from care and treatment occurs and when, how, why and for whom mHealth can change these contexts. However, realist research begins with an initial programme theory and ends with a more refined version of this theory (Wong, 2017). As such, the findings cannot be interpreted in 'full' realist terms because the data collection processes were not informed by an initial programme theory and as such not meant to be interpreted through a 'full' realist logic. However, the configurational findings of papers I and II still provide improved explanations and a nuanced understanding of engagement with HIV care and potential impacts of mHealth and as such may have transferability to other similar settings. Further, the refinement of the programme theory in DPhil paper IV has produced a 'fuller' realist understanding of mHealth, which is currently being tested in the realist evaluation of HamRaah.

Given the interpretative nature of the methods used in this study, the findings may be exposed to confirmation bias, both during the social constructivist data collection phase, and the realist analysis and synthesis phase. The empirical findings produced through qualitative interviews and focus group discussions accessed the socially constructed understandings and shared realities of interviewed stakeholders with regard to contexts of HIV care, daily adherence, and possibilities for mHealth. I may have been exposed to confirmation bias during the interview process, given my shared background with the participants, being affected by similar social, economic, and political pressures (and in particular the impact of economic sanctions on daily lives in Iran). Similarly, during the realist analysis and synthesis processes, I may have been exposed to confirmation bias, rooted in my hermeneutic engagement with the literature. However, throughout this research, discussions were held with research assistants and mentors in an iterative process of data analysis and collaborative review of the developed themes. While the initial programme theory developed in this thesis was initially developed through the qualitative engagements with people living with HIV and their providers, the findings of the more refined programme theory, developed in the realist synthesis, were not validated through re-engagement with respondents. However, the realist

evaluation that follows (see Figure 1.11) will further test the developed programme theory, with the possibility to refine, confirm, or refute the findings presented in this thesis.

Lastly, several practical and personal challenges impacted this research project. I received my confirmation of status in November of 2019, and was on track to submit my thesis by the end of 2020. From January of 2020, the length of time it took to complete this thesis was impacted by several factors, including the COVID-19 pandemic, my move back to Iran and the various national crises, having to take time off due to loss and mental health challenges of the pandemic, and ultimately the unexpected loss of my dear father in 2022. One year after this immense loss, and through all world events since 2020, I am grateful that this project is nearing completion, while I am also aware that some of the findings discussed here must be considered in light of the rapidly evolving field of digital health, and massive expansion of technology-driven remote healthcare services, especially in response to the exigencies of the COVID-19 pandemic.

6.3 Further Research

The immediate next step that follows the work presented as part of this thesis is the full analysis of data collected through the randomised controlled pilot trial, feasibility study, and realist evaluation that was conducted in Iran (see Figure 1.11). The findings of these papers will bring this project full circle in terms of applying and testing the developed realist programme theory and producing efficacy data on the mHealth intervention. Further, the middle-range programme theory produced here permits empirical testing and can enhance the reproducibility of intervention outcomes across other settings. Thus, the knowledge produced in this thesis can be used by other researchers and practitioners to configure interactive mHealth programmes across different settings and to test and trigger the core mechanisms, such as the emergence of a therapeutic relationship and a logic of care, to produce the desired outcomes in terms of enhanced engagement with HIV care or similar long-term treatments.

As discussed in the limitations section, when considering the value proposition of mHealth, it is important to assess the value created for both patients and providers. This thesis has only explored insights in terms of the value added to the lives of people living with HIV. The question of how and whether human-supported mHealth will add value for providers

remains a crucial question to be asked in future research. Indeed, evidence suggests that mobile messaging can substantially burden providers when interventions are added onto the already strained daily work routines of healthcare workers (Mano & Morgan, 2022). There appears to be a higher burden on female health workers (Rittenberg et al., 2022), especially in settings that such healthcare provisions are offered through informal means (Hampshire et al., 2017), as opposed to creating a formalised and staffed programme. As such, an important next step would be to formulate a new research question on the usefulness of mHealth for healthcare providers—relative to the additional burden they may carry as a result of these interventions. Building a therapeutic relationship appears to be vital for engagement with digital interventions. Simultaneously, given the added burden that human-supported digital health can place on providers, the use of their time and ability to provide care should be considered judiciously. Additionally, the economic feasibility of such interventions is an important consideration that can be evaluated in future research.

It would be illuminating for future research to carefully examine aspects of care that can (or cannot) be managed by interventions that use interactive chatbots (Brown & Halpern, 2021; Müssener, 2021). The programme theory and recommendations developed in this thesis can be used to ask important questions in the design of interactive digital health programmes, including those that consider AI-operated chatbots for provision of care and support. For instance, can AI chatbots earn patient trust? In what contexts and to what extents might chatbots be preferred to human providers? Can the new generative models of AI chatbots, such as ChatGPT, emulate aspects of a therapeutic relationship, such as empathic engagement, and deliver certain elements that represent a logic of care, such as openness and continuity? Nuanced answers to these questions can build on already existing but contradictory evidence to inform the future of AI for conditions that are marred by stigma. For instance, evidence suggests that internalised shame can be overcome to seek mental health care by a wider spectrum of groups (Minerva & Giubilini, 2023). The anonymity offered by AI, combined with the perception of receiving objective and thorough information could help dismantle misinformation as a barrier to treatment for stigmatised conditions. In contrast, other researchers argue that AI-operated systems cannot and should not replace human interaction in mental healthcare (Brown & Halpern, 2021). Yet, it would be important to ask policy and practice relevant questions in terms of when, for whom, in what context, and to what extent

can artificial intelligence replace the human touch and relationship, and when, for whom, in what context, and to what extent can technology-based approaches support rather than replace or burden healthcare workers.

6.4 Policy Implications

The findings of this thesis have a number of implications for policy and programming within Iran and other global settings. The work presented in this thesis was conducted in two parallel arms, using primary data from Iran and global secondary evidence. The central question addressed was: *how can mobile phones be used to enhance the contexts in which HIV care is engaged with globally and in Iran?* The first two aims of the study addressed the context of Iran, and the third aim considered the global context. In light of the findings, I discuss the implications for policy and programming in Iran and other global settings.

6.4.1 Policy Contexts: Iran

The first set of findings, based on data collected from Iran, can be considered in terms of the socioecological contexts that lead to interrupting treatment retention and adherence for people living with HIV in Iran. Pragmatic considerations for HIV programming have so far been effective in reducing the population size of people who inject drugs, providing methadone treatment and needle exchanges, creating a decentralised universal antiretroviral therapy programme, and offering psychosocial support through triangular clinics and peer supported adherence clubs (UNAIDS, 2020a). These efforts have managed to reduce the rate of new HIV infections and AIDS related mortality, in contrast to the rest of the MENA region in which new HIV infections and AIDS related mortality continues to expand (Figure 1.3). Yet, there remains significant gaps in terms of HIV diagnosis and retention in care, as only 72 per cent of people diagnosed with HIV are actively retained on treatment. This thesis identifies and considers mHealth strategies to prevent disengagement from HIV treatment and care. This strategy is in line with the recommendations provided by the Global Fund, based on the recent evaluation of the national HIV policy and programming, to include digital approaches for

promoting treatment retention (UNDP, 2020). Thus, the findings of my thesis generate pertinent and useful policy considerations.

The contexts that were identified as triggering denial, fear, and despair and thereby leading to disengagement from HIV care, are amenable to change through policy and practice strategies that can be temporally, politically, culturally, and economically apposite. The contexts can be broadly categorised in three spheres. First, stigma and discrimination against people living with HIV. Second, wider societal negative perceptions regarding HIV and lack of awareness regarding antiretroviral therapy and available programmes. Third, dwindling social support and economic security. The findings of this thesis suggest that discrimination against people living with HIV is rampant in medical and dental care facilities, in contrast to HIV care settings where considerable support and empowering resources are offered. To combat discrimination, two key steps were taken by the MoHME: a *'Legal Environment Assessment'* study for recommending amendments to laws and regulations, and an *'Information, Education, and Communication'* campaign for health care providers. An anti-discrimination directive was drafted by MoHME to all medical universities to end HIV related discrimination in healthcare settings. The process is hoped to be strengthened by offering training to healthcare providers to change attitudes that are stigmatising and discriminatory. Additionally, a bylaw to *'Prevent Discrimination and Stigma against People Living with HIV'* was submitted to the parliament within the duration of this research project, and presented by policy makers during the evaluation that I conducted for the Global Fund as part of an independent team of international evaluators. However, it remains unclear how effective these efforts can be in terms of reducing societal HIV-related stigmatisation, especially without public debates on HIV and wider awareness raising campaigns.

Public debates, awareness raising campaigns, and legal reform can be most effective in reducing stigma and discriminations. A handful of national TV programmes have provided information on antiretroviral therapy, shedding light on the possibility of having a 'normal' life with a 'normal' life-expectancy to debunk the myth of HIV as a 'death sentence'. These programmes have invariably talked about prevention strategies, including the use of the word 'condom' on TV to shine light on the importance of prevention of sexually transmitted diseases (MacFarquhar, 2002). Sex before marriage is criminalised in Iran, just as sex between the same sexes, but these are not prosecutable when 'committed' in the private realms of life,

within which these praxes are indeed prevalent. Prosecution is only permitted in cases of sexual offence, public sexual acts, and organised sex crimes (see Appendix A, Document A7). In the introduction to this thesis, the decriminalisation of personal drug possession, medicalisation of drug use, recognition of transsexual rights and provision of sex-change surgeries were highlighted as examples of pragmatic policy making and variegated reasonings through Shi'a jurisprudence (Axworthy, 2013). These venues can further be used towards more decriminalisations and reduced involvement of the state in the social aspects of life. However, the current politicisation of issues and polarisation of the society, combined with the Islamic Republic's sensitivity towards what it views as imperialistic means of policymaking through international pressure and universal directives, have led to a gridlock with very little progress on issues that can indeed be solved without conflict and through compromise.

In settings where human rights approaches are met with resistance and efforts to change 'bad' laws can have counterproductive effects, it is demonstrably more productive to build on good policies and laws (El Feki, 2022). While legal reform in Iran is met with resistance, it is important to take advantage of progress that can be made in the economic, medical, and technological realms. Economic policies and social protection measures have indeed been shifting, with cash transfer policies targeting the bottom deciles of the households more progressively to protect against the economic insecurity that was identified as part of this research. Yet, these progressive measures continue to lose their potency in the face of rising inflation and economic sanctions that produce added inflationary pressures (Ameli, 2023). Medical progress has had the most significant impact on the lives of people living with HIV in Iran as the uptake of the latest medical guidelines has been met with little resistance within the policy context of Iran, making Iran one of the countries that has adopted most medical policy recommendations, such as PrEP and Dolutegravir, for improved HIV prevention and treatment (HIV Policy Lab, 2021). The medical community holds significant societal authority and political power, with some progressive members who have tirelessly fought for progressive change, including the wellbeing of the HIV community in Iran (Samarasekera, 2021). Technological progress, when combined with medical goals, has the highest potential to achieve change and implement progress. The Iranian government is highly keen to move towards 'smart' provisions of public services as a means to confront challenges

that range from fighting corruption to expanding universal health coverage. While such policy prioritisations are combined with an overly optimistic view of technologies, they do open a realm of possibility to deliver services more equitably, including to marginalised populations. Following the COVID-19 pandemic, technology uptake within healthcare was particularly rapid, especially within the realm of remote consultations, at-home lab tests, and basic primary care check-ups, that were increasingly booked through smartphone applications. Some of these services managed to secure coverage by national insurance programmes, but most are privately financed. However, the medical community and the national health system showed considerable enthusiasm in adopting these programmes.

Within the aforementioned contexts, the findings of this study can potentially inform the adoption of mHealth strategies to provide HIV care and social support more efficiently at scale, by connecting currently available resources to those in need of such resources. However, to be offered through formalised staffing and free of charge at the point of service to marginalised populations, these programmes would need to be considered as part of the national budget for HIV programming, which funds the universal antiretroviral therapy programme, adherence clubs, triangular clinics, and the full-service provisions as part of the national HIV strategy programming. While there is the possibility for adoption and expansion, the current health system is facing staff shortages, especially with regard to nursing and primary care. Additionally, given that economic sanctions have slashed government budgets, expansion of universal health coverage is met with obstacles, and the nation-wide cash transfer programme continues to lose its real value against inflation (Salehi-Isfahani, 2020). Lastly, the political and economic pressures are producing a rising 'brain drain' wave of the professional and medical workforce, making technological solutions that depend on human resources a challenging strategy to pursue. For instance, two of the members of the current research team (one psychology graduate who delivered HamRaah, and one research assistant who oversaw the trial recruitment) recently emigrated from Iran. As such, there needs to be a more nuanced understanding of the costs, benefits, and sustainability of human supported digital health programmes. This research project hopes to produce more insights with regard to the promises and perils of human supported mHealth for HIV care in Iran. However, as mentioned in the previous section, more research needs to be conducted from the provider and health system perspective.

6.4.2 Policy Contexts: Global

The WHO produced a set of recommendations, including the use of mobile messaging, to support antiretroviral adherence and HIV care retention (WHO, 2015b). These guidelines distinguished between two- and one-way messaging approaches, but failed to open the category of two-way or interactive messaging further in terms of who or what operating mode is sending and receiving messages to and from people living with HIV. Importantly, the studies that have followed from the 'WelTel' two-way messaging intervention have sometimes been delivered via human providers and sometimes via automated systems (Lester et al., 2010; Nordberg et al., 2021; Van der Kop et al., 2013). Various meta-analyses and systematic reviews have compared two-way versus one-way messaging designs, ultimately without resolving the growingly conflicting evidence base (Amankwaa et al., 2018; Finitsis et al., 2014; T. Horvath et al., 2012; S. B. Lee & Valerius, 2020). This thesis finds that what underpins such mixed results is disregarding the *human* element and overlooking relational changes that occur between people living with HIV, their providers, and the larger health system.

To this end, the findings of this thesis that emerged from the global synthesis of evidence, shed light on the importance of human relationship and the contexts of care that can be influenced by developing a therapeutic relationship with providers. These findings build on previous work that looked into the value and measurability of therapeutic relationships within primary care settings (Greenhalgh & Heath, 2010a, 2010b). By incorporating insights from primary care and care for other long-term conditions, such as diabetes (Mol, 2008), this finding has a reasonable potential to (re)launch a new debate within the field of HIV care and the application of digital health approaches for long-term and stigmatised conditions. These findings come at a particularly pertinent time, as AI-based approaches are becoming more prominent in the field of healthcare.

Further, following the COVID-19 pandemic the guidelines and available regimens for antiretroviral therapy are changing. The updated WHO guidelines recommend reduced in-person visits and longer-term antiretroviral medication disposal (WHO, 2021). In the near future, daily adherence to antiretroviral therapy may be less of an issue given that long-acting injectable antiretrovirals will become more widely accepted and available. Long-acting injectables will still require long-term engagement with HIV care, which could be enhanced through having an interactive and flexible mHealth connection to providers (as opposed to

structured and daily one-way reminders) that can induce a therapeutic relationship and enhance holistic care. Crucially, the introduction to this thesis outlined the inequities and injustices that prevent global south countries from accessing novel therapeutics and medicines that are lifesaving. It will likely take a considerable amount of time and effort for long acting injectables to be available to people living with HIV in low- and middle-income countries, just as the slow global expansion of access to Dolutegravir, the preferred single-pill first-line antiretroviral therapy that has limited side effects and better uptake. Thus, daily adherence will likely remain relevant in the lives of people living with HIV in much of the global south countries. Evidence such as those produced in this thesis, could inform critical decisions by stakeholders, policymakers, regulators, health organisations, healthcare workers, and patients in terms of managing resources, coordinating technologies, delivering, and engaging with HIV care.

6.5 Dissemination and Impact

This research has attempted to avoid two common tropes within global health research: neo-colonial structures (Abimbola et al., 2021) and orientalist representations (Said, 1978). To avoid reproducing orientalist narratives, the thinking, interpreting, conceptualising, presenting, and disseminating of findings go beyond a dualised lens of 'Eastern vs. Western', 'rational vs. ideological', 'democratic vs. totalitarian', and 'moderation vs. fanaticism'. Care has been taken to understand differing viewpoints, belief systems, and lifestyles, to find common grounds and opportunities for advancing beyond polarised stances on HIV-related praxes. To avoid colonialist structures, the funding for this study was provided by Tehran University of Medical Sciences, and as such the research project was aligned with local research priorities and policy relevant questions. Thus, the colonialism that lingers on through global health research structures that are characterised by global north-south power imbalances, misalignment of priorities, and unsustainable solutions for local contexts were avoided, while simultaneously a fruitful international collaboration was established. Instead of imposing an idea from outside the policy context of Iran, the research questions for this project were formed through consultation with local stakeholders. This enhanced the potential adoption of

my thesis findings in terms of proposed solutions with potential sustainable impact that is aligned with local needs, and Global Fund's recommendations.

Further, it is hoped that the findings of this research project can be translated into an informed policy debate at the international and national levels, on the relevance of human supported digital health and HIV care. At the international level, in addition to the four publications within peer-reviewed journals, I will disseminate insights through social media accounts and potential media engagement. The findings have been presented at the International AIDS Conference (2022) and CEBI research group in the Department of Social Policy and Intervention. At the national level, I will translate the journal publications into Persian, as this was requested through Twitter by several Iranians living with HIV who came across the English versions of the published papers. Further, I will draft a policy brief, and a summary of findings that can be shared through mobile messaging with all relevant stakeholders and study participants. In a final presentation at the Iranian Research Centre for HIV/AIDS, I will share HamRaah's programme theory and programming relevant findings.

6.6 Conclusion

To end AIDS across the globe, we have the necessary tools for prevention, diagnosis, and care. However, 'what we lack is an equity plan linked to a delivery system.' In the current era, technologies such as mobile phones provide valuable opportunities to enhance the delivery of equitable care. Remarkably, however, we have yet to see the capacities of mobile phones to be used effectively and sustainably for HIV care. In this thesis, I have argued that there is a need to keep sight of the complexities of introducing digital approaches within healthcare and specifically HIV care. By adopting a realist framework of inquiry, I contextualised engagement with HIV care in Iran and conceptualised how mHealth can change care contexts. These findings highlight the importance of understanding the nuances of experience, through cognitive and affective mechanisms, that impact health decisions within the international, national, social, economic, and structural contexts of living with HIV. Technological solutions can then be designed in a way that can add value and be sustainably implemented within these contexts.

I further proposed a pilot trial and nested realist evaluation of a human supported mHealth trial in Iran, in an attempt to triangulate methods and answer efficacy questions in addition to diagnosing how mHealth would interact with the complexities of HIV care and everyday living with HIV. I further used secondary evidence to explore the value of human-supported mHealth from the perspective of people living with HIV. By producing a middle-range theoretical explanation, I show that human supported mHealth offers value by kindling a therapeutic relationship with providers when they proactively and responsively engage patients through tailored, flexible, open, and ongoing messaging. Using these findings, I provide recommendations on when and how to use human support and when and how to emulate aspects of a therapeutic relationship in interactive digital health designs. The findings are particularly timely both for the policy and programming context of HIV care in Iran, whereby there is a need to keep people living with HIV retained in care, and for the current global context of technologies in healthcare, whereby there is a need to consider when, how, for whom, and in what context digital health approaches need to be supported by humans versus machines, such as those operated by generative artificial intelligence.

A

Appendix A: Research Ethics

Document A1

Tehran University of Medical Sciences

Vice-Chancellor in Research Affairs- Tehran University of Medical Sciences

Research Ethics Certificate

Approval ID:	IR.TUMS.VCR.REC.1397.558	Approval Date:	2018-11-05
Evaluated by:	Vice-Chancellor in Research Affairs- Tehran University of Medical Sciences		
Status:	Approved		
Approval Statement:	The project was found to be in accordance to the ethical principles and the national norms and standards for conducting Medical Research in Iran. Notice: 1. Although the proposal has been approved by the research ethics committee, meeting the professional and legal requirements is the sole responsibility of the PI and other project collaborators. 2. This certificate is reliant on the proposal/documents received by this committee on 2018-11-05. The committee must be notified by the PI as soon as the proposal/documents are modified.		
Proposal Title:	The acceptability and effectiveness of a mobile-health intervention to improve adherence to treatment and medication for people living with HIV		
Principal Investigator:	Name: Minoo Mohraz Email: minoomohraz@ams.ac.ir		

Dr. Mohammad Ali Sahraian
Director of Institutional Research Ethics Committee
Vice-Chancellor in Research Affairs- Tehran University of Medical Sciences

Dr. Shokoufeh Nikfar
Secretary of Institutional Research Ethics Committee
Vice-Chancellor in Research Affairs- Tehran University of Medical Sciences

Document A2

Oxford Tropical Research Ethics Committee

University of Oxford
Research Services, University Offices
Wellington Square, Oxford OX1 2JD
Tel. +44 (0)1865 (2)82106
E-mail: oxtrec@admin.ox.ac.uk

Vira Ameli
Green Templeton College
43 Woodstock Road
Oxford
OX2 6HG

30 August 2018

Dear Ms. Ameli

Full Title of Study: Community participatory approach to develop a mobile-health intervention to improve adherence to antiretroviral therapy for people living with HIV (PLHIV) in Tehran, Iran

OxTREC Reference: 537-18

Thank you for your email of the 30 August 2018, and for your minimal risk application form.

I am pleased to confirm that approval has now been granted for this study. This is valid for the first five years and is subject to receiving the local ethical approval (if this approval has not yet been received).

The documents approved for this study are as follows:

Documents:	Version:	Date:
Minimal risk application form (including appendices)		30/08/18

Any subsequent changes to the application must be submitted to the Committee as an Amendment. This should include a letter to give the reasons for the proposed modifications and all revised documents with changes tracked.

Please ensure that you submit a completed Annual Report form on every anniversary of this approval and a final End of Study Report. The relevant forms can be found on the OxTREC website: https://researchsupport.admin.ox.ac.uk/governance/ethics/apply/oxtrec.

Finally, please note the following **important information**:

Data safety—all studies
It is the responsibility of the PI to ensure that all data collected during the course of the study is stored and transferred safely and securely. Further guidance and advice is available from the Research Data Team.

Studies that will involve storing human tissue samples in Oxford
As you are planning to import the samples into England, you will need to make arrangements before the samples are transferred to store them under the governance of a Human Tissue Authority (HTA) licence. It is a legal requirement that any tissue or fluid made up of or

containing human cells to be used for the purpose of research is stored on premises licensed by the HTA unless covered by an exemption. OxTREC approval is not a recognised exemption. Further information may be found on the University's human tissue governance web pages: https://researchsupport.admin.ox.ac.uk/governance/human-tissue.

Yours sincerely

Dr Rebecca Bryant
Research Ethics Manager, OxTREC

Document A3

Oxford Tropical Research Ethics Committee

University of Oxford
Research Services, University Offices
Wellington Square, Oxford OX1 2JD
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E-mail: oxtrec@admin.ox.ac.uk

Ms Vira Ameli
Green Templeton College
43 Woodstock Rd.
Oxford OX2 6HG

06 March 2019

Dear Ms Ameli

Full Title of Study: A pilot study to test the feasability and acceptibility of a mobile-health intervention to achieve high retention in care and adherence to antiretroviral therapy for people newly diagnosed with HIV in Tehran, Iran

OxTREC Reference: 506-19

Thank you for your email of the 4th March 2019, and for your minimal risk application form.

I am pleased to confirm that approval has now been granted for this study. This is valid for the first five years and is subject to receiving the local ethical approval (if this approval has not yet been received).

The documents approved for this study are as follows:

Documents:	Version:	Date:
Minimal risk application form (including PIS and consent form)		27 Feb 2019
2 x questionnaire items		

Any subsequent changes to the application must be submitted to the Committee as an Amendment. This should include a letter to give the reasons for the proposed modifications and all revised documents with changes tracked.

Please ensure that you submit a completed Annual Report form on every anniversary of this approval and a final End of Study Report. The relevant forms can be found on the OxTREC website: https://researchsupport.admin.ox.ac.uk/governance/ethics/apply/oxtrec.

Finally, please note the following **important information**:

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It is the responsibility of the PI to ensure that all data collected during the course of the study is stored and transferred safely and securely. Further guidance and advice is available from the Research Data Team.

Tel: +44 (0)1865 (2)82106
Email: oxtrec@admin.ox.ac.uk
Web: https://researchsupport.admin.ox.ac.uk/governance/ethics

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As you are planning to import the samples into England, you will need to make arrangements before the samples are transferred to store them under the governance of a Human Tissue Authority (HTA) licence. It is a legal requirement that any tissue or fluid made up of or containing human cells to be used for the purpose of research is stored on premises licensed by the HTA unless covered by an exemption. OxTREC approval is not a recognised exemption. Further information may be found on the University's human tissue governance web pages: https://researchsupport.admin.ox.ac.uk/governance/human-tissue.

Yours sincerely

Dr Rebecca Bryant
Research Ethics Manager, OxTREC

Document A4

INFORMED CONSENT SHEET

(QUALITATIVE STUDY)

TITLE OF STUDY

A qualitative study to understand stakeholder perspectives of engagement with and adherence to antiretroviral therapy, and possibilities to use mobile phones for HIV care in Tehran, Iran.

PRINCIPAL INVESTIGATOR

Vira Ameli

Iranian Research Centre for HIV/AIDS & University of Oxford

Address: Tehran Province, Tehran, District 6, Imam Khomeini Hospital, Keshavarz Blvd.

Phone: +98 21 6694 7984

Email: vira.ameli@spi.ox.ac.uk

INTRODUCTION

You are being asked to take part in a research study, which is joint project of Universities of Oxford and Tehran University of Medical Sciences. Before you decide to participate in this study, it is important that you understand why the research is being done and what it will involve. Please read the following information carefully. Please ask the researcher if there is anything that is not clear or if you need more information. This study has been reviewed by the Oxford Tropical Research Ethics Committee (OxTREC) at the University of Oxford, as well as by Tehran University of Medical Sciences.

PURPOSE OF THE STUDY

The most important factor in sustainable management of HIV is adherence to antiretroviral therapy (ART). Poor adherence increases the chances of treatment failure, transmission, progression to AIDS, and death. The World Health Organization recommends programs using mobile/cellular technologies to support patients in improving treatment adherence. This study

hopes to first understand the context and impediments to successful antiretroviral therapy in Iran, and second gain an insight into the applicability and suitability of using mobile communication technologies to address the needs of people living with HIV in Iran.

Why have I been chosen?

You have been chosen to participate in this study because you are either a patient receiving antiretroviral therapy, or healthcare provider for people living with HIV, at Imam Khomeini hospital. Therefore, you will have knowledge about the needs of people living with HIV with regards to adherence to antiretroviral therapy. This program is being tested for the first time in Tehran, Iran, and aims to improve adherence to antiretroviral therapy in this patient population. Your participation in the qualitative phase of the study will help inform and improve the design of the program and ensure that the program will be delivered in a culturally and contextually acceptable way, and address the needs of the larger community of people living with HIV in Iran.

Do I have to take part?

Your participation in this study is completely voluntary. It is up to you to decide whether or not to take part in this study. If you decide to take part in this study, you will be asked to sign a consent form. After you sign the consent form, you are still free to withdraw at any time and without giving a reason. Withdrawing from this study will not affect the relationship you have, if any, with the researcher, your healthcare provider, or any of the clinic staff. If you withdraw from the study before data collection is completed, your data will be destroyed and not used.

What will my participation entail?

You will be invited to participate in a 2-hour long in-depth conversation with the lead researchers of the study, and five to eight other patients or healthcare providers. The meeting will have an open discussion format where the following questions will be discussed:

i. What are your views regarding the challenges and support mechanisms for adhering to Antiretroviral Therapy (ART)?

ii. How does the context of living with HIV affect individuals in their engagement with and adherence to antiretroviral therapy?

iii. What are your thoughts regarding a program using mobile/cellular technology to improve adherence to ART and retention in care?

iv. What, in your belief, are the potential challenges, cultural, and logistical barriers to implementing an adherence intervention using mobile technology?

Are there any possible risks in taking part?

This project will not subject you to any risks or harms. You will provide us with two hours of your time, which will be invaluable in allowing us to learn from your knowledge. Your voice will be recorded. However, the recorded information you share with us will be anonymised and never shared with personal identifiers, with any governmental, non-governmental, research organization or body. You may decline to answer any or all questions and you may terminate your involvement at any time if you choose.

Are there any possible benefits in taking part?

This project will not have any direct benefits for you. However, the information you will share with us will help inform and improve the design and delivery of a program, which could support patients in improving their adherence to antiretroviral therapy.

Will my taking part in this study be kept confidential?

Every effort will be made by the researcher to preserve your confidentiality including the following. You will be invited to choose nicknames (instead of your real name) to be used in the group discussions. No real names will be used on any research materials. Your voice and responses to the discussion questions will be recorded. Please do not mention any identifying information or names during the conversation. The recorded information you share with us will be anonymised and never shared with personal identifiers. This may include sensitive information, such as sexual orientation, sexual practices, religious beliefs, physical/mental health information.

Any sensitive and non-sensitive information collected will be anonymised and never shared with any governmental, non-governmental, or research body or organization. All care will be taken in keeping notes, interview transcriptions, and any other participant information in a locked file cabinet in the personal possession of the researcher, and in an anonymised format.

Participant data will be kept confidential, and not shared with anyone, except in cases where the researcher believes that the participant is putting others at risk of harm. If a participant is a risk to him/herself, or if they are suffering from mental health concerns, they will be encouraged (but not required) to seek counseling from Imam Khomeini hospital's on-site psychiatry unit.

How will I be compensated for my time and participation?

In order to show our appreciation for your time, we will be providing a warm lunch on your interview day. Additionally, we can provide a gift-pass to a swimming pool club in Tehran's city centre.

What will happen to the results of the study?

Results of the research will be published. You will not be identified in any report or publication. If you wish to be given a copy of any reports resulting from the research, please ask us to put you on our circulation list.

How will the data I provide be protected?

Tehran University of Medical Sciences and the University of Oxford are responsible for ensuring the safe and proper use of any personal data you provide, solely for research purposes. Any publications that will arise from this study will solely report the anonymised data.

Who has ethically reviewed this study?

This study has been reviewed by the Oxford Tropical Research Ethics Committee (OxTREC) at the University of Oxford, as well as by Tehran University of Medical Sciences.

CONTACT INFORMATION

If you have questions at any time about this study, or you experience adverse effects as the result of participating in this study, you may contact the researcher whose contact information is provided on the first page. If you have questions regarding your rights as a research participant, or if problems arise which you do not feel you can discuss with the

Primary Investigator, please contact Tehran University of Medical Sciences' Ethics review board, at +982181633613 or +982181633626

CONSENT

I have read and understood the Participant Information Sheet. **Participant's Initials: _____**

I have had the opportunity to ask any questions about the study and have received satisfactory answers or the additional information I requested. **Participant's Initials: _____**

I understand that I may withdraw from the study at any time and will not be asked for reasons of withdrawal. **Participant's Initials: _____**

I understand that this study has been reviewed and approved by Tehran University of Medical Sciences Ethics Committee, and the Oxford Tropical Research Ethics Committee (OxTREC) at the University of Oxford. **Participant's Initials: _____**

I understand how my interview will be stored, who will have access to my interview, and what will happen to my interview at the end of this study. **Participant's Initials: _____**

I understand that the research will be written up as a doctoral thesis and how personal data from this research will be published and archived. **Participant's Initials: _____**

I understand how to raise concerns or complaints about this study. **Participant's Initials: _____**

I understand that sensitive personal data may be collected during this interview. This may include information on sexual orientation, sexual practices, religious beliefs, physical/mental health information. Any sensitive information collected will be anonymised and never shared with any governmental, non-governmental, or research organization. **Participant's Initials: _____**

I understand that in this project and all future works using this interview, all personal and sensitive data will be anonymised. **Participant's Initials: _____**

I understand that my voice will be recorded during the focus group discussions and interviews, and that the audio recording will be transcribed, anonymised and discarded within 48 hours after the recording. **Participant's Initials: _____**

I voluntarily consent to participate in this study and recording, and hereby assign to the researcher all copyright in my contribution for use in all work stemming from this project and future projects. **Participant's Initials: _____**

I voluntarily consent to participate in this study and recording, and hereby assign to the researcher all copyright in my contribution for use in all work stemming from this project and future projects.

Participant's signature _____ Date _____

Investigator's signature _____ Date _____

Document A5

Semi-Structured Guides for the Qualitative Study

Questions asked from people living with HIV:

Adherence related questions:

i. What factors (issues / problems / contexts) make engagement with and adherence to Antiretroviral Therapy (ART) more difficult?

ii. What factors facilitate your adherence to Antiretroviral Therapy?

iii. What are the current mechanisms through which the clinic supports you in adhering to your treatment?

Intervention related questions:

i. What do you think of a program, which connects you to the clinic staff through mobile text messaging to support your adherence to treatment?

ii. What do you think the frequency of the mobile messages should be?

iii. Would you like to receive reminders through mobile messages?

iv. Would you like to receive counselling through mobile messages?

v. Are there any personal, cultural and/or logistical issues that would make a program using mobile communication not acceptable?

Questions asked from care providers and peer supporters:

Adherence related questions:

i. What do you think is the main barrier(s) to ART retention and adherence for patients receiving care at this centre?

ii. What do you think about the current healthcare mechanisms in place to help improve adherence to ART?

Intervention related questions:

i. How do you think a program using mobile-messaging communication could be helpful in improving treatment retention, engagement with care, and adherence to ART?

ii. Do you think such a program would be feasible to establish within the clinic structure?

iii. What are your thoughts regarding the frequency of the messages?

iv. What are your thoughts regarding the content of the messages?

v. Are there any logistical barriers that you can foresee in implementing such a program?

vi. Are there any personal, cultural, or logistical barriers that you can foresee in implementing such a program?

Document A6

INFORMED CONSENT SHEET

(HamRaah PILOT)

TITLE OF STUDY

HamRaah: a pilot study to test the feasability and acceptibility of a mobile-health intervention to improve engagement with HIV care in Tehran, Iran.

PRINCIPAL INVESTIGATOR

Vira Ameli

Iranian Research Centre for HIV/AIDS & University of Oxford

Address: Tehran Province, Tehran, District 6, Imam Khomeini Hospital, Keshavarz Blvd.

Phone: +98 21 6694 7984

Email: vira.ameli@spi.ox.ac.uk

INTRODUCTION

You are being asked to take part in a research study, which is joint project of Universities of Oxford and Tehran University of Medical Sciences. Before you decide to participate in this study, it is important that you understand why the research is being done and what it will involve. Please read the following information carefully. Please ask the researcher if there is anything that is not clear or if you need more information. This study has been reviewed by the Oxford Tropical Research Ethics Committee (OxTREC) at the University of Oxford, as well as by Tehran University of Medical Sciences.

PURPOSE OF THE STUDY

The most important factor in sustainable management of HIV is adherence to antiretroviral therapy (taking your medications every day at the right time and dose). Poor adherence increases the chances of treatment failure, transmission, progression to AIDS, and death. The World Health Organization recommends programs using mobile/cellular technologies to support patients in improving treatment adherence. This study hopes to gain an insight into

the applicability of these programs to the Iranian population and test their suitability for the needs of people living with HIV in Iran.

Why have I been chosen?

You have been chosen to participate in this study because you are a patient, who is recently been diagnosed with HIV, and are currently receiving antiretroviral therapy at Imam Khomeini hospital. This program is being tested for the first time in Tehran, Iran, and aims to improve adherence to antiretroviral therapy. Your participation in this pilot study will help inform the effectiveness of this program for yourself and other people living with HIV in your community.

Do I have to take part?

Your participation in this study is completely voluntary. It is up to you to decide whether or not to take part in this study. If you decide to take part in this study, you will be asked to sign a consent form. After you sign the consent form, you are still free to withdraw at any time and without giving a reason. Withdrawing from this study will not affect the relationship you have, if any, with the researcher, your healthcare provider, or any of the clinic staff. If you withdraw from the study before data collection is completed, your data will be destroyed and not used.

What will my participation entail?

You will be invited to participate in a 24-week long study. This study will entail the following components:

1. During the study period you will be asked to fill in a survey questionnaire, which will be sent to you once at the onset of your participation in the study, and once at the termination of the program – should you choose to participate in the full 24-week trial. We will then use this data to measure the impact of the program on your adherence to Antiretroviral therapy.
2. Depending on your random allocation to the two arms of the study, we *may* contact you on a weekly basis to remind you of the available clinic support, via text-messages, delivered through participant's platform of choice, which can be fully encrypted and secure. Additionally, to safeguard your privacy, you can choose a pin to ensure that our staff are in contact with you, and not with any third party accessing your phone.
3. At the termination of the study you will be offered a free viral load test, which will be sponsored by the research group. This will help both you and us to understand the impact of the program on your treatment adherence and health status.

4. You may be asked to visit the at the termination of the study, in order to participate in a one-hour long interview with the lead researcher, or in a 2-hour discussion with other patients like yourself who participated and completed the study. Your voice will be recorded, but discarded in 48 hours, when all information is transcribed. No personal identifiers will be recorded in the transcripts.
5. All data collected through the questionnaires, in-person interviews, and group discussions will be anonymised. Text-messaging communication will also be anonymised and we can stay in touch through a nickname chosen by you.

Are there any possible risks in taking part?

This project will not subject you to any physical risks or harms. We understand that you worry about disclosure of your HIV status to your cohabitants, partner, family, or friends, and text-messaging communication may elevate the risk of unintended disclosure. This is because text-messages could be read by third party subjects, to whom you would not have planned to disclose your HIV status. If these possibilities put you or your relationships at risk, you may choose to decline participation and terminate your involvement at any time if you choose.

Are there any possible benefits in taking part?

This project aims to provide support in order to improve your adherence to antiretroviral therapy. The effectiveness of this program within the community of people living with HIV in Iran, and in the context of Iran's healthcare system is not yet known. However, any positive impacts on adherence to treatment, could reduce your viral load, and improve your immune function and health. Additionally, your participation in this study will help inform and improve the design and delivery of this program, helping future patients in Iran improving their adherence to antiretroviral therapy.

Will my taking part in this study be kept confidential?

Every effort will be made by the researcher to preserve your confidentiality, including the following: You will be invited to choose nicknames (in addition to the enrollment number that the researchers will assign to you) to be used on all research material. No real names will be used on any research materials. Your nicknames will be saved so that all your responses to the surveys, and all text-messaging communication is anonymous.

The online questionnaires are fully encrypted, which means that no party other than authorised parties can access the information you enter. Your real name will NOT be entered in the online survey. Your voice and responses during the interviews and discussions will be recorded. However, these voice recordings, will be transcribed, and destroyed within 48 hours after the recording. Please do not mention any identifying information or names during the conversation. This ensures that the transcribed and collected information will be anonymised and never shared with personal identifiers, with any governmental, non-governmental, research organization or body.

All care will be taken in keeping consent forms, interview transcriptions, and any other participant information in a locked file cabinet in the personal possession of the researcher, and in the anonymised format. Participant data will be kept confidential, and not shared with anyone, except in cases where the researcher believes that the participant is putting others at risk of harm. If a participant is a risk to him/herself, or if they are suffering from mental health concerns, they will be encouraged (but not required) to seek counseling from Imam Khomeini hospital's on-site psychiatry unit.

How will I be compensated for my time and participation?

In order to show our appreciation for your time, we will be providing a free viral load test at the termination of the study. Additionally, during interview days we will be providing a warm lunch to show our appreciate for your commute.

What will happen to the results of the study?

Results of the research will be published. You will not be identified in any report or publication. If you wish to be given a copy of any reports resulting from the research, please ask us to put you on our circulation list.

How will the data I provide be protected?

Tehran University of Medical Sciences and the University of Oxford are responsible for ensuring the safe and proper use of any personal data you provide, solely for research purposes. Any publications that will arise from this study will solely report the anonymised data.

Who has ethically reviewed this study?

This study has been reviewed by the Oxford Tropical Research Ethics Committee (OxTREC) at the University of Oxford, as well as by Tehran University of Medical Sciences.

CONTACT INFORMATION

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CONSENT

I have read and understood the Participant Information Sheet. **Participant's Initials: _____**

I have had the opportunity to ask any questions about the study and have received satisfactory answers or the additional information I requested. **Participant's Initials: _____**

I understand that I may withdraw from the study at any time and will not be asked for reasons of withdrawal. **Participant's Initials: _____**

I understand that this study has been reviewed and approved by Tehran University of Medical Sciences Ethics Committee, and the Oxford Tropical Research Ethics Committee (OxTREC) at the University of Oxford. **Participant's Initials: _____**

I understand how my data will be stored, who will have access to my data, and what will happen to my data at the end of this study. **Participant's Initials: _____**

I understand that the online survey service is fully encrypted, and the data is collected without any personal identifiers. **Participant's Initials: _____**

I understand that the I can choose which mobile messaging service to used and choose an encrypted (such as Telegram and WhatsApp) to protect my privacy and security **Participant's Initials: _____**

I understand that I will be given a nickname to ensure anonymity when communicating through mobile messaging **Participant's Initials: _____**

I understand that I will be given a pin to make sure third parties will not be responding on my behalf.

Participant's Initials: _____

I understand that my voice will be recorded during the focus groups and interviews, and that the audio recording will be transcribed, anonymised, and discarded within 48 hours after the recording. **Participant's Initials: _____**

I understand that the research will be written up as a doctoral thesis and how personal data from this research will be anonymised and published. **Participant's Initials: _____**

I understand how to raise concerns or complaints about this study. **Participant's Initials: _____**

I understand that sensitive personal data may be collected during this study. This may include drug use history, and physical/mental health information. Any sensitive information collected will be anonymised and never shared with any governmental, non-governmental, or research organization. **Participant's Initials: _____**

I understand that in this project and all future works using the data from this study, all personal and sensitive data will be anonymised, all audio recording arising from the discussions will be discarded, and all online information are encrypted and collected without any personal identifiers. **Participant's Initials: _____**

I voluntarily consent to participate in this study and recording, and hereby assign to the researcher all copyright in my contribution for use in all work stemming from this project and future projects.

Participant's signature _____ Date _____

Investigator's signature _____ Date _____

Document A7

Legal Information on Criminalisation of Homosexuality:

Article 102 of Iran's *Criminal procedure code (2013)* states that "prosecutor is not allowed to prosecute or investigate crimes which are related to homosexuality, **unless** there is a petition from a victim of sexual offence or rape, the crime is committed in public, or in cases of organised crimes. In addition to the aforementioned prohibition from prosecution, article 106 of *Criminal procedure code* states that if the prosecutor or any judge undertakes any investigation or prosecution not compatible with article 102, they will be sentenced to administrative punishment. Moreover, **in practice**, any evidence captured through the above-mentioned illegal forms of investigation is invalid and not usable against the accused, unless it is related to a sexual offence, rape, or an organised crime. Furthermore, all investigations of sexual offence crimes must be conducted by judges, and police officers are banned from doing this investigation. In according to article 102 (subsection 1), if any person confesses to a sexual offence crime (such as homosexuality), it is incumbent upon the prosecutors or judges to prevent him/her from confessing and failing to do so will sentence the official prosecutors or judges as mentioned above.

B

Appendix B: Realist Synthesis

Table B1 Detailed overview of the five iterative stages of the realist synthesis

Stage 1: Developing initial programme theory An initial programme theory (IPT) summarises the initial understanding of how a program works. The IPT (see Figure S1) for this synthesis was underpinned by patient perspectives from an earlier qualitative analysis, expert advice, brainstorming within the research team, and identified theories in the literature. To provide explanations on how mHealth programs can impact on engagement with and adherence to treatment, five candidate theories (each with its own limitations) were selected (Table S2) given that they were frequently applied to the studies of mHealth and living with HIV. These theories, in addition to insights from our consultations and qualitative interviews informed our initial programme theory (Ameli, Haberer, et al., 2021; Ameli, Taj, et al., 2021). As the review progressed, more candidate theories (Table S3) were considered, and, as we became aware of the limitations of available data, our theoretical focus narrowed. Importantly, the scope of the synthesis was narrowed at the onset by the initial program theory in two major ways: a) narrowing the focus to aspects of living with HIV and lifetime treatment that can be modified by mobile messaging, and b) limiting it to the causal explanations on how mobile messaging affects care *for* people living with HIV, setting aside the question of how the intervention alters the larger health system, to manage the scope of how much information can be covered by the synthesis.
Stage 2: Searching for evidence An experienced information specialist (CD) guided the designing, piloting, and conducting of the search for evidence. A broad search strategy was developed to find explanatory evidence on HIV AND mHealth across various study designs and documents. Eight electronic databases (including Medline, EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, Scopus, Web of Science, Global Health, the Cochrane Database of Systematic Reviews and WHO Global Index Medicus) were systematically searched to maximise comprehensiveness and sensitivity across a range of disciplines. The searches were run twice: first in June of 2019, and a second time in January of 2021 to identify new documents that may have risen during the initial post-pandemic growth of mHealth research. Additional documents were identified through supplementary

search strategies, such as citation tracking (snowballing) and seeking expert advice. As the review progressed, further searches were undertaken iteratively, across multiple disciplines, to identify relevant substantive theories that could provide deeper insights regarding the emerging findings.

Stage 3: Selecting and appraising documents

A three-step process was used to a) identify, b) screen, and c) include documents. All retrieved documents were exported onto Rayyan QCRI platform for sorting. (Ouzzani et al., 2016) After removing duplicate records, the principal author (VA) screened all titles, abstracts, and keywords for eligibility. A second reviewer (BV) screened a random 10% subsample of the documents in the identification and screening stages to check for systematic errors. The screening of titles, abstracts, and full texts used a focused inclusion and exclusion criteria. Documents were included when providing evidence on two-way digital health interventions to support treatment adherence and engagement with care by connecting patients to providers for interactive check-ins and communication. Studies of two-way messaging were excluded when they did not involve human support. Full text articles were further screened for relevance (whether some part[s] of the document contributed to refinement of the programme theory) and rigour (whether the data used was trustworthy). The relevant substantive theoretical literature identified through the narrowing of the theoretical lens were included when providing insights that could enrich the programme theory and recommendations for future design and evaluation of human supported digital health.

Stage 4: Extracting and organising data

The documents contributing data were organised within three layers. The core documents provided data from primary studies that use mobile messaging with a human provider to support treatment and care. The topical core included studies and key reviews that provided insights on the contexts and mechanisms of human supported digital health for HIV treatment support. The theoretical core provided insights on the theoretical lens through which to understand the overall findings of the synthesis. The characteristics of the main documents are summarised in the Appendix I. Read, coding, and analysis of the emerging

codes occurred concurrently and iteratively. Coding was first applied to the document texts to organise concepts, guided by the initial programme theory, and then refined iteratively to reflect and inform the interactive relationship between context, mechanism, and outcomes that emerged from the data. Documents were organised and coded using MAXQDA software.

Stage 5: Synthesising the evidence

During this stage, the coded data extracts were configured to produce explanations of the relationship between context, mechanism, and outcomes, which form the building blocks of the refined programme theory. Concurrently and iteratively broader theoretical literature was searched to enhance and substantiate the emerging explanatory relationships. The iterative process of synthesis continued until theoretical saturation was reached, at which point many of the overlapping context-mechanism-outcome configurations (CMOCs) were collated and collapsed where appropriate. To mitigate subjectivity in the analysis, the reasoning behind the analytic stage of developing CMOCs and refining the programme theory was discussed in various rounds between two authors (VA and GW). VA is a doctoral student, who is investigating the possibilities of caring for patients through mobile phones, and GW a clinically active family physician (general practitioner).

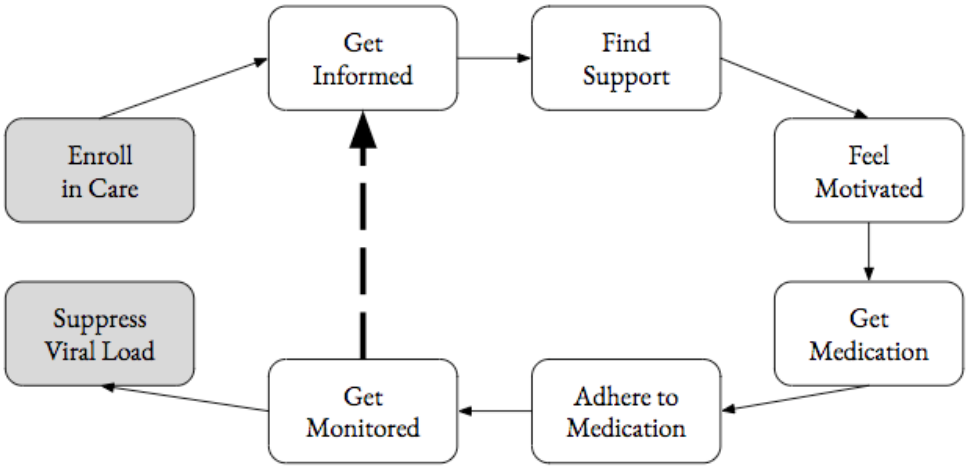

Figure B1: Initial program theory – steps taken in lifetime antiretroviral therapy

This initial programme theory was developed based on patient perspectives, expert advice, and identified theories in the literature, the initial program theory (IPT) for this review was

developed, describing the aspects of lifetime antiretroviral therapy that can be modified by mHealth to achieve and maintain viral load suppression. The theory held that participants who can access information, find support that is needed, continue to feel motivated, and get medication, are more likely to adhere better, and continue monitoring their progress, which leads to viral load suppression. Once monitoring is received further access to information is required for the patient to continue remaining within the cycle of lifetime therapy successfully.

To narrow the breadth of focus in the refinement of the program theory, two deliberate attempts were made: a) narrowing the focus to aspects of living with HIV and lifetime treatment that can be modified by mobile messaging, and b) limiting it to the causal explanations on how mobile messaging affects care *for* people living with HIV, setting aside the question of how the intervention alters the larger health system, to manage the scope of how much information can be covered by the synthesis. Further, given the focus on adherence and retention within the lifetime cycle of treatment, no attempt was made to study the causal pathways that lead to the first step of enrolment in care and last step of suppression of viral load; the former being a function of access, awareness, and agency, the latter being a by-product of the biomedical effectiveness of antiretroviral therapy. Viral load suppression is an indication of successful antiretroviral use; however, the purpose of this review is to understand the repeated cycle of decisions made by individuals to be retained within the cycle of care and treatment, and the ways in which mHealth can enhance this.

Table B2 Candidate theories that informed initial programme theory

Theory	**Description**	**Limitation**
Health Belief Model	Likelihood of engaging in health promoting behaviour based on perceived benefits, barriers, threats, in addition to self-efficacy and cues to action	It does not account for individual attitudes, emotions, habits, and how some of these are caused by the social context
Theory of Planned Behaviour / Theory of Reasoned Action	Likelihood of engaging in behaviour based on attitudes, intention, norms, perceived power, and perceived control	It assumes that person has acquired the opportunity and resources to execute the change in behaviour
Social cognitive theory / Social Learning Theory	Posits that learning occurs in a social context with a dynamic	It assumes that a change in the environment will

	and reciprocal interaction of the person, environment, and behaviour. The unique feature of SCT is the emphasis on social influence and its emphasis on external and internal social reinforcement.	automatically lead to change in person. The theory does not focus on emotions or motivation.
Information Motivation Behavioural Skills Model	Likelihood of engaging in health behaviour depends on information and knowledge about the behaviour, and the behavioural motivation and skills necessary to perform the intervention	It does not account for individual attitudes, emotions, habits, and how some of these are caused by the social context
Technology Acceptance Model	Likelihood of accepting a technology based on perceived usefulness and ease of use	Overlooks structural and economic barriers and does not question whether more technology is necessary

Table B3 Further candidate theories considered as the review progressed

Theory	**Description**	**Limitation**
Diffusion of Innovations	Developed by E.M. Rogers to explain how a new idea, behaviour, or product gains momentum and diffuses through a population or system. The five main factors that influence adoption in different settings to different extents include: Relative advantage, compatibility, complexity, trialability, and observability of the innovation. An adaptation of this theory developed by Davis as Technology	It doesn't consider an individual's resources or social support to adopt an innovation, while also overlooking structural and economic barriers, not questioning whether

	Acceptance Model has been widely used in technology and digital health research.	more technology is necessary.
Theory of Practice	Pierre Bourdieu's theory of practice set the grounds for bringing together the objectivist and subjectivist views of social reality. By considering the recursive relationship between structure and agency, he considered the "relationship between the objective structures and the cognitive and motivating structures which they produce, and which tend to reproduce them". He proposed a relationship with three essential concepts: '[(habitus)(capital)] + field = practice'. The interactive concept of social capital and habitus could have helped explain the changes in the environment through digital health that advances social care and enhances belonging.	The concepts presented would be backed by or match the available data within the literature on digital health and mobile messaging interventions. The conceptualisation of habitus is criticised for being deterministic.
Technology Structuration theory	Barley applied Anthony Gidden's Structuration theory to the technological change brought about by the introduction of the CT scanner in US hospital settings, showing how the introduction of this new technology was an 'occasion for structuring'. He used the script as a 'unit of analysis' to demonstrate how new configurations of social action emerged in response to the resources and opportunities created by the CT Scanner, but that the introduction of the CT scanner was not deterministic of the emerging outcomes. Using mobile messages as a unit of analysis and following the emerging patterns of change could have been a fruitful exercise to	The nature of the literature and available data on mobile messaging and digital health interventions would not fit an approach, such as the one taken by Barley, and through the non-deterministic streams of research that used his work on Technology Structuration theory.

	answer the how caring for and living with HIV is influence through the introduction of proactive and regular mobile messaging with providers.	
Actor Network Theory	View people and technologies within an interactive network, and the dynamically emerging relational configurations that can shape outcomes. The Actor Networks can continuously change with time and can settle within an alignment when people's needs and incentives are aligned with the technology's offerings.	It views technologies and people as equivalent change-makers, a 'symmetry' that fails to analytically consider human cognitive and affective reasonings. It overlooks structural and economic barriers and does not question whether more technology is necessary.

Table B4 Overview of main search strategy

(mhealth **OR** m-health **OR** mobile health or smartphone* **OR** mobile phone* **OR** mobile device* **OR** cellphone* or cell phone* **OR** mobile app* **OR** text messag* **OR** mobile messag* **OR** SMS **OR** digital health **OR** telemedicine **OR** telehealth or telecare **OR** technology-delivered **OR** technology-based **OR** social media **OR** online **OR** web-based **OR** e-Health **OR** electronic health **OR** e Health **OR** Internet-based **OR** telemonitoring)

AND

(HIV **OR** human immunodeficiency virus **OR** AIDS **OR** Acquired Immunodeficiency syndrome **OR** PLWHA **OR** PLHIV **OR** HAART **OR** antiretroviral*)

AND

(Adher* **OR** Retention **OR** Retain* **OR** engag*)

Table B5 Main Searches

Medline Searches:

1. (mhealth or m-health or mobile health or smartphone* or mobile phone* or mobile device* or cellphone* or cell phone* or mobile app* or text messag* or mobile messag* or SMS or digital health or telemedicine or telehealth or telecare or technology-delivered or technology-based or social media or online or web-based or e-Health or electronic health or e Health or Internet-based or telemonitoring).ti,ab,kw.
2. Telemedicine/
3. exp Cell Phone/
4. (HIV or human immunodeficiency virus or AIDS or Acquired Immunodeficiency syndrome or PLWHA or PLHIV or HAART or antiretroviral*).ti,ab,kw.
5. HIV/
6. hiv infections/ or acquired immunodeficiency syndrome/
7. Antiretroviral Therapy, Highly Active/
8. (Adher* or Retention or Retain* or engag*).ti,ab,kw.
9. "Treatment Adherence and Compliance"/
10. 4 or 5 or 6 or 7
11. 1 or 2 or 3
12. 8 or 9
13. 10 and 11 and 12

Total hits: 2158 (2021), 1674 (2019)

PsychINFO Searches

1. (mhealth or m-health or mobile health or smartphone* or mobile phone* or mobile device* or cellphone* or cell phone* or mobile app* or text messag* or mobile messag* or SMS or digital health or telemedicine or telehealth or telecare or technology-delivered or technology-based or social media or online or web-based or e-Health or electronic health or e Health or Internet-based or telemonitoring).ti,ab,id. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh]
2. exp Mobile Health/
3. exp Telemedicine/
4. exp Electronic Health Services/

5. (HIV or human immunodeficiency virus or AIDS or Acquired Immunodeficiency syndrome or PLWHA or PLHIV or HAART or antiretroviral*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh]
6. hiv/ or aids/
7. drug therapy/
8. exp treatment compliance/
9. (Adher* or Retention or Retain* or engag*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh]
10. 1 or 2 or 3 or 4
11. 5 or 6 or 7
12. 8 or 9
13. 10 and 11 and 12

Total hits: 857 (2021), 698 (2019)

Global Health Searches

1. (mhealth or m-health or mobile health or smartphone* or mobile phone* or mobile device* or cellphone* or cell phone* or mobile app* or text messag* or mobile messag* or SMS or digital health or telemedicine or telehealth or telecare or technology-delivered or technology-based or social media or online or web-based or e-Health or electronic health or e Health or Internet-based or telemonitoring).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
2. mobile health.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
3. telemedicine/
4. mobile telephones/
5. (HIV or human immunodeficiency virus or AIDS or Acquired Immunodeficiency syndrome or PLWHA or PLHIV or HAART or antiretroviral*).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
6. human immunodeficiency viruses/
7. acquired immune deficiency syndrome.sh.
8. hiv infections/
9. exp highly active antiretroviral therapy/
10. (Adher* or Retention or Retain* or engag*).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]

11. 1 or 2 or 3 or 4
12. 5 or 6 or 7 or 8 or 9
13. 10 and 11 and 12

Total hits: 864 (2021) , 672 (2019)

Embase Searches

1. (mhealth or m-health or mobile health or smartphone* or mobile phone* or mobile device* or cellphone* or cell phone* or mobile app* or text messag* or mobile messag* or SMS or digital health or telemedicine or telehealth or telecare or technology-delivered or technology-based or social media or online or web-based or e-Health or electronic health or e Health or Internet-based or telemonitoring).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
2. telemedicine/
3. exp telehealth/
4. exp mobile phone/
5. (HIV or human immunodeficiency virus or AIDS or Acquired Immunodeficiency syndrome or PLWHA or PLHIV or HAART or antiretroviral*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
6. Human immunodeficiency virus/
7. exp acquired immune deficiency syndrome/
8. exp antiretroviral therapy/
9. exp patient compliance/
10. (Adher* or Retention or Retain* or engag*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
11. 1 or 2 or 3 or 4
12. 5 or 6 or 7 or 8
13. 9 or 10
14. 11 and 12 and 13

Total hits: 2572 (2021), 2205 (2019)

Scopus

(TITLE-ABS-KEY ((mhealth OR m-health OR "mobile health" OR smartphone* OR "mobile phone*" OR "mobile device*" OR "cellphone*" OR "cell phone*" OR "mobile app*" OR "text messag*" OR "mobile messag*" OR sms OR "digital health" OR telemedicine OR telehealth OR telecare OR technology-delivered OR technology-based OR "social media" OR online OR web-based OR e-health OR "electronic health" OR "e Health" OR internet-based OR telemonitoring))) AND (TITLE-ABS-KEY (hiv OR "human immunodeficiency virus" OR aids OR "Acquired Immunodeficiency syndrome" OR plwha OR plhiv OR haart OR antiretroviral*)) AND (TITLE-ABS-KEY (adher* OR retention OR retain* OR engag*))

Total hits: 2340 (2021), 1803 (2019)

PubMed

1. Title/Abstract: mhealth OR m-health OR "mobile health" OR smartphone* OR "mobile phone*" OR "mobile device*" OR "cellphone*" OR "cell phone*" OR "mobile app*" OR "text messag*" OR "mobile messag*" OR sms OR "digital health" OR telemedicine OR telehealth OR telecare OR technology-delivered OR technology-based OR "social media" OR online OR web-based OR e-health OR "electronic health" OR "e Health" OR internet-based OR telemonitoring (189803 hits)
2. MeSH terms: Telemedicine (25805 hits)
3. MeSH terms: Cell Phone (9693 hits)
4. MeSH terms: Cell Phone Use (118 hits)
5. Title/Abstract: HIV or “human immunodeficiency virus” OR AIDS OR “acquired immunodeficiency syndrome” OR PLWHA OR PLHIV OR HAART OR antiretroviral* (397926 hits)
6. MeSH terms: HIV (95782 hits)
7. MeSH terms: HIV Infections (272933 hits)
8. MeSH terms: Antiretroviral therapy, highly active (20488 hits)
9. MeSH terms: Antiretroviral agents (65471)

10. Title/Abstract: adher* OR retention OR retain* OR engag* (678452)
11. MeSH terms: Treatment adherence and compliance (230643)

Total hits: 2230 (2021), 1646 (2019)

CINAHL

S13: S4 AND S9 AND S12

S12: S10 OR S11

S11: (MH "Patient Compliance+")

S10: TI (Adher* or Retention or Retain* or engag*) OR AB (Adher* or Retention or Retain* or engag*)

S9: S5 OR S6 OR S7 OR S8

S8: (MH "Antiretroviral Therapy, Highly Active")

S7: (MH "Anti-Retroviral Agents+")

S6: (MH "HIV Infections+")

S5: TI (HIV or "human immunodeficiency virus" or AIDS or "Acquired Immunodeficiency syndrome" or PLWHA or PLHIV or HAART or antiretroviral*) OR AB (HIV or "human immunodeficiency virus" or AIDS or "Acquired Immunodeficiency syndrome" or PLWHA or PLHIV or HAART or antiretroviral*)

S4: S1 OR S2 OR S3

S3: (MH "Cellular Phone+")

S2: (MH "Telehealth+")

S1: TI (mhealth or m-health or "mobile health" or smartphone* or "mobile phone*" or "mobile device*" or cellphone* or "cell phone*" or "mobile app*" or "text messag*" or "mobile messag*" or SMS or "digital health" or telemedicine or telehealth or telecare or technology-delivered or technology-based or "social media" or online or web-based or e-Health or "electronic health" or "e Health" or Internet-based or telemonitoring) OR AB (mhealth or m-health or "mobile health" or smartphone* or "mobile phone*" or "mobile device*" or cellphone* or "cell phone*" or "mobile app*" or "text messag*" or "mobile messag*" or SMS or "digital

health" or telemedicine or telehealth or telecare or technology-delivered or technology-based or "social media" or online or web-based or e-Health or "electronic health" or "e Health" or Internet-based or telemonitoring)

Total hits: 961 (2021), 750 (2019)

Proquest – Dissertations and theses global

noft(mhealth OR m-health OR "mobile health" OR smartphone* OR ("mobile phone" OR "mobile phones") OR ("mobile device" OR "mobile devices") OR "cellphone*" OR ("cell phone") OR ("mobile app" OR "mobile application" OR "mobile applications" OR "mobile apps") OR ("text message" OR "text messages" OR "text messaging") OR ("mobile messaging") OR sms OR "digital health" OR telemedicine OR telehealth OR telecare OR technology-delivered OR technology-based OR online OR web-based OR e-health OR "electronic health" OR "e Health" OR internet-based OR telemonitoring) AND noft(hiv OR "human immunodeficiency virus" OR aids OR "Acquired Immunodeficiency syndrome" OR plwha OR plhiv OR haart OR antiretroviral*) AND noft(adher* OR retention OR retain* OR engag*)

Total hits: 513 (2021)

Google Scholar

(text-messag* OR mobile messag* OR SMS OR whatsapp OR digital health OR mobile health OR mHealth) AND (Two-way OR two way OR bidirectional OR interactive) AND (HIV OR HAART OR antiretroviral*) 191 results

Total hits: 191 (2021)

Table B6 Secondary Searches

PubMed

1. (HIV[Title/Abstract]) OR (antiretroviral*[Title/Abstract]) (359058)
2. (therapeutic relationship[Title/Abstract]) OR (therapeutic alliance[Title/Abstract]) (6161 hits)
3. "mhealth"[Title/Abstract] OR "m-health"[Title/Abstract] OR "mobile health"[Title/Abstract] OR "smartphone*"[Title/Abstract] OR "mobile phone*"[Title/Abstract] OR "mobile device*"[Title/Abstract] OR "cellphone*"[Title/Abstract] OR "cell phone*"[Title/Abstract] OR "mobile app*"[Title/Abstract] OR "text messag*"[Title/Abstract] OR "mobile messag*"[Title/Abstract] OR "sms"[Title/Abstract] OR "digital health"[Title/Abstract] OR "telemedicine"[Title/Abstract] OR "telehealth"[Title/Abstract] OR "telecare"[Title/Abstract] OR "technology-delivered"[Title/Abstract] OR "technology-based"[Title/Abstract] OR "social media"[Title/Abstract] OR "online"[Title/Abstract] OR "web-based"[Title/Abstract] OR "e health"[Title/Abstract] OR "electronic health"[Title/Abstract] OR "e health"[Title/Abstract] OR "internet-based"[Title/Abstract] OR "telemonitoring"[Title/Abstract] (410845 hits)

Total hits: 101 (2023)

Google Scholar

(text-messag* OR mobile messag* OR SMS OR whatsapp OR digital health OR mobile health OR mHealth) AND ("therapeutic alliance" OR "therapeutic relationship") AND (HIV OR "cascade of care" OR antiretroviral*)

Total hits: 25 (2023)

(“mHeath” OR “mobile health” OR “digital health”) AND (“therapeutic relationship” OR “therapeutic alliance”) AND (“HIV” OR “antiretroviral therapy”) 892 results

Total hits: 892 (2023)

Table B7 Study characteristics

Core Primary Studies

Study characteristics (core primary studies of mobile messaging between providers and people living with HIV to improve engagement with antiretroviral therapy)								
Author Year	**Study Methods**	**Population / Sample**	**Country**	**Setting**	**Intervention**	**Research Aim(s)**	**Research Finding(s)**	**Contribution to CMOC(s)**
(Lester et al., 2010)	Randomised Controlled Trial, (Multisite)	538 adults initiating antiretroviral therapy. SMS intervention (n=273), Standard care (n=265)	Kenya	Three different clinics in Kenya: Rural, low-income, faith-based high-income	2-way interactive text-messaging (WelTel Kenya)	To assess whether mobile phone communication between health-care workers and patients initiating ART in Kenya2,12 improved drug adherence and suppression of plasma HIV-1 RNA load.	Patients who received SMS support had significantly improved ART adherence and rates of viral suppression compared with the control individuals. Findings formed the seminal study that showed mobile	2b, 4, 5

							phones, offering two-way patient-provider text messaging, might be effective to improve care in resource-limited settings.	
(Van Der Kop et al., 2012)	Conversation analysis, (SMS bi-directional messages)	Of the 538 adults initiating antiretroviral therapy, 271 participants generated 11,873 responses; 377 of which indicated a problem.	Kenya	Three different clinics in Kenya: Rural, low-income, faith-based high-income	2-way interactive text-messaging (WelTel Kenya)	1) Describe problems participants identified through mobile phone support and reasons why participants did not respond to the messages; 2) investigate factors associated	271 participants generated 11,873 responses; 377 of which indicated a problem. Health issues were the primary reason for problem responses (72%). Rural	1b, 2a, 3a, 3b

						with indicating a problem and not responding; and 3) examine participant perceptions of the intervention.	residence and age were associated with indicating a problem. Higher educational level was associated with a decreased rate of non-response. Benefits included reminding patients to take medication and promoting a feeling that "someone cares".	

(Smillie et al., 2014 a)	Qualitative, (Interviews)	People living with HIV (n = 15) and healthcare providers (HCP) (n = 5)	Kenya	Clinic in Nairobi, Kenya by African Medical & Research Foundation (AMREF)	2-way interactive text-messaging (WelTel Kenya)	Exploring the experiences of people living with HIV who have attempted to engage in HIV care, the use of cell phones in everyday life, and perceptions of communicating via text message with healthcare providers	Results indicated that while individuals have many motivators for engaging in care after diagnosis, structural and individual barriers including poverty, depression and fear of stigma prevent them from doing so. All participants had access to a mobile phone, and most were comfortable communicating through text	1b, 2a, 4

							messages, or were willing to learn. Both people living with HIV and HCP felt that increased communication via the text messaging intervention has the potential to enable early identification of problems, leading to timely problem solving that may improve retention and engagement in care during the first year after diagnosis.	

(Smillie 2014 b)	Qualitative, (Interviews pre- & post-intervention)	Wel-Tel Canada pilot study (n=20) adults in Wel-Tel Canada pilot study	Canada	Woman & Family-cantered HIV clinic in Vancouver, British Columbia	2-way interactive text-messaging (WelTel Canada)	Understand the attitudes of people living with HIV in British Columbia, Canada who faced multiple barriers to engagement in HIV care, and their experiences using the Wel-Tel intervention as a tool to help manage their care	Participants described the intervention as a useful way to communicate with health care providers, thus increasing the ability to access services, report side effects, and attend appointments. Using low-cost interactive text messaging has the potential to serve as an affordable and easy-to-use	2b, 3b

							conduit to link individuals to HCPs (outreach workers, nurses, case managers) who are equipped to assist with health promotion and navigating the health care system	
(M. Murray et al., 2015)	Mixed methods pilot, (Acceptability, feasibility, pre-intervention focus groups and post-intervention interviews)	5 Healthcare providers from a pool of 11 healthcare providers participating in pilot WelTel Canada	Canada	Woman & Family-cantered HIV clinic in Vancouver, British Columbia	2-way interactive text-messaging (WelTel Canada)	To explore intervention acceptability and feasibility from the HCP perspective through a baseline focus group and end of study interviews	HCPs identified that the WelTel intervention engaged patients in building relationships, while organising and streamlining	2a, 2b, 4

						with HCP impacted by the intervention.	existing mHealth efforts and dealing with privacy issues.	
(Rana et al., 2016)	Quasi experimental 6-month pilot pre-test post-test	20 PLHIV with higher risk of loss to follow up, including those with a recent HIV diagnosis or those re-engaging in HIV care at a large urban clinic in New England.	USA	Large Urban Clinic in New England	Clinic-based bi-directional texting with provider response within 48h window	to investigate the use of a clinic-based bi-directional texting intervention with appointment and medication adherence reminders to improve engagement in HIV care among patients who were newly diagnosed with HIV, re-	Findings support the use of a clinic-based bi-directional mHealth intervention among patients at risk for disengaging with medical care given the prevalence of cell phone use, text messaging, and acceptability of the	1a,1b, 2a, 5

						engaging with HIV medical care, or those considered by their medical providers to be at risk for non-adherence to medications or appointments.	intervention among the study participants.	
(Bayona et al., 2017)	Conversation analysis, (SMS, WhatsApp, and Facebook bi-directional messages)	40 men who have sex with men living with HIV	Peru	NGO-run HIV Clinic	Counsellor-linked bi-directional messaging	To analyze data generated from an existing mHealth intervention to gain a more detailed understanding of patient experiences during the early stages of the cascade, including linkage,	Findings identify the main themes that support was sought by participants: (a) mental health symptoms (b) coping behaviours; (c) interpersonal support; (d) physical symptoms; (e)	2a, 3a, 3b, 4

						engagement, and retention in HIV care among recently diagnosed	HIV knowledge; and (f) care coordination. Participants sent text messages describing depressive symptoms and seeking mental health services during this initial stage of HIV care.	
(King et al., 2017)	Quasi experimental, Repeated measures study	80 people living with HIV who completed the study	Canada	Woman & Family-cantered HIV clinic in Vancouver, British Columbia	2-way interactive text-messaging (WelTel Canada)	To assess whether the standardized WelTel SMS text-message intervention applied to a vulnerable, predominantly female,	Built on the WelTel (Lester, 2010) study by showing that mobile phones, offering two-way patient-provider	1b, 5

						population improved cART adherence and VL	messaging, may be an effective tool for improving cART adherence and reducing VLs among high-risk, vulnerable HIV-positive persons in Canada.	
(Bardosh et al., 2017)	Qualitative. (Interviews, implementation evaluation)	32 key informants involved in six WelTel projects	Kenya & Canada	Various	2-way interactive text-messaging (WelTel Kenya & Canada)	to provide a unique, comparative (Global North and South) perspective on the "real-world" complexity of implementation, and on the challenges and potential for	(Ruan et al., 2017) Ruan, 2017 2017	1b, 2a, 2b, 3b, 4

						scale-up, of an established mHealth application.		
	Randomised Controlled Trial (Feasibility and Acceptability)	100 people living with HIV, 50 in the intervention arm and 50 in control.	China	Major HIV Clinic in Hunan province	2-way interactive text-messaging	To examine the acceptability and efficacy of interactive short message service (SMS) in improving medication adherence in antiretroviral treatment (ART)-naïve individuals	This study shows that SMS intervention can improve HIV/ AIDS-related knowledge and ART adherence. People who receive SMS are more likely to get	1a, 2a, 3a, 3b

						living with HIV/AIDS in Hengyang, Hunan, China	higher scores and improve their ART adherence than patients who get the standard care alone.	
(Chiang et al., 2018)	Theoretical Evaluation of intervention protocol	700 patients were recruited, 349 people allocated to intervention and 351 to the control group	N/A	N/A	2-way interactive text-messaging (WelTel Kenya)	To characterize how WelTel may promote medication adherence by applying the Behaviour Change Wheel model. (Chiang_Eval _Wel_2018, P. 1: 2392)	An evaluation of WelTel using the Behaviour Change Wheel that suggests most of its impact is delivered primarily through its personalized communicatio n component, in which 8 different behaviour change	1a, 5

							techniques were identified and linked with 5 intervention functions (environmental restructuring, enablement, education, persuasion, and training). Its mechanisms of action in promoting antiretroviral therapy adherence may involve addressing all Capability Opportunity Motivation-Behaviour	

							influences on behaviour (physical and psychological capability, physical and social opportunity, reflective and automatic motivation).	
(Van der Kop, et al., 2018)	Randomised Controlled Trial	700 patients, 349 people were allocated to the intervention group and 351 to the control group	Kenya	Two clinics in informal settlements in Nairobi, Kenya	2-way interactive text-messaging (WelTel Retain Kenya)	This weekly text-messaging service did not improve retention of people in early HIV care. The intervention might have a modest role in improving	This weekly text-messaging service did not improve retention of people in early HIV care. The intervention might have a modest role in improving	2a, 4

						self-perceived health-related quality of life in individuals in HIV care in similar settings.	self-perceived health-related quality of life in individuals in HIV care in similar settings	
(Gross et al., 2019)	Randomised Controlled Trial (Multi-country)	521 enrolled participants who had failed second-line antiretroviral therapy	9 LMICs in Africa, Asia, and Americas	17 Various sites	Two-way text messaging intervention, with triggered counselling	To asses whether mobile phone communication between health-care workers and non-adherent patients improved drug adherence and suppression of viral loads in a multi-site RCT across 9 different LMICs.	Two-way MPI did not significantly improve week 48 suppression, but it did modestly affect virological failure. People failing second-line ART might not achieve benefits from phone-based triggers or enhanced	2a, 4

							adherence support (or both). More effective strategies are needed. (Gross_RCT_ 2019, P. 1: 5131)	
(Lima et al., 2019)	Quantitative (Descriptive)	102 patients	Brazil	Outpatient infectious disease clinics	Interactive text-messaging	To assess an instant messaging application as a tool of care for people living with HIV/AIDS, based on analysis of interactions between nurse and patients	There were 816 interactions, with conversations about physical activity, sharing signs and symptoms, report of engagement with treatment and request of information on the intake of medicine.	3a, 3b, 4

							Most participants showed satisfactions with the follow-up, with willingness to continue receiving the messages.	
(Pasipanodya et al., 2020)	Qualitative (Focus groups, cultural tailoring)	12 patients and 11 providers	USA	Family Health Centers of San Diego, large community health organisation	text messaging (tailoring)	to refine an existing text-messaging intervention, examine barriers and facilitators to ART adherence among African Ameri-cans and perspectives on features to	Participant-suggested features for refinement included: i) matching content to participants' comfort with receiving messages referencing HIV or medication-taking, ii)	3a, 3b, 5

						integrate into the extant intervention	culturally-tailoring content for African Americans, iii) tracking adherence, and iv) encouraging adherence interactions between patients and providers.	

Topically Relevant Primary studies, Reviews, and Commentaries

Study characteristics (highly relevant mobile messaging studies, key reviews of evidence, and expert commentaries on mHealth intervention designs and features that improve engagement with antiretroviral therapy)								
Author Year	**Document type**	**Study Population / Letter Title**	**Country**	**Setting**	**Intervention**	**Research Aim(s)**	**Research Finding(s)**	**Contribution to CMOC(s)**
(Lester, 2009)	Comment/Opinion					Mobilizing cell phones to improve antiretroviral adherence and follow-up in Kenya: a randomized controlled trial in progress		2a, 2b
(Lester et al., 2009)	Protocol	People living with HIV in Kenya	Kenya	Rural + Urban	2-way interactive text-messaging (WelTel Kenya)	To report protocol for WelTel Kenya		1b, 2b

(Chiasson et al., 2010)	Narrative review	Studies using digital media for HIV in the US	United States	Any	Digital media	To describe the role of digital media for HIV care in the US	Of the 7 published randomised trials of intensive individual-level online HIV behavioural interventions, 5 have demonstrated short-term increases in knowledge, self-efficacy, and outcome expectancies, in addition to some reduction in HIV risk behaviours, an increase in HIV testing.	1a, 3a, 5

(Chi & Stringer, 2010)	Comment	Mobile phones to improve HIV treatment adherence						1b, 2a, 4
(Coomes et al., 2012)	Narrative review	published SMS-based intervention research that aimed to improve healthcare quality and outcomes for PLWH and other chronic health conditions	Global	Any	SMS interventions	To review and provide a conceptual framework for SMS-based intervention research that aimed to improve healthcare quality and outcomes for PLWH and other chronic health conditions,	Posit that SMS-based intervention that incorporates the elements ofinteractivity, frequency, timing, and tailoring of messages could be implemented to encourage greater medication adherence as well as impact other mutually reinforcing behaviours	1a, 4, 5

							and factors (e.g. increasing patient involvement and social support, reducing risk behaviours, an promoting general health and well-being) to support better healthcare quality and clinical outcomes for PLWH.	
(T. Horvath, 2012)	Systematic review	Studies on mHealth SMS interventions to promote ART adherence	Global	Any	Text-messaging	To determine whether mobile phone text-messaging is efficacious in enhancing	Find high-quality evidence from the two RCTs that mobile phone text-messaging at	5

						adherence to ART in patients with HIV infection	weekly intervals is efficacious in enhancing adherence to ART, compared to standard care.	
(Pellowski & Kalichman, 2012)	Systematic review	Studies on technology-delivered interventions for people living with HIV	Global	Any	Technology-delivered interventions	To identify recent technology based interventions for people living with HIV	identified several gaps in the literature particularly the lack of technology-based interventions focusing on engagement and retention to care as well as sexual risk reduction.	2b
(Browne, 2013)	Editorial	Dialling for Doses: Enhancing Community-						1b, 2a, 2b, 4

		Based Adherence Support With Mobile Technologies						
(Lester, 2013)	Letter	Ask, Don't Tell - Mobile Phones to Improve HIV Care						1b, 4
(Mbuagbaw et al., 2013)	Meta-analysis	3 randomised controlled trials conducted between 2010 and 2012 in rural and urban centres in Cameroon and Kenya (two studies) were used.	Global	Rural + Urban	Text-messaging	To analyse the effects of text messaging versus usual care in improving adherence to antiretroviral therapy (ART) in people living with HIV using individual patient data meta-analysis	Text messaging has a significant effect on adherence to ART, and this effect is influenced by level of education, gender, timing (weekly vs daily) and interactivity. We recommend	1a, 1b, 5

							the use of interactive weekly text messaging to improve adherence to ART, which is most effective in those with at least a primary level of education.	
(Bastawrous & Armstrong, 2013)	Overview of reviews	mHealth recipients in LMICs	LMICs	Any	mHealth	To provide an overview of the peer-reviewed literature, published between 1 August 2006 and 1 August 2011, for the application of mobile/cell phones (from basic text-	Identifies potential for evidence-based trials of SMS interventions to change health behaviour	5

						messaging systems to smartphones) in healthcare in both resource-poor and high-income countries.		
(Van der Kop et al., 2013)	Protocol	People living with HIV in Kenya	Kenya	Informal Settlements	2-way interactive text-messaging (WelTel Retain)	To report protocol for WelTel Retain	N/A	1b, 2b, 3b
(Kahol, 2014)	Editorial	Mobile phone messaging to improve health						1a
(Finitsis et al., 2014)	Systematic Review and Meta-Analysis	Studies of text-messaging interventions to promote	Global	Any	Text-messaging	Synthesis of evidence on text-messaging interventions for promoting	Text-messaging can support antiretroviral therapy adherence.	1a, 1b, 2b, 5

		ART adherence				ART adherence	Researchers should consider the adoption of less frequent messaging interventions with content and timing that is individually tailored and designed to evoke a reply from the recipient. Future research is needed in order to determine how best to optimise efficacy.	

(Graham et al., 2015)	Development + Pilot testing of intervention	MSM living with HIV	Kenya	Urban	Case management + SMS	To test efficacy of peer and provider support through SMS	After adjustment for baseline viral suppression and confounding, the intervention group had a sixfold increased odds of viral suppression during follow-up	5
(Mursleen et al., 2015)	Economic Analysis, (Cost-effectiveness)	Population data from two SMS studies for adults initiating antiretroviral therapy in Kenya	Kenya	Various	2-way SMS-based patient engagement	To evaluate the cost-effectiveness of SMS-based adherence interventions and explore the added value of retention benefits	Effective SMS interventions would likely increase the efficiency of ART programs by improving HIV treatment outcomes at relatively low	3b

							costs, and they could facilitate achievement of the UNAIDS goal of 90% viral suppression among those on ART by 2020.	
(DeKoekkoek et al., 2015)	Integrative review	Studies on mHealth SMS interventions to promote medication adherence	Global	Any	mHealth text-messaging	To report on how text-messaging promotes adherence and provide detailed guidance for nurses to provide SMS content	Text messaging is an effective tool to improve adherence	5
(Mwai, 2015)	Letter	Scaling up WelTel: an evidence-based, patient-						2b

		centred mHealth intervention						
(Amico, 2015)	Literature review	Literature (2012-2015) on technology interventions that promote ART adherence	Global	Any	Technology-delivered interventions	Summarising recent advances in the evidence base for technology-driven, -delivered or -enhanced ART adherence intervention approaches	Emerging and future work should seek to uncover "active ingredients," or the specific aspects of the technology that appear to impact ART adherence, and the context or profiles of individuals most likely to benefit from such approaches	3a

(J. I. Campbell & Haberer, 2015)	Narrative review	People living with HIV in resource limited settings	Global	Resource Limited	Cellular-based and electronic adherence monitoring	To review recent advances in HIV-related cellular-based and electronic adherence monitoring technologies that are being studied and/or deployed in resource limited settings	Described technologies that rely upon cell phones and/or that electronically monitor adherence. Importantly, while some technologies have been used in both research and clinical settings (e.g. linkage to care and education), others (e.g. EAMs) have yet to enter clinical care. Additionally, a potential exists to	2a, 2b, 3a, 3b, 4, 5

							combine these technologies, as demonstrated by the linkage of SMS reminders with real-time adherence monitoring.	
(Simoni et al., 2015)	Narrative review of reviews	Reviews of eHealth and mHealth studies for HIV treatment and prevention	Global	Any	eHealth and mHealth solutions for HIV treatment and prevention	To discuss the opportunities and challenges of digital technology for HIV treatment and prevention	Concludes that more evidence is needed as few technology-based HIV intervention studies reference theoretical or conceptual models, limiting our understanding of	3b

							mechanisms of effect and key elements of successful intervention.	
(Mbuagbaw et al., 2015)	Overview of systematic reviews and framework for evidence transfer	Systematic reviews on text messaging interventions to improve health or health related outcome for HIV and other chronic diseases	Global	Any	Mobile phone text messaging	To evaluate Text messaging interventions for improving HIV and other chronic disease health outcomes	Text messaging has a significant effect on adherence to ART, and this effect is influenced by level of education, gender, timing (weekly vs daily) and interactivity. Recommend the use of interactive weekly text messaging to improve adherence to	1a, 1b, 5

							ART, which is most effective in those with at least a primary level of education.	
(Muessig et al., 2015)	Systematic Review	Studies using technologic modalities across the HIV care cascade	Global	Any	eHealth, mHealth and "Web 2.0" social media strategies	To evaluate technology interventions across the HIV care cascade	Describe the technology modes applied and the stages of the HIV care cascade addressed, including both primary and secondary prevention activities. Overall trends include use of new tools including social networking sites,	3b

							provision of real-time assessment and feedback, gamification and virtual reality	
(Hall et al., 2015)	Systematic review of reviews	Reviews of text-messaging for health	Global	Any	Text-messaging	Assess mobile text-messaging for health	Majority of published text-messaging interventions were effective when addressing diabetes self-management, weight loss, physical activity, smoking cessation, and medication adherence for antiretroviral therapy.	1a, 3b, 5

							However, we found limited evidence across the population of studies and reviews to inform recommended intervention characteristics. Although strong evidence supports the value of integrating text-messaging interventions into public health practice, additional research is needed to	

							establish longer-term intervention effects, identify recommended intervention characteristics, and explore issues of cost.	
(Jongbloed et al., 2015)	Review of reviews	Studies and reviews on people living with HIV	Global	Any	Digital health	Synthesis of recent evidence on digital technology for HIV care after diagnosis	Simple two-way interactive text messaging, to provide support rather than as a medication reminder, is an evidence-based technological	1b, 4

							intervention for engagement in care that is able to reach the majority of people with HIV. (Jongbled_Rev_2016, P. 10: 1794)	
(Kanters et al., 2016)	Systematic Review and network Meta-Analysis	RCTs of interventions that aimed to improve adherence to antiretroviral therapy	Global	Any	Any	Comparative effectiveness of adherence interventions with the aim of informing the WHO's global guidance on interventions to increase adherence	Identified a number of effective interventions to improve adherence to antiretroviral therapy both generally and in LMICs where most people receiving treatment reside.	4

(Abaza & Marscholle k, 2017)	Comparative review	Studies on people with any health need	Global	Any	mHealth	Comparing LMIC and HIC mHealth literature	SMS and app solutions are the most common forms of mHealth applications. SMS solutions are prevalent in both high and LMICs while app solutions are mostly used in high income countries.	3b

(Haberer et al., 2017)	Overview of evidence	evidence from individual studies, systematic reviews, meta-analyses, and the World Health Organization Consolidated Guidelines for HIV	LMICs	Any	Interventions for improving adherence to antiretroviral therapy	In July 2015, the Bill and Melinda Gates Foundation convened a meeting to discuss the most promising ART adherence interventions for use at scale in resource-limited settings. This article summaries that discussion with recent updates. It is not a systematic review, but rather provides	Numerous interventions build on existing health care infrastructure and leverage available resources. Those most widely studied and implemented to date involve peer counselling, adherence clubs, and short message service (SMS). Many additional interventions could have an important impact on	3a, 3b, 4, 5

						practical considerations for programme implementation based on evidence from individual studies, systematic reviews, meta-analyses, and the World Health Organization Consolidated Guidelines for HIV, which include evidence from randomised controlled trials in low- and middle-income countries	ART adherence with further development, including standardised counselling through multi-media technology, electronic dose monitoring, decentralised and differentiated models of care, and livelihood interventions. Optimal targeting and tailoring of interventions will require improved	

							adherence measurement.	
(Van der Kop et al., 2017)	Cross-sectional Gender comparative analysis	1068 individuals living with HIV who were screened for trial participation, 690 (64.6%) of whom were female	Kenya	informal urban settlement with limited access to services	2-way interactive text-messaging (WelTel Retain)	Pre-trial analysis of data from the WelTel Retain study on retention in HIV care to assess gender-based differences in phone access, phone sharing	men and women were equally able to participate in an mHealth intervention. Equitable access in these urban slums may indicate the 'gender	2a

						and concerns about receiving text messages from a healthcare provider.	digital divide' is narrowing.	
(Yah et al., 2017)	Scoping Review	Studies using tele monitoring and mHealth approaches for real-time monitoring of HIV and TB services	Global	Any	Telemonitoring and mHealth	To evaluate telemonitoring / mHealth approaches as a real-time strategy in HIV and TB interventions	Provide recommendations and indicate that improved integrated HIV and TB telemonitoring systems sustainability hold great promise in health systems strengthening including patient-centered early diagnosis and care delivery	2b, 4

							systems, uptake and retention to medications services and improving patients' survival and quality of life.	
(Cooper et al., 2017)	Systematic Review	Studies on people living with HIV	Global	Any	mHealth	Review impact of mHealth on self-management of HIV	Our review found evidence that mHealth interventions can have significant impact on outcomes including adherence to ART [23, 24, 26, 27, 30, 34, 45, 55], viral load [26, 34, 45], engagement	3a, 5

							with care [36], HIV knowledge, social support and sexual risk behaviours [33], smoking cessation [53], quality of life [52], depression, anxiety and self-efficacy [54].	
(Henny et al., 2018)	Rapid Review	Studies on people on HIV continuum of care	Global	Any	eHealth	Review impact of eHealth on HIV continuum of care	We have identified several key characteristics that are associated with eHealth interventions that show preliminary or proven evidence of	1b, 3a, 4

							efficacy for improving HIV care-related outcomes, particularly adherence to HIV medication. These key characteristics include (a) having a two-way interactive component between providers and client, (b) designing eHealth interventions based on behavioural theory, and (c) integrating	

							content that facilitates behaviour change using knowledge and cognition.	
(Watkins et al., 2018)	Realist Review	Studies on people living with chronic diseases and on long-term treatment	Global	Any	mHealth	Synthesise primary evidence on monitoring of chronic diseases using two-way digital text or voice communication between a patient and health worker.	Four articles were identified—monitoring of hypertension and HIV/AIDS from: Kenya, Pakistan, Honduras and Mexico and South Africa. Six components were found in	2a, 5

							all four interventions: reminders, patient observation of health state, motivational education/advice, provision of support communication, targeted actions and praise and encouragement.	
(Quintana et al., 2018)	Systematic Review	Studies on people receiving antiretroviral therapy	Global	Any	mHealth	Review mHealth impact on Antiretroviral adherence	To better retain satisfactory adherence within the HIV population, and especially in low-resource	3a

							settings, we recommend that future interventions incorporate multiple strategies: mobile-based reminders, social support structures, and personalised content.	
(Amankwaa et al., 2018)	Systematic Review and Meta-Analysis	Studies on people receiving antiretroviral therapy	Global	Any	SMS and voice call	Review impact of SMS and voice call interventions on antiretroviral adherence	Scheduled mobile phone text-messaging have demonstrated significant improvement in adherence to ART. Mobile SMS adherence interventions	2b, 3a, 3b

							that allow for two-way communication may, however, be more acceptable than standalone SMS reminders, which are seen to be intrusive, producing habituation and response fatigue.	

(Marcolino et al., 2018)	Systematic Review of Systematic Reviews	Studies on people with any health need	Global	Any	mHealth	Review effectiveness and confit-effectiveness of mHealth	The current evidence shows benefits of mHealth in chronic disease management, improving symptoms and peak flow variability in asthma patients and chronic pulmonary diseases symptoms; heart failure symptoms, reducing deaths and hospitalizatio n and improving quality of life; glycemic	1a, 1b

							control in diabetes patients; and improving BP in hypertensive patients. SMS reminders improved attendance rates at reduced costs and improved adherence to tuberculosis and HIV therapy in some scenarios, with evidence of decrease of viral load.	
(Mills & Lester, 2019) 2019	Comment/Opinion		Mobile phone-enabled adherence in HIV/AIDS		Not Applicable		3b	

(C. Kruse et al., 2019)	Systematic Review and Meta-Analysis	Studies using mHealth for public health in LMICs	LMIC(s)	Any	mHealth	Identify barriers to the use of mHealth technologies such as text messaging, calls, and apps to change and, where possible, improve the health behaviours and health outcomes of populations in developing countries.	demonstrates the barriers faced by developing countries in the use of mHealth to improve health outcomes. This systematic review shed light on the most prominent health outcomes that can be improved using mHealth technology interventions in developing	5

							countries. SMS technology is readily available at low cost in developing countries and can be easily adopted to interventions that improve the health outcomes already identified.	
(Taylor et al., 2019)	Systematic Review and Meta-Analysis	Studies using text messaging for delivery of STI/HIV interventions	Global	Any	Text messaging	to evaluate the effectiveness of text messaging to support STI/HIV prevention and treatment interventions	The effectiveness of SMS interventions to improve STI / HIV outcomes remains equivocal, and	5

							due to the lack of precision of our pooled results and inconsistency of findings due to patient characteristic variability, it is incumbent upon program planners to evaluate the effectiveness of any program to ensure it is achieving the intended result.	
(Smith & van Velthoven, 2020)	Letter	Best practices in digital health to improve antiretroviral		Various	Various			1b, 4

		treatment adherence						
(Drake et al., 2020)	Narrative Review	Studies on people accessing HIV and sexual health care	LMIC(s)	Any	SMS	Review in-person data collection for HIV-related research and monitoring evaluation	Based on the review, key considerations in selecting and designing an SMS system for data collection in LMICs are summarised, and identified 2 broad areas that have high potential to benefit from SMS as an approach to collect HIV-related data: 1. Surveillance, 2. Monitoring	5

(S. B. Lee & Valerius, 2020)	Narrative Review	Studies on people receiving antiretroviral therapy	Global	Any	mHealth	Review Current implementation of mHealth in HIV care	There seems to be a role of mHealth in the management of HIV in lower-income nations; however, the optimal design of an intervention needs to be delineated. In higher-income countries, where the 2 significant risk factors were injection drugs and men who have sex with men, the benefit was less clear, and more research is needed.	3b

(Gerke et al., 2020)	Randomised controlled trial	Youth and young adults with high risk of HIV outcomes	USA	Urban	Peer and provider support + SMS	To test efficacy of case management via SMS for youth living with HIV	Associations between greater frequency of texting with a medical case manager and greater likelihood of viral load suppression and kept medical visits at 12-month follow- up.	5
(Graham et al., 2020)	Randomised controlled trial	MSM living with HIV	Kenya	Urban	Peer and provider support + SMS	To design an intervention that was named: Shikamana after a Kiswahili word meaning "to form a bond or stick together."	The intervention was feasible and acceptable among MSM in Kenya.	5

						Providing encouragement, empathy, and information		
(Shah et al., 2019)	Systematic Review and Meta-Analysis	Studies on people receiving antiretroviral therapy	Global	Any	mHealth	Review effectiveness of mHealth in promoting adherence to antiretroviral therapy	Specific interventions, of proven effectiveness should be considered for implementation, rather than mobile phone-based interventions in general. Interventions targeting a wider range of barriers to adherence may be more effective than existing interventions.	1a, 1b

(Wang et al., 2019)	Systematic Review and Meta-Analysis	Studies on people receiving antiretroviral therapy	Global	Any	eHealth (including mHealth)	Review effectiveness of eHealth (including mHealth) in promoting adherence to antiretroviral therapy	Overall, eHealth interventions reported significant, but small, positive effects on ART adherence (Cohen d=0.25; 95% CI 0.05 to 0.46; P=.01) compared with PLWH in usual care. This finding was also stable in 3 sensitivity analyses. Specifically, SMS, telephone call, and EAMD were not able	1b

							to significantly increase ART adherence of PLWH; however, the study of combining SMS and telephone call was highly effective in improving ART adherence.	

Theoretical readings and insightful relevant studies

Study characteristics (Core theoretical readings on therapeutic relationship/alliance, including primary studies exploring therapeutic relationship/alliance and/or mHealth within similar/relevant but different clinical settings)						
Author Year	**Document Type**	**Document Title**	**Clinical Setting**	**Key Arguments / Findings**	**Key Insight**	**Contribution to CMOC(s)**
(C. Rogers, 1951)	Book	Client-centered therapy: its current practices, implications, and theory	Psychotherapy	Conceptualising how the therapeutic relationship can be therapeutic in various settings, including education and group therapy settings	Rogerian conceptualisations of the therapeutic relationship, which itself is therapeutic, through its provision of: unconditional positive regard, empathy, and congruence.	2a, 2b, overall thinking and recommendations
(Balint, 1955)	Original research	The doctor, his patient, and the illness	Any	Introducing the application of therapeutic relationship to the clinical relationship between GPs and patients, thinking of the 'doctor' as the treatment.	Introducing 'apostolic function' of doctors, which is rooted in personal background and professional training. Highlighting the importance of using reflection and discussion to understand the emotional and clinical	2a, 2b, overall thinking and recommendations

					roots of symptoms, especially through considering positionally and doctor's reflexive thoughts and feelings that are formed in a therapeutic relationship. Suggested that some patients need 'the doctor as the drug', emphasising the relational connection of patients to doctors, and that the doctor's persona could influence the 'side effects' of the 'doctor as the drug'.	

(Bordin, 1979)	Original research	The generalisability of the psychoanalytic concept of the working alliance	Psychotherapy	To elaborate on the psychoanalytic concept of the working alliance, arguing that "various modes of psychotherapy can be meaningfully differentiated in terms of the kinds of working alliances embedded in them. Moreover, the strength, rather than the kind of working alliance, will prove to be the major factor in change achieved through psychotherapy.	Bordin developed a 'pan-therotical reformulation' in which the 'Working Alliance' was seen as a basis for a general theory of psychotherapy in its multitude of forms. Bordin's concept of the alliance involved agreements and collaboration between the therapist and the client; thus, it was a "true" bidirectional relationship, beyond the uni-directional provision of empathy, unconditional positive regard, and congruence. His definition of the alliance was made up of three interlocking components: bonds, tasks, and goals.	2a, 2b, 4, 5, overall thinking and recommendations

(A. Horvath, 2000)	Conceptual and historic review of therapeutic alliance	The therapeutic relationship: From transference to alliance	Psychotherapy	To provide an overview of the historic roots of the therapeutic relationship, its evolving nature, and conceptual transformations.	The review provided an orientation within the evolving conceptualisations of therapeutic relationship: from the Freudian transference, to a 'real" relationship that helps the therapeutic process, to the more recent conceptualisations that see the therapeutic relationship itself as therapeutic.	overall thinking and recommendations
(Federman et al., 2001)	Intention to discontinue care among primary care patients: influence of physician behaviour and process of care	Intention to discontinue care among primary care patients: influence of physician behaviour and process of care	Any	"patient reports that the physician did not listen to what the patient had to say (OR, 8.8; 95% CI, 2.5 to 30.7). In subgroup analysis, patients who were prescribed medications at their last visit but who did not receive an explanation of the purpose of the medication were more	mHealth could help with providing a feeling of being listened to, and also providing detailed and ongoing information on treatment and care, thereby preventing prime reasons for drop-out and disengagement.	1b, 3a, 5

				likely to be unwilling to return (OR, 4.9; 95% CI, 1.8 to 13.3)"		
(Roter & Larson, 2002)	Assessing strengths, limitations and scope of RIAS for interaction analysis	The Roter interaction analysis system (RIAS): utility and flexibility for analysis of medical interactions	Any	Patient-provider communication can be broadly divided into affective and instrumental, or 'care' talk and 'cure' talk. Interaction analysis can perform a sentence-by-sentence coding of verbatim transcripts of patient-provider encounters.	Future mHealth studies could use interaction analysis to examine the interactions that take place in messing or other mHealth communication applications. Distinguishing between 'care' and 'cure' talk can examine the extent of affective versus instrumental exchanges between patients and providers. RIAS can help gauge the presence or absence of a key	2a, overall thinking and recommendations

					element that adds value to the therapeutic relationship: empathy towards socio-emotional needs.	
(Deveugele et al., 2004)	Cross-sectional study. The communicative behaviour was gauged by means of the Roter interaction analysis system (RIAS).	Is the communicative behaviour of GPs during the consultation related to the diagnosis?: A cross-sectional study in six European countries	Any	A key difference across countries was found on consultations about psychosocial problems and affective behaviour, such as social talk, agreement, rapport building and facilitation.	6	overall thinking and recommendations
(Robb & Greenhalgh, 2006)	Qualitative study	You have to cover up the words of the doctor": the mediation of trust in interpreted	Any	Trust was a prominent theme in almost all the narratives in the interpreted consultation settings. “The critical importance of voluntary trust for open and effective	The interdependence of trust and therapeutic relationship in various clinical relationships, including interpretation services. There may also be different types trust, which can be fruitfully	2a, 2b, overall thinking and recommendations

		consultations in primary care		communication, and the dependence of the latter on a positive interpersonal relationship and continuity of care, should be acknowledged in the design and funding of interpreting services and in the training of both clinicians, interpreters and administrative staff."	explored in future studies of mHealth.	
(Mol, 2008)	Book	The Logic of Care	Diabetes	Juxtaposes logic of care against logic of choice, arguing that clinical care for chronic illnesses needs to focus less on providing choice and shifting responsibilities of finding good care to patients. Instead, Mol proposes that a logical of care put patients and physicians on the same side to provide,	The proposition of the logic of care by Mol is one theory to underpin the defining attributes of a therapeutic relationship in the chronic disease context. This logic can be used to develop and examine a therapeutic relationship when caring for people living with HIV and	1a, 1b, 2a, 2b, 3a, 3b, 4, 5, overall thinking and recommendations

				continuous, holistic, and affective care.	when doing so through mobile phones.	
(Reis et al., 2008)	Three-country study of a new scale designed to assess patient perceptions of physician responsiveness	Measuring Responsiveness in the Therapeutic Relationship: A Patient Perspective	Any	Patient perceptions of physician responsiveness significantly predicted both patient satisfaction and subjective health status. More important is the finding that even when general satisfaction was controlled, responsiveness still accounted for significant variance in ratings of subjective health-related problems.	Enriched the programme theory on the importance of 'responsiveness' and 'trust' in the context of a therapeutic relationship. Showing that when providers are responsive to patient needs, and importantly when patients perceive providers as responsive to their needs, trust can develop. Responsiveness and trust are two important aspects of the success of long-term care and health-related benefits from continuous care.	1b, 2a, 2b, 4

(Greenhalgh & Heath, 2010)	Meta narrative review of literature on therapeutic relationship and how to measure its quality	Measuring quality in the therapeutic relationship	Any	A critical review of the literature that explores the therapeutic relationship is provided. considered Different research traditions in terms of their respective philosophical assumptions, methodological strengths and limitations and empirical findings are considered.	This document contributed significantly to orienting us in our conception of the therapeutic relationship and how it can relate to the particular question of this realist synthesis. It also provided an excellent and efficient means of exploring different research traditions to enrich the findings. This review provided an excellent source for snowballing references.	Overall thinking and reading

(Greenhalgh & Heath, 2010a)	Meta narrative review of literature on therapeutic relationship and how to measure its quality through objective measures	Measuring quality in the therapeutic relationship—part 1: objective approaches	Any	The 'objective' research traditions from the above document are considered in terms of their strengths and limitations to 'measure' the therapeutic relationship.	This article was a focused summary of the objective measures and further narrowed our snowballing. The discussion on 'trust' and its impact on patient satisfaction enriched our CMOCs on a trusting relationship.	2a, 2b
(Greenhalgh & Heath, 2010b)	Meta narrative review of literature on therapeutic relationship and how to measure its quality through subjective measures	Measuring quality in the therapeutic relationship—part 2: subjective approaches	Any	The 'subjective' research traditions from the above document are considered in terms of their strengths and limitations to 'measure' the therapeutic relationship.	This article was a focused summary of the subjective measures and further narrowed our snowballing.	Overall thinking and reading

(Verhoeks et al., 2019)	Systematic review	Women's expectations and experiences regarding e-health treatment: A systematic review		review showed that barriers to e-health treatment were lower for women than barriers to face-to-face treatment, such as feelings of shame and time constraints. However, they expressed a wish for more support during e-health treatment, preferably blended care with human support and face to face care.	e-Health lowers the threshold for women to seek healthcare. Women were able to develop an online therapeutic relationship. However, combining e-health interventions with face-to-face sessions may enhance women's motivation to complete treatment.	Overall thinking and recommendations
(Tremain et al., 2020)	Narrative Review	The Therapeutic Alliance in Digital Mental Health Interventions for Serious Mental Illnesses: Narrative Review		Results indicated that a therapeutic alliance can be cultivated in digital interventions for those with serious mental illnesses, however programs cannot simply replace providers. A number of design and implementation considerations may enhance the digital	More research is required to further understand the nature and specific role of a therapeutic alliance in digital interventions for serious mental illnesses, particularly in informing their design. This review revealed several key research priorities to advance the therapeutic	Overall thinking and recommendations

				therapeutic alliance, including human support and technological features.	alliance in digital interventions.	
(Müssener, 2021)	Critical reflections on digital therapeutic relationship	Digital encounters: Human interactions in mHealth behaviour change interventions	Any	The user feelings associated with digital therapeutic relationships and how such interactions might affect user's capacity for behavioural change are raised. There is considerable distinction made on whether a human professional is included as part of the intervention. The complexity of the	Some technological features and human-like considerations for enhancing digital encounters in mHealth interventions are provided.	1a, 1b, 2a, 2b, 3a, 3b, 4 Overall thinking and recommendations

				therapeutic alliance within the digital realm of communication is expanded on, using a variety of evidence sources on various diseases.		

Table B8 Context – Mechanism – Outcome – Configurations (CMOCs)

Context – Mechanism – Outcome Configurations (CMOCs)	Contributing sources
1) Engagement with tailored content and responsive providers	
1a) When mobile messages offer a tailored content and use a personalised language (C) patients are more likely to engage with the content (O) because they perceive the content to be individually relevant to them (M)	6, 10, 11, 18, 20, 21, 25, 28, 29, 37, 39, 51, 60, 76, 70, 71, 72, 77
A third element of messaging design investigated here was that of individual tailoring of message content. Interventions that used participant input to generate personalised message content saw larger effects on outcomes than those that sent uniform messages to all participants. While providers are certainly the experts of disease, patients are the experts of themselves. Interventionists who sought the participants' own words and preferences may have produced intervention content that was less intrusive and more relatable for participants. (Finitsis et al., 2014) Our evaluation of WelTel using the Behaviour Change Wheel suggests that most of its impact is delivered primarily through its personalised communication component (environmental restructuring, enablement, education, persuasion, and training). (Chiang et al., 2018) Five of the 15 reviews focused on medication adherence, which is an important public health issue (49). Park et al. (36) included a wide range of chronic conditions (e.g. diabetes, asthma, HIV/AIDS) for	

which SMS messages were tested for medication adherence and found that 18 out of 29 studies using TMIs reported statistically significant improvements in medication adherence rates or biomarkers; however, 11 studies reported no differences. The authors note that many of these 11 nonsignificant studies used basic and repetitive SMS content compared to more varied and motivational content in the studies with positive outcomes. (Hall et al., 2015b) Whittaker et al [20] listed advantages of using mobile interventions: convenience, ease, cost-effectiveness, scalability, personalisation, and "the ability to send time-sensitive messages with an 'always on' device." Hamine et al [34] observed that mHealth tools can impact patients who are less inclined to engage with traditional health services. The most popular mHealth intervention was behaviour change interventions using text messaging. (Marcolino et al., 2018) Tailoring, and personalizing content may help foster a digital therapeutic alliance between the user's personal needs and goals and interactions with the intervention.36 Individuals seem more motivated to engage with and process information more thoroughly if the content is personally relevant and meaningful.37.... Digital interventions need to be as engaging and trustworthy as possible to effect behaviour change..... Being able to select the frequency of the messages is stressed as one feature that might affect the experience of the intervention as more personalised. (Müssener, 2021)	

1b) When mHealth offers communication with a human provider (as opposed to an automated system) who is responsive to patients' expressed needs (C) patients value the openness, flexibility, and responsiveness of interactions offered by the intervention (O) because they perceive these modes of care as useful (M)	2, 3, 6, 8, 9, 19, 23, 24, 25, 27, 29, 37, 40, 47, 51, 55, 60, 61, 70, 71, 72, 75, 77
Many participants indicated that they appreciated knowing that there was an actual person on the other end sending the messages to them, which made it more personal than if it was just an automated system as this one participant conveys: "I was talking to a human being, so that's what makes it more worth it. If I'm talking to a recording and they're recording me, it's almost like that wasn't worth it at all." (Rana et al., 2016) Versatility of the SMS technology was described as a "lifeline" that allowed patients to engage on their own terms, when and how they needed assistance. They could be very active on the platform, and then remain silent until a future need arose. The benefits of SMS also allowed some more vulnerable patients in Canada to "open-up" about complex issues, due to the "emotional safety", as one nursing staff described it, of the SMS technology. These benefits were widely discussed as a form of "patient empowerment." (Bardosh et al., 2017) Imagine that patients are sick, and a unidirectional text-messaging service keeps telling them they are important and cared for. It is better to show patients you care, rather than just tell them. (Lester, 2013)	

Text message interventions that include a link to a health care professional, interactivity and three or more BCTs all showed improvements in objective adherence measures. (Shah et al., 2019) Results supported all three hypotheses. Patient perceptions of physician responsiveness significantly predicted both patient satisfaction and subjective health status. More important is the finding that even when general satisfaction was controlled, responsiveness still accounted for significant variance in ratings of subjective health-related problems. (Reis et al., 2008) Additionally, if the sender is known and identifiable, this could influence the participant's trust in and perception of the credibility and value of the intervention and the information it provides, and strengthen the belief that the messages were sent by a person, even if sent from an automated service. (Müssener, 2021)	

2) Therapeutic relationship with trusted providers who care	
2a) When providers are willing to use mHealth to proactively check-in for affective and clinical care (C) especially in the early stages of care (C) patients can build rapport, trust, and a therapeutic relationship with providers (O) because they feel heard, cared for, and seen. (M)	2, 3, 5, 6, 7, 9, 10, 12, 13, 16, 19, 23, 35, 44, 48, 66, 70, 72, 73, 74,
First, why did the intervention work? The SMS queries were too infrequent to actually remind patients to take their drugs pill by pill. Possibly the SMS intervention worked by improving communication and rapport between health providers and patients (patients reported during the pilot phase that "it feels like someone cares"). (Chi & Stringer, 2010) Another participant felt the messaging conveyed a responsible connection that someone was keeping them accountable for their actions: "It feels a little bit more accountable when someone's actually taking their time to text message you." (Rana et al., 2016) The most positive feedback from early enrolees in the SMS-protocol is that the participants feel "like someone cares" ("Mobilizing Cell Phones to Improve Antiretroviral Adherence and Follow-up in Kenya: A Randomised Controlled Trial in Progress.," 2009) The fact that participants in our study shared intimately personal details about their emotional and mental state with their assigned HIV counselor shows the potential role that a bi-directional text messaging intervention can have for engaging patients during the early steps of the HIV cascade. (Bayona et al., 2017)	

Patients were reported to regularly text about the “joys and challenges of life” (Interview, Clinician, Canada) while staff could also use the service to check-in with patients who were going through difficult periods, either clinically or emotionally. “the more you talk, the more friendly you become” (Kuongea ni Kuongeza Urafiki, in Swahili). Similar euphemisms were used in Canada. Complex issues could be triaged on the phone, connecting patients to multiple healthcare providers, while also allowing patients with chronic conditions, like HIV, to build stronger rapport with their providers. In Kenya, and to a lesser degree in Canada, one of the most emphasised benefits was the ability for patients to circumvent long wait times for immediate health needs.(Bardosh et al., 2017) Patient reports of their physician not listening to what they have to say, not acknowledging their concerns, and not spending time with them all predict reluctance to return to that physician. (Federman et al., 2001) People’s opinions differ, and some studies described that participants felt that these interventions provided them with feelings of support and connectedness, as they reported that someone was giving their time (to send them messages), which made them feel that someone was thinking of them and cared about them. (Müssener, 2021) In care-specific terms, care is bad when people are being neglected. When there is not enough time to listen. When physical parameters are isolated from their context; when patients’ daily lives are not taken into consideration. (Mol, 2008)	

2b) When mobile messaging provides the means to connect and maintain an ongoing therapeutic relationship between patients and providers (C) long-term engagement in care can enhance between them (O) because they can maintain and deepen their trusting relationship with providers and the health system (M)	1, 4, 5, 9, 16, 17, 22, 23, 27, 29, 33, 35, 45, 50, 71, 73
"By initiating conversations with their assigned counsellor and in responding to standardised messages, participants were able to elicit and manage their interpersonal support to bolster their wellbeing. Additionally, patients were able to schedule and reschedule appointments and ask questions about lab results by sending text messages to their counsellor. Overall, these conversations reflect that participants were actively engaging in their own care. (Bayona et al., 2017) Many of our participants had support from family and friends and had already established relationships with their HCPs prior to the intervention, a factor shown to promote long-term engagement in care (Mallinson, Rajabiun, & Coleman, 2007). What participants required was a method to help them facilitate and maintain this relationship to care. When asked what they liked about the WelTel intervention, most described appreciating the feeling that someone cared, that someone was looking out for them, and that they were not alone. (Smillie, Van Borek, Abaki, et al., 2014) Feedback suggests that the majority of health providers, patients and decision-makers highly value the intervention, particularly its capacity for keeping vulnerable patients connected to the health care system, and allowing effective remote patient follow up and triage. (Mwai, 2015)	

Another possible factor is the extent to which bidirectional communication bolsters the patient-provider relationship, increasing trust [11]. Evidence suggests that patients are better able to manage their care and are more likely to achieve adherence goals when they perceive their providers care about and like them [48,49]. It is possible that messaging back and forth with clinic staff sufficiently evokes a relationship dynamic as to further bolster the extant patient-provider relationship. (Finitsis et al., 2014) a long-term relationship with a primary care physician has certain conceptual parallels with close relationships in general (although to be sure there are important differences). These parallels prominently include the importance of understanding, acceptance and support of the patient's health care needs as a key element of responsive relationships between patient and physician. (Reis et al., 2008)	

3) Enabling trusted, timely, and convenient sharing of information, concerns, and perspectives	
3a) When patients can openly message their questions to their trusted providers (C), especially in the early stages of care (C) knowledge and management of treatment can improve (O), because they can get trusted clarification and clinical guidance (M)	2, 7, 10, 14, 15, 18, 32, 34, 35, 43, 46, 47, 50, 51
"The fifth theme, HIV knowledge, included the codes of transmission, misinformation, and clinician expertise. Messages in which participants expressed what they knew or understood about HIV modes of transmission were coded as such. The code of misinformation was used when messages described false beliefs, stereotypes, or other false information about HIV that was regarded as true by participants. Messages were coded as clinician expertise when participants described a doctor or nurse explaining and clarifying HIV information to them or when counsellors provided education to participants. The text message exchanges that occurred within this theme emerged from both replies to standard text messages and natural conversations. The distribution of these exchanges in time ranged from a single message reply by participants to a 30-minute text conversation. (Bayona et al., 2017) Although in the HIV clinic, PLWH receive routine teaching sessions for ART preparation and some pamphlets, at the initial stage of ART, SMS could regularly send drug use instructions to patients, and timely answers to their questions effectively improves the awareness of drug use. (Ruan et al., 2017) Participants identified informational support from providers as helpful for understanding HIV and supporting ART adherence. Many providers	

additionally reported facilitating open communication and endorsed engaging in active problem-solving as helpful for bolstering adherence. (Pasipanodya et al., 2020) Mobile devices may improve patient-provider communication, facilitating assistance in disease management. It may increase the likelihood of delivering health interventions to hard-to-reach populations. (Marcolino et al., 2018) In care specific terms, care is bad..... when patients are left to their own devices and have to face complex (and sometimes impossible) tasks of combining the divergent instructions given to them by different specialists. (Mol, 2008) Compared with the control group, the mean scores for both HIV-related and ART medication knowledge of the SMS intervention group demonstrated a better improvement over time than those of the control group after the intervention (P,0.0001). The effect sise of SMS intervention over time for HIV-related knowledge and medication knowledge was 0.35 and 0.48, respectively (Ruan et al., 2017) At 4 months, the intervention arm had higher self-reported adherence (past 7 days: 77% versus 56%, p = .022) and higher CD4 counts (extracted from clinical records; 578 cells/ml versus 362 cells/ml, p= .0007). Utilisation of intervention data was not reported, although the authors attribute intervention effects to increasing patient knowledge and literacy around HIV medication and adherence. (Amico, 2015)	

3b) When providers regularly and responsively communicate with patients (C), especially in the early stages of care (C) patients are more able to get the support and help needed to overcome challenges and barriers that arise (O) because they can get timely help and advice (M) and use the conduit of messaging to share concerns more easily in various forms (M).	4, 2, 7, 9, 10, 14, 15, 27, 31, 35, 36, 38, 39, 40, 42, 43, 49, 50, 52, 57
The interactive text message offered the ART-naïve individuals a conduit for timely communication with healthcare providers as to informational, emotional, and technical supports to overcome the multitude of barriers they faced at the start of ART. (Ruan et al., 2017) "The WelTel intervention provided a conduit for many to deal with challenges in a timely manner, thus facilitating the ability to attend appointments, communicate with their HCPs, and take medications..... Participants described feeling comforted knowing that the HCPs were there for them when they were in crisis, and that they were referred to support services when needed. (Smillie, Van Borek, Abaki, et al., 2014) The results of our study reveal a potential role for an mHealth intervention to serve as ancillary support to clinicians, especially when patients are entering the ART adherence step of the HIV cascade during which they may experience medication side effects. The participants in our study sent messages describing their symptoms and counsellors were able to ask questions to determine whether an emergency was occurring and needed immediate clinical	

attention, or if the person could wait until the following day to receive care. (Bayona et al., 2017) The added capability to send and receive photos was especially helpful in assessing rashes and improved patient understanding of their own symptoms. We found that a qualitative analysis of participant–counsellor text message exchanges was important to reveal not only the nature of support provided by the counsellors during this mHealth intervention, but also to reveal concerns, challenges, and solutions that were most impactful during the early stages of the cascade for our recently diagnosed participants. (Bayona et al., 2017) The role of applications as a conduit for health care support was also emphasised [71,84]. (S. B. Lee & Valerius, 2020) Recent research has shown that by facilitating communication between patients and health services, and supporting connection with peers [48], two-way communication technology is a formidable vehicle for psychosocial support [44, 51, 58, 59]. (Jongbloed et al., 2015) Some participants experienced mHealth interventions as more convenient, reliable, flexible, less judgmental, and faster, and stated that they provided more frequent support. In mHealth interventions the 'professional' takes up less, or no, space in treatment, i.e. the professional is less present in physical space, but might be more present in terms of availability. mHealth interventions might, if the user requires it, offer more frequent 'contact' compared with face to face. (Müssener, 2021)	

4) Strategizing holistically for multidisciplinary care	
4) When providers are willing and able to counsel patients and work towards holistic care (C) patients can have more of their needs met (O) because their care is multidisciplinary and not fragmented (M).	1, 3, 5, 7, 9, 12, 13, 14, 19, 20, 23, 24, 35, 40, 41, 43, 45, 47, 55
This model recognises that multiple social barriers inhibit medication adherence, calling upon the need for HCPs to work collectively in strategizing engagement opportunities for each individual. Respect for adherence to this model of care was the most important concern for HCP [Healthcare provider] participants. (M. C. M. Murray et al., 2015) "I think that part of our job is… to give the medication and make sure we tailor the best medications as per personality and personal barriers… views and values, etc. but I think the other part is really the multidisciplinary… support of the group because….it's HIV and not another chronic disease: they need a lot of support for their treatment because many of them have social barriers… we all know that if you don't have any housing that even if you are sick and your CD4 is 20, you will not be able to get your ARVs or take your ARVs or probably care." (M. C. M. Murray et al., 2015) While it is possible that the effect of the interventions is attributable to the text messages, the possible role of phone counselling should be acknowledged. Phone counselling enables personalised support to be delivered. Concerns can be addressed, and content tailored accordingly in a way that is not possible with automated messages. In the Gross trial, participants were sent daily, and then weekly, SMS messages in the local language asking, 'Everything ok?', to which they were expected to respond by calling a central number. In both trials, failure	

to respond to messages triggered an attempt at phone counselling by healthcare workers. In the Lester trial, 4171 out of 11983 (35%) responses would have required a phone call. In the Gross trial, 248 out of 250 participants (99%) met the criteria for phone contact at least once. Despite both studies involving a significant amount of phone counselling, they have been described as 'SMS interventions' and the content and possible effect of phone counselling are not discussed. (Smith & van Velthoven, 2020) New studies have taken a "whole person" approach to technological engagement in care interventions that acknowledge and support multiple health needs and priorities, such as co-morbidities and substance use. (Jongbloed et al., 2015) We found the most important differences for consultations about psychosocial problems as compared to all other diagnostic categories. In these consultations, doctors show more affective behaviour, are more concerned about having a good relationship with their patients, ask more questions and give less information than in other consultations. The percentages of utterances in the other diagnostic categories were pretty similar. The communicative behaviour of doctors reflects a global pattern in every consultation. This pattern is the most stable for affective behaviour (social talk, agreement, rapport building and facilitation). Within instrumental behaviour (the other categories), the directions and the information the doctor gives are adapted to the problems presented. (Deveugele et al., 2004)	

References

Abaza, H., & Marschollek, M. (2017). mHealth Application Areas and Technology Combinations*. A Comparison of Literature from High and Low/Middle Income Countries. *Methods of Information in Medicine*, *56*(7), e105–e122.

Abimbola, S., Asthana, S., Cortes, C. M., Guinto, R. R., Jumbam, D. T., Louskieter, L., Kabubei, K. M., Munshi, S., Muraya, K., Okumu, F., Saha, S., Saluja, D., & Pai, M. (2021). Addressing power asymmetries in global health: Imperatives in the wake of the COVID-19 pandemic. *PLoS Medicine*, *18*(4). https://doi.org/10.1371/JOURNAL.PMED.1003604

Abimbola, S., Patel, B., Peiris, D., Patel, A., Harris, M., Usherwood, T., & Greenhalgh, T. (2019). The NASSS framework for ex post theorisation of technology-supported change in healthcare: worked example of the TORPEDO programme. *BMC Medicine 2019 17:1*, *17*(1), 1–17. https://doi.org/10.1186/S12916-019-1463-X

Abrams, H. B., Bock, K., & Irey, R. L. (2015). Can a Remotely Delivered Auditory Training Program Improve Speech-in-Noise Understanding?. *American Journal of Audiology*, *24*(3), 333–337. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med11&NEWS=N&AN=26649542

Abu-Raddad, L. J., Akala, F. A., Semini, I., Riedner, G., Wilson, D., & Tawil, O. (2010). *Characterizing the HIV/AIDS Epidemic in the Middle East and North Africa*.

Agwu, A. L., & Fairlie, L. (2013). Antiretroviral treatment, management challenges and outcomes in perinatally HIV-infected adolescents. *Journal of the International AIDS Society*, *16*(1). https://doi.org/10.7448/IAS.16.1.18579

AIDSinfo, & UNAIDS. (2023). *Global factsheets 2022*. https://aidsinfo.unaids.org/

Alabaster, O. (2016). Deadly Stigma: HIV Infections in Middle East on the Rise. *VICE*. https://www.vice.com/en/article/xy84jn/hiv-infections-are-growing-in-the-middle-east-thanks-to-prejudice-and-a-lack-of-sex-ed

Aliabadi, N., Carballo-Dieguez, A., Bakken, S., Rojas, M., Brown, W., Carry, M., Mosley, J. P., Gelaude, D., & Schnall, R. (2015). Using the Information-Motivation-Behavioral Skills Model to Guide the Development of an HIV Prevention Smartphone Application for High-Risk MSM. *AIDS Education and Prevention : Official Publication of the International Society for AIDS Education*, *27*(6), 522. https://doi.org/10.1521/AEAP.2015.27.6.522

Altman, D. (1999). Globalization, Political Economy, and HIV/AIDS on JSTOR. *Theory and Society*, *28*(4), 559–584. https://www.jstor.org/stable/3108562

Amankwaa, I., Boateng, D., Quansah, D. Y., Akuoko, C. P., & Evans, C. (2018). Effectiveness of short message services and voice call interventions for antiretroviral therapy adherence and other outcomes: A systematic review and meta-analysis. *PloS One*, *13*(9), e0204091.

Ameli, V. (2014). Social and behavioral factors associated with injection drug use among Iranian men living in Kermanshah city.

Ameli, V. (2023). Unilateral Sanctions as Sustainable Development Decelerators, The Routledge Handbook of the Political Economy of Sanctions (K. Kirkham, Ed.). Routledge. https://www.routledge.com/The-Routledge-Handbook-of-the-Political-Economy-of-Sanctions/Kirkham/p/book/9781032355634

Ameli, V., Haberer, J., Sabin, L., Meinck, F., Barlow, J., Taj, L., & Mohraz, M. (2021). Tailored mHealth intervention for improving treatment adherence for people living with HIV in Iran (HamRaah): protocol for a feasibility study and randomised pilot trial with a nested realist evaluation. *BMJ Open*, *11*, 42296. https://doi.org/10.1136/bmjopen-2020-042296

Ameli, V., Taj, L., Barlow, J., Sabin, L., Meinck, F., Haberer, J., & Mohraz, M. (2021). 'You just prefer to die early!': How socioecological context impedes treatment for people living with HIV in Iran. *BMJ Global Health*, *6*(11), e006088. https://doi.org/10.1136/BMJGH-2021-006088

Amico, K. R. (2015). Evidence for Technology Interventions to Promote ART Adherence in Adult Populations: a Review of the Literature 2012-2015. *Current HIV/AIDS Reports*, *12*(4), 441–450.

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), 188. https://doi.org/10.1186/1471-2458-14-188

Arrivillaga, M., Ross, M., Useche, B., Springer, A., & Correa, D. (2011). Applying an Expanded Social Determinant Approach to the Concept of Adherence to Treatment: The Case of Colombian Women Living With HIV/AIDS. *Women's Health Issues*, *21*(2), 177–183. https://doi.org/10.1016/J.WHI.2010.09.003

Arum, C., Fraser, H., Artenie, A. A., Bivegete, S., Trickey, A., Alary, M., Astemborski, J., Iversen, J., Lim, A. G., MacGregor, L., Morris, M., Ong, J. J., Platt, L., Sack-Davis, R., van Santen, D. K., Solomon, S. S., Sypsa, V., Valencia, J., Van Den Boom, W., … Strathdee, S. A. (2021). Homelessness, unstable housing, and risk of HIV and hepatitis C virus acquisition among people who inject drugs: a systematic review and meta-analysis. *The Lancet Public Health*, *6*(5), e309–e323. https://doi.org/10.1016/S2468-2667(21)00013-X/ATTACHMENT/928DA60E-2BC9-4CB6-BD66-11C429DFEEB5/MMC1.PDF

Attride-Stirling, J. (2001). Thematic networks: An analytic tool for qualitative research. *Qualitative Research*, *1*(3), 385–405. https://doi.org/10.1177/146879410100100307

Axworthy, M. (2013). *Revolutionary Iran: A History of the Islamic Republic*. Oxford University Press.

Bach-Mortensen, A. M., Goodair, B., & Barlow, J. (2022). Outsourcing and children's social care: A longitudinal analysis of inspection outcomes among English

children's homes and local authorities. *Social Science & Medicine*, *313*, 115323. https://doi.org/10.1016/J.SOCSCIMED.2022.115323

Bach-Mortensen, A. M., Goodair, B., & Barlow, J. (2023). For-profit outsourcing and its effects on placement stability and locality for children in care in England, 2011–2022: A longitudinal ecological analysis. *Child Abuse & Neglect*, *144*, 106245. https://doi.org/10.1016/J.CHIABU.2023.106245

Badawy, S. M., Barrera, L., Sinno, M. G., Kaviany, S., O'Dwyer, L. C., & Kuhns, L. M. (2017). Text Messaging and Mobile Phone Apps as Interventions to Improve Adherence in Adolescents With Chronic Health Conditions: A Systematic Review. *JMIR MHealth and UHealth*, *5*(5), e66. https://doi.org/10.2196/mhealth.7798

Balint, M. (1955). The Doctor, His Patient, and the Illness. *The Lancet*, 683–688.

Bardosh, K. L., Murray, M., Khaemba, A. M., Smillie, K., & Lester, R. (2017). Operationalizing mHealth to improve patient care: a qualitative implementation science evaluation of the WelTel texting intervention in Canada and Kenya. *Globalization and Health*, *13*(1), 87.

Barker, C., Dutta, A., & Klein, K. (2017). Can differentiated care models solve the crisis in HIV treatment financing? Analysis of prospects for 38 countries in sub-Saharan Africa. *Journal of the International AIDS Society*, *20*(0), 21648. https://doi.org/10.7448/IAS.20.5.21648

Bar-Lev, S. (2008). *"We Are Here to Give You Emotional Support": Performing Emotions in an Online HIV/AIDS Support Group*. https://doi.org/10.1177/1049732307311680

Barley, S. R. (1986). Technology as an occasion for structuring: Evidence from observations of CT scanners and the social order of radiology departments. *Administrative Science Quarterly*, *31*(1), 78–108. https://doi.org/10.2307/2392767

Bärnighausen, T., Tanser, F., Herbst, K., Mutevedzi, T., Mossong, J., & Newell, M.-L. (2013). Structural barriers to antiretroviral treatment: a study using population-based CD4 cell count and linked antiretroviral treatment programme data. *The Lancet*, *382*, S5. https://doi.org/10.1016/s0140-6736(13)62253-9

Bassett, I. V, Coleman, S. M., Giddy, J., Bogart, L. M., Chaisson, C. E., Ross, D., Jacobsen, M. M., Robine, M., Govender, T., Freedberg, K. A., Katz, J. N., Walensky, R. P., & Losina, E. (2016). Sizanani: A Randomized Trial of Health System Navigators to Improve Linkage to HIV and TB Care in South Africa. *Journal of Acquired Immune Deficiency Syndromes (1999)*, *73*(2), 154–160. https://doi.org/https://dx.doi.org/10.1097/QAI.0000000000001025

Bastawrous, A., & Armstrong, M. J. (2013). Mobile health use in low- and high-income countries: an overview of the peer-reviewed literature. *Journal of the Royal Society of Medicine*, *106*(4), 130–142.

Batmanghelidj, E. (2022). *The Inflation Weapon How American Sanctions Harm Iranian Households*. www.sanctionsandsecurity.org

Bayona, E., Menacho, L., Segura, E. R., Mburu, G., Roman, F., Tristan, C., Bromley, E., & Cabello, R. (2017). The Experiences of Newly Diagnosed Men Who Have Sex with Men Entering the HIV Care Cascade in Lima, Peru, 2015-2016: A Qualitative Analysis of Counselor-Participant Text Message Exchanges. *Cyberpsychology, Behavior and Social Networking*, *20*(6), 389–396.

Beckmann, N. (2012). Medicines of hope? The tough decision for anti-retroviral use for HIV in Zanzibar, Tanzania. *Journal of Eastern African Studies*, *6*(4), 690–708. https://doi.org/10.1080/17531055.2012.729786

Behrouzan, O. (2010). An Epidemic of Meanings: The Significance of History, Gender and Language in HIV/AIDS Epidemics. In *The Fourth Wave: Violence, Gender, Culture and HIV in the 21st Century*. UNESCO.

Behrouzan, O. (2016). *Prozak diaries : psychiatry and generational memory in Iran*. Stanford University Press.

Benatar, S. (2016). Politics, power, poverty and global health: Systems and frames. *International Journal of Health Policy and Management*, *5*(10), 599–604. https://doi.org/10.15171/ijhpm.2016.101

Bere, T., Nyamayaro, P., Magidson, J. F., Chibanda, D., Chingono, A., Munjoma, R., Macpherson, K., Ndhlovu, C. E., O'Cleirigh, C., Kidia, K., Safren, S. A., & Abas, M. (2017). Cultural adaptation of a cognitive-behavioural intervention to improve

adherence to antiretroviral therapy among people living with HIV/AIDS in Zimbabwe: *Nzira Itsva*. *Journal of Health Psychology*, *22*(10), 1265–1276. https://doi.org/10.1177/1359105315626783

Berg, M. (1999). Patient care information systems and health care work: a sociotechnical approach. *International Journal of Medical Informatics*, *55*(2), 87–101. https://doi.org/10.1016/S1386-5056(99)00011-8

Berkman, A., Garcia, J., Muñoz-Laboy, M., Paiva, V., & Parker, R. (2005). A critical analysis of the Brazilian response to HIV/AIDS: Lessons learned for controlling and mitigating the epidemic in developing countries. In *American Journal of Public Health* (Vol. 95, Issue 7, pp. 1162–1172). https://doi.org/10.2105/AJPH.2004.054593

Berthaud, V., Johnson, L., Jennings, R., Chandler-Auguste, M., Osijo, A., Baldwin, M. T., Matthews-Juarez, P., Juarez, P., Wilus, D., & Tabatabai, M. (2022). The effect of homelessness on viral suppression in an underserved metropolitan area of middle Tennessee: potential implications for ending the HIV epidemic. *BMC Infectious Diseases*, *22*(1), 1–7. https://doi.org/10.1186/S12879-022-07105-Y/FIGURES/1

Bhaskar, R. (1978). *A Realist Theory of Science*. Verso.

Bigna, J. J. R., Noubiap, J. J. N., Plottel, C. S., Kouanfack, C., & Koulla-Shiro, S. (2014). Factors associated with non-adherence to scheduled medical follow-up appointments among Cameroonian children requiring HIV care: a case-control analysis of the usual-care group in the MORE CARE trial. *Infectious Diseases of Poverty*, *3*(1), 44. https://doi.org/https://dx.doi.org/10.1186/2049-9957-3-44

BMJ. (1998, August 8). Ex-ministers to face trial in French “blood scandal.” *BMJ : British Medical Journal*, *317*(7154), 302. /pmc/articles/PMC1174664/

Boender, T. S., Sigaloff, K. C. E., McMahon, J. H., Kiertiburanakul, S., Jordan, M. R., Barcarolo, J., Ford, N., Rinke de Wit, T. F., & Bertagnolio, S. (2015). Long-term Virological Outcomes of First-Line Antiretroviral Therapy for HIV-1 in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis. *Clinical*

Infectious Diseases : An Official Publication of the Infectious Diseases Society of America, *61*(9), 1453–1461. https://doi.org/10.1093/cid/civ556

Bogna, F., Raineri, A., & Dell, G. (2020). Critical realism and constructivism: merging research paradigms for a deeper qualitative study. *Qualitative Research in Organizations and Management: An International Journal*, *15*(4), 461–484. https://doi.org/10.1108/QROM-06-2019-1778

Bordin, E. S. (1979). The generalizability of the psychoanalytic concept of the working alliance. *Psychotherapy: Theory, Research & Practice*, *16*(3), 252–260. https://doi.org/10.1037/H0085885

Borhani, M., & Ahmadzadeh, R. (2019). The criterion of recognising the corruptor's example and its adaptation to drug crimes. *Criminal Law and Criminology Studies*, *48*(2).

Bourdieu, P. (1977). Outline of a Theory of Practice. In *Outline of a Theory of Practice*. Cambridge University Press. https://doi.org/10.1017/CBO9780511812507

Brinkley-Rubinstein, L., Chadwick, C., & Graci, M. (2013). The connection between serious life events, anti-retroviral adherence, and mental health among HIV-positive individuals in the Western Cape, South Africa. *Http://Dx.Doi.Org/10.1080/09540121.2013.793270*, *25*(12), 1581–1585. https://doi.org/10.1080/09540121.2013.793270

Brion, J. M., Menke, E. M., & Kimball, C. (2013). Grief and HIV Medication Adherence: The Work of Transcending Loss. *Http://Dx.Doi.Org/10.1080/15325024.2012.719341*, *18*(6), 499–520. https://doi.org/10.1080/15325024.2012.719341

Bronfenbrenner, U. (1979). *The Ecology of Human Development*. Harvard University Press.

Brown, J. E. H., & Halpern, J. (2021). AI chatbots cannot replace human interactions in the pursuit of more inclusive mental healthcare. *SSM - Mental Health*, *1*, 100017. https://doi.org/10.1016/J.SSMMH.2021.100017

Browne, S. H. ,. (2013). Editorial commentary: Dialing for doses: Enhancing community-based adherence support with mobile technologies. *Clinical Infectious Diseases*, *56*(9), 1327–1329.

Byng, R., Kirkpatrick, T., Lennox, C., Warren, F. C., Anderson, R., Brand, S. L., Callaghan, L., Carroll, L., Durcan, G., Gill, L., Goodier, S., Graham, J., Greer, R., Haddad, M., Harris, T., Henley, W., Hunter, R., Leonard, S., Maguire, M., … Shaw, J. (2023). Evaluation of a complex intervention for prisoners with common mental health problems, near to and after release: the Engager randomised controlled trial. *The British Journal of Psychiatry*, *222*(1), 18–26. https://doi.org/10.1192/BJP.2022.93

Byng, R., Lennox, C., Kirkpatrick, T., Quinn, C., Anderson, R., Brand, S. L., Callaghan, L., Carroll, L., Durcan, G., Gill, L., Goodier, S., Graham, J., Greer, R., Haddad, M., Harris, T., Henley, W., Hunter, R., Maguire, M., Leonard, S., … Shaw, J. (2022). Development and evaluation of a collaborative care intervention for male prison leavers with mental health problems: the Engager research programme. *Programme Grants for Applied Research*, *10*(8). https://doi.org/10.3310/MMWC3761

Cairney, P. (2016). Health and Advocacy: What Are the Barriers to the Use of Evidence in Policy? *The Politics of Evidence-Based Policy Making*, 51–84. https://doi.org/10.1057/978-1-137-51781-4_3

Campbell, C., & Cornish, F. (2010). Towards a “fourth generation” of approaches to HIV/AIDS management: creating contexts for effective community mobilisation. *AIDS Care*, *22 Suppl 2*, 1569–1579. https://doi.org/10.1080/09540121.2010.525812

Campbell, C., Skovdal, M., Madanhire, C., Mugurungi, O., Gregson, S., & Nyamukapa, C. (2011). “We, the AIDS people...”: How antiretroviral therapy enables Zimbabweans living with HIV/AIDS to cope with stigma. *American Journal of Public Health*, *101*(6), 1004–1010. https://doi.org/10.2105/AJPH.2010.202838

Campbell, J. I., & Haberer, J. E. (2015). Cell Phone-Based and Adherence Device Technologies for HIV Care and Treatment in Resource-Limited Settings: Recent Advances. *Current HIV/AIDS Reports*, *12*(4), 523–531.

Carrico, A. W., Antoni, M. H., Durán, R. E., Ironson, G., Penedo, F., Fletcher, M. A., Klimas, N., & Schneiderman, N. (2006). Reductions in depressed mood and denial coping during cognitive behavioral stress management with HIV-Positive gay men treated with HAART. *Annals of Behavioral Medicine : A Publication of the Society of Behavioral Medicine*, *31*(2), 155–164. https://doi.org/10.1207/S15324796ABM3102_7

Carrieri, D., Mattick, K., Pearson, M., Papoutsi, C., Briscoe, S., Wong, G., & Jackson, M. (2020). Optimising strategies to address mental ill-health in doctors and medical students: "Care under Pressure" realist review and implementation guidance. *BMC Medicine*, *18*(1), 1–10. https://doi.org/10.1186/S12916-020-01532-X/FIGURES/2

Carroll, A., Stokes, D., & Darley, A. (2021). Use of complexity theory in health and social care: a scoping review protocol. *BMJ Open*, *11*(7), e047633. https://doi.org/10.1136/BMJOPEN-2020-047633

Case, A., & Deaton, A. (2015). Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(49), 15078–15083. https://doi.org/10.1073/pnas.1518393112

Case, A., & Deaton, A. (2020). *Deaths of Despair and the Future of Capitalism | Princeton University Press*. Princeton University Press. https://press.princeton.edu/books/hardcover/9780691190785/deaths-of-despair-and-the-future-of-capitalism

Castro, A., & Farmer, P. (2005). Understanding and Addressing AIDS-Related Stigma: From Anthropological Theory to Clinical Practice in Haiti. *American Journal of Public Health*, *95*(1), 53. https://doi.org/10.2105/AJPH.2003.028563

Castro, E. M., Santiago, L. E., Jiménez, J. C., Dávila-Vargas, D., & Rosal, M. C. (2015). A Social-Ecological View of Barriers and Facilitators for HIV Treatment

Adherence: Interviews with Puerto Rican HIV Patients. *PLoS ONE*, *10*(9). https://doi.org/10.1371/JOURNAL.PONE.0125582

CDC. (2019). *Viral Suppression | HIV by Age | HIV by Group | .* https://www.cdc.gov/hiv/group/age/viral-suppression.html

Chaiyachati, K. H., Ogbuoji, O., Price, M., Suthar, A. B., Negussie, E. K., & Bärnighausen, T. (2014). Interventions to improve adherence to antiretroviral therapy: a rapid systematic review. *Wolters Kluwer Health*, *28*(2), 187–204. https://doi.org/10.1097/QAD.0000000000000252

Chi, B. H. , & Stringer, J. S. A. ,. (2010). Mobile phones to improve HIV treatment adherence. *The Lancet*, *376*(9755), 1807–1808.

Chiang, N., Guo, M., Amico, K. R., Atkins, L., & Lester, R. T. (2018). Interactive Two-Way mHealth Interventions for Improving Medication Adherence: An Evaluation Using The Behaviour Change Wheel Framework. *JMIR MHealth and UHealth*, *6*(4), e87. https://doi.org/https://dx.doi.org/10.2196/mhealth.9187

Chiasson, M. A., Hirshfield, S., & Rietmeijer, C. (2010). HIV prevention and care in the digital age. *Journal of Acquired Immune Deficiency Syndromes (1999)*, *55 Suppl 2*, S94-7. https://doi.org/https://dx.doi.org/10.1097/QAI.0b013e3181fcb878

Chipanta, D., Pettifor, A., Edwards, J., Giovenco, D., Topazian, H. M., Bray, R. M., Millington, M. C., Estill, J., Keiser, O., & Justman, J. E. (2022). Access to Social Protection by People Living with, at Risk of, or Affected by HIV in Eswatini, Malawi, Tanzania, and Zambia: Results from Population-Based HIV Impact Assessments. *AIDS and Behavior*, *26*(9), 3068–3078. https://doi.org/10.1007/S10461-022-03645-1

Christopoulos, K. A., Riley, E. D., Tulsky, J., Carrico, A. W., Moskowitz, J. T., Wilson, L., Coffin, L. S., Falahati, V., Akerley, J., & Hilton, J. F. (2014). A text messaging intervention to improve retention in care and virologic suppression in a U.S. urban safety-net HIV clinic: Study protocol for the Connect4Care (C4C) randomized controlled trial. *BMC Infectious Diseases*, *14*, 718. https://doi.org/https://dx.doi.org/10.1186/s12879-014-0718-6

Cluver, L., Meinck, F., Toska, E., Orkin, F. M., Hodes, R., & Sherr, L. (2018). Multitype violence exposures and adolescent antiretroviral nonadherence in South Africa. *AIDS (London, England)*, *32*(8), 975–983. https://doi.org/10.1097/QAD.0000000000001795

Cluver, L., Pantelic, M., Toska, E., Orkin, M., Casale, M., Bungane, N., & Sherr, L. (2018). STACKing the odds for adolescent survival: health service factors associated with full retention in care and adherence amongst adolescents living with HIV in South Africa. *Journal of the International AIDS Society*, *21*(9). https://doi.org/10.1002/jia2.25176

Coetzee, B., & Kagee, A. (2013). The Development of an Inventory to Assess the Structural Barriers to Clinic Attendance and Pill-taking Amongst Users of Antiretroviral Therapy. *AIDS and Behavior*, *17*(1), 319–328. https://doi.org/10.1007/s10461-012-0374-z

Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M. C., Kumarasamy, N., Hakim, J. G., Kumwenda, J., Grinsztejn, B., Pilotto, J. H. S., Godbole, S. V, Mehendale, S., Chariyalertsak, S., Santos, B. R., Mayer, K. H., Hoffman, I. F., Eshleman, S. H., Piwowar-Manning, E., Wang, L., … HPTN 052 Study Team. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. *The New England Journal of Medicine*, *365*(6), 493–505. https://doi.org/10.1056/NEJMoa1105243

Cohn, S., Clinch, M., Bunn, C., & Stronge, P. (2013). Entangled complexity: why complex interventions are just not complicated enough. *Journal of Health Services Research & Policy*, *18*(1), 40–43. https://doi.org/10.1258/JHSRP.2012.012036

Colasanti, J., Kelly, J., Pennisi, E., Hu, Y. J., Root, C., Hughes, D., Del Rio, C., & Armstrong, W. S. (2016). Continuous Retention and Viral Suppression Provide Further Insights Into the HIV Care Continuum Compared to the Cross-sectional HIV Care Cascade. *Clinical Infectious Diseases*, *62*(5), 648–654. https://doi.org/10.1093/CID/CIV941

CommsMEA. (2018). *Iran mobile penetration reaches 53.2 million mobile users in March 2018 – Mobile penetration reaches over 110% in the country*.

https://www.commsmea.com/business/people/17817-iran-mobile-penetration-reaches-532-million-mobile-users-in-march-2018

Connell, R. (2005). *Masculinities*.

Conway, B. (2007). The Role of Adherence to Antiretroviral Therapy in the Management of HIV Infection. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *45*(Supplement 1), S14–S18. https://doi.org/10.1097/QAI.0b013e3180600766

Coomes, C. M., Lewis, M. A., Uhrig, J. D., Furberg, R. D., Harris, J. L., & Bann, C. M. (2012). Beyond reminders: a conceptual framework for using short message service to promote prevention and improve healthcare quality and clinical outcomes for people living with HIV. *AIDS Care*, *24*(3), 348–357.

Cooper, V., Clatworthy, J., Whetham, J., & Consortium, E. (2017). mHealth Interventions To Support Self-Management In HIV: A Systematic Review. *The Open AIDS Journal*, *11*(101480215), 119–132.

Cornelius, J. B., Dmochowski, J., Boyer, C., St Lawrence, J., Lightfoot, M., & Moore, M. (2013). Text-messaging-enhanced HIV intervention for African American adolescents: a feasibility study. *The Journal of the Association of Nurses in AIDS Care : JANAC*, *24*(3), 256–267. https://doi.org/https://dx.doi.org/10.1016/j.jana.2012.06.005

Corporate Europe Observatory. (2022). *TRIPS 'Waiver failure': EU betrayal of global south on vaccine access obscured by lack of transparency | Corporate Europe Observatory*. https://corporateeurope.org/en/2022/07/trips-waiver-failure-eu-betrayal-global-south-vaccine-access-obscured-lack-transparency

Courtenay, W. H. (2000). Constructions of masculinity and their influence on men's well-being: A theory of gender and health. *Social Science and Medicine*, *50*(10), 1385–1401. https://doi.org/10.1016/S0277-9536(99)00390-1

Craig, P., Dieppe, P., Macintyre, S., Mitchie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: The new Medical Research Council guidance. *BMJ*, *337*(7676), 979–983. https://doi.org/10.1136/BMJ.A1655

Cresswell, K., & Sheikh, A. (2013). Organizational issues in the implementation and adoption of health information technology innovations: an interpretative review. *International Journal of Medical Informatics*, *82*(5). https://doi.org/10.1016/J.IJMEDINF.2012.10.007

Da Silva, J. (2022). Successful transition to tenofovir/lamivudine/dolutegravir (TLD) in PEPFAR-supported countries. *International AIDS Conference*. https://programme.aids2022.org/Abstract/Abstract/?abstractid=10414

Dahab, M., Charalambous, S., Hamilton, R., Fielding, K., Kielmann, K., Churchyard, G. J., & Grant, A. D. (2008). "That is why I stopped the ART": Patients' & providers' perspectives on barriers to and enablers of HIV treatment adherence in a South African workplace programme. *BMC Public Health*, *8*. https://doi.org/10.1186/1471-2458-8-63

Dalkin, S. M., Greenhalgh, J., Jones, D., Cunningham, B., & Lhussier, M. (2015). What's in a mechanism? Development of a key concept in realist evaluation. *Implementation Science*, *10*(1). https://doi.org/10.1186/s13012-015-0237-x

Davis, F. D. (1989). Perceived Usefulness, Perceived Ease of Use, and User Acceptance of Information Technology. *MIS Quarterly*, *13*(3), 319. https://doi.org/10.2307/249008

De Guzman, A. (2001). Reducing social vulnerability to HIV/AIDS: Models of care and their impact in resource-poor settings Reducing social vulnerability to HIV/AIDS: models of care and their impact in resource-poor settings. *AIDS CARE*, *13*(5), 663–675. https://doi.org/10.1080/09540120120063287

DeBeck, K., Cheng, T., Montaner, J. S., Beyrer, C., Elliott, R., Sherman, S., Wood, E., & Baral, S. (2017). HIV and the criminalisation of drug use among people who inject drugs: a systematic review. *The Lancet. HIV*, *4*(8), e357–e374. https://doi.org/10.1016/S2352-3018(17)30073-5

Dejong, J., & Mortagy, I. (2013). The struggle for recognition by people living with HIV/AIDS in Sudan. *Qualitative Health Research*, *23*(6), 782–794. https://doi.org/10.1177/1049732313482397

DeKoekkoek, T., Given, B., Given, C. W., Ridenour, K., Schueller, M., & Spoelstra, S. L. (2015). mHealth SMS text messaging interventions and to promote medication adherence: an integrative review. *Journal of Clinical Nursing*, *24*(19), 2722–2735.

Denzin, N. K., & Lincoln, Y. (2011). Handbook of Qualitative Research - Contents and Index. In *Handbook of Qualitative Research*.

Development, U. N. C. on T. and. (2022). *World Investment Report 2022*.

Deveugele, M., Derese, A., De Bacquer, D., Van Den Brink-Muinen, A., Bensing, J., & De Maeseneer, J. (2004). Is the communicative behavior of GPs during the consultation related to the diagnosis?: A cross-sectional study in six European countries. *Patient Education and Counseling*, *54*(3), 283–289. https://doi.org/10.1016/J.PEC.2004.02.004

Devi, B. R., Syed-Abdul, S., Kumar, A., Iqbal, U., Nguyen, P.-A., Li, Y.-C. J., & 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. https://doi.org/doi: 10.1016/j.cmpb.2015.08.003.

Devine, P. G., Plant, E. A., & Harrison, K. (1999). The Problem of "Us" Versus "Them" and AIDS Stigma. *Http://Dx.Doi.Org/10.1177/00027649921954732*, *42*(7), 1212–1228. https://doi.org/10.1177/00027649921954732

Dillingham, R., Ingersoll, K., Flickinger, T. E., Waldman, A. L., Grabowski, M., Laurence, C., Wispelwey, E., Reynolds, G., Conaway, M., & Cohn, W. F. (2018). PositiveLinks: A Mobile Health Intervention for Retention in HIV Care and Clinical Outcomes with 12-Month Follow-Up. *AIDS Patient Care and STDs*, *32*(6), 241–250. https://doi.org/10.1089/APC.2017.0303/ASSET/IMAGES/LARGE/FIGURE2.JPEG

Dingwall, R., Iphofen, R., Lewis, J., Oates, J., & Emmerich, N. (2014). Towards Common Principles for Social Science Research Ethics A Discussion Document for the Academy of Social Sciences. In *Academy of Social Sciences Working Group (R*.

Dobbs, R., Hatami, H., Allas, T., Arab, S., & Mahtafar, A. (2016). *Iran: The $1 Trillion Growth Opportunity?*

Drake, A. L., Rothschild, C., Jiang, W., Ronen, K., & Unger, J. A. (2020). Utility of Short Message Service (SMS) for Remote Data Collection for HIV in Low- and Middle-Income Countries. *Current Hiv/Aids Reports*, *17*(6), 654–662.

Duddy, C., & Wong, G. (2023). Grand rounds in methodology: when are realist reviews useful, and what does a 'good' realist review look like? *BMJ Quality & Safety*, *32*(3), 173–180. https://doi.org/10.1136/BMJQS-2022-015236

Earnshaw, V. A., Eaton, L. A., Collier, Z. K., Watson, R. J., Maksut, J. L., Rucinski, K. B., Kelly, J. F., & Kalichman, S. C. (2020). HIV Stigma, Depressive Symptoms, and Substance Use. *AIDS Patient Care and STDs*, *34*(6), 275–280. https://doi.org/10.1089/apc.2020.0021

Earnshaw, V. A., Smith, L. R., Chaudoir, S. R., Amico, K. R., & Copenhaver, M. M. (2013). HIV stigma mechanisms and well-being among PLWH: A test of the HIV Stigma Framework. *AIDS and Behavior*, *17*(5), 1785–1795. https://doi.org/10.1007/S10461-013-0437-9/TABLES/3

Elwood, S. A., & Martin, D. G. (2000). "Placing" Interviews: Location and Scales of Power in Qualitative Research. *The Professional Geographer*, *52*(4), 649–657. https://doi.org/10.1111/0033-0124.00253

Emanuel, J. E., Grady, C., Crouch, A. R., Lie, K. R., Miller, G. F., & Wendler, D. (2008). *The Oxford Textbook of Clinical Research Ethics*.

Erdbrink, T. (2018). Iran Eases Death Penalty for Drug Crimes, Saving Potentially Thousands of Lives - The New York Times. *The New York Times*. https://www.nytimes.com/2018/01/10/world/middleeast/iran-drugs-death-penalty.html

Fadhil, A. (2023). A Conversational Interface to Improve Medication Adherence: Towards AI Support in Patient's Treatment. *MedRxiv (Preprint)*. https://arxiv.org/ftp/arxiv/papers/1803/1803.09844.pdf

FAO. (2023). *The State of Food Security and Nutrition in the World 2023*. FAO; IFAD; UNICEF; WFP; WHO; https://doi.org/10.4060/CC3017EN

Farmer, P. (2021). *Infections and Inequelities* (Issue February). https://www.ucpress.edu/book/9780520229136/infections-and-inequalities

Farrokhi, M., Gholami, M., Mohraz, M., McFarland, W., Baesi, K., & Abbasian, L. (2019). HIV drug resistance among naïve HIV-infected patients in Iran. *Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences*, *24*, 31. https://doi.org/10.4103/jrms.JRMS_689_18

Federman, A. D., Cook, E. F., Phillips, R. S., Puopolo, A. L., Haas, J. S., Brennan, T. A., & Burstin, H. R. (2001). Intention to Discontinue Care Among Primary Care Patients: Influence of Physician Behavior and Process of Care. *Journal of General Internal Medicine*, *16*(10), 668. https://doi.org/10.1111/J.1525-1497.2001.01028.X

Ferdows, A. K. (1983). Women and the Islamic Revolution. *International Journal of Middle East Studies*.

Ferlatte, O., Salway, T., Oliffe, J. L., & Trussler, T. (2017). Stigma and suicide among gay and bisexual men living with HIV. *AIDS Care*, *29*(11), 1346–1350. https://doi.org/10.1080/09540121.2017.1290762

Feyissa, G. T., Lockwood, C., Woldie, M., & Munn, Z. (2019). Reducing HIV-related stigma and discrimination in healthcare settings: A systematic review of quantitative evidence. *PLoS ONE*, *14*(1). https://doi.org/10.1371/JOURNAL.PONE.0211298

Finch, E. (2001). Issues of Confidentiality in Research into Criminal Activity: the Legal and Ethical Dilemma. *Mountbatten Journal of Legal Studies*.

Finitsis, D. J., Pellowski, J. A., & Johnson, B. T. (2014). Text Message Intervention Designs to Promote Adherence to Antiretroviral Therapy (ART): A Meta-Analysis of Randomized Controlled Trials. *PLoS ONE*, *9*(2), e88166. https://doi.org/10.1371/journal.pone.0088166

Fisher, J. D., & Fisher, W. A. (2000). *Theoretical Approaches to Individual-Level Change in HIV Risk Behavior*. 3–55. https://doi.org/10.1007/978-1-4615-4137-0_1

Fisher, J. D., Fisher, W. A., Misovich, S. J., Kimble, D. L., & Malloy, T. E. (1996). Changing AIDS risk behavior: effects of an intervention emphasizing AIDS risk reduction information, motivation, and behavioral skills in a college student

population. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *15*(2), 114–123.

Flyvbjerg, B. (2001). *Making social science matter: Why social inquiry fails and how it can succeed again* (Steven Sampson, Ed.; Vol. 7, Issue 2). Cambridge University Press. https://doi.org/10.5172/jmo.2001.7.2.70

Francois, P. (2019). *How We Can Secure the Broadest Access to Quality-Assured and Affordable Medicines to Defeat HIV - Opinion - The Global Fund to Fight AIDS, Tuberculosis and Malaria*. The Global Fund. https://www.theglobalfund.org/en/opinion/2019/2019-10-16-how-we-can-secure-the-broadest-access-to-quality-assured-and-affordable-medicines-to-defeat-hiv/

Friedland, J., Renwick, R., & Mccoll, M. (2010). AIDS Care : Psychological and Socio-medical Aspects of AIDS / HIV Coping and social support as determinants of quality of life in HIV / AIDS C oping and social support as determ inants of quality of life in H IV / AID S. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*, *8*(September 2012), 37–41. https://doi.org/10.1080/09540129650125966

Furlong, P., & Marsh, D. (2010). A skin not a sweater: ontology and epistemology in political science. In D. Marsh & G. Stoker (Eds.), *Theory and Methods in Political Science* (3rd ed.). Palgrave MacMillan.

Fynn, R. W., De Jager, D., Chan, H. A., Anand, S., & Rivett, U. (2006). Remote HIV/AIDS patient monitoring tool using 3G/GPRS packet-switched mobile technology. *IET Seminar Digest*, *2006*(11370), 129–137. https://doi.org/10.1049/ic.2006.0670

Gagnon, M., Jacob, J. D., & McCabe, J. (2015). Locating the qualitative interview: reflecting on space and place in nursing research. *Journal of Research in Nursing*, *20*(3), 203–215. https://doi.org/10.1177/1744987114536571/ASSET/IMAGES/LARGE/10.1177_1744987114536571-FIG1.JPEG

Galárraga, O., Genberg, B. L., Martin, R. A., Barton Laws, M., & Wilson, I. B. (2013). Conditional economic incentives to improve HIV treatment adherence: literature

review and theoretical considerations. *AIDS and Behavior*, *17*(7), 2283–2292. https://doi.org/10.1007/s10461-013-0415-2

Gardner, E. (2011). The Spectrum of Engagement in HIV Care and itsRelevance to Test-and-Treat Strategies forPrevention of HIV Infection. *Clinical Infectious Diseases*.

Gardner, E. M., Mclees, M. P., Steiner, J. F., Del Rio, C., & Burman, W. J. (2011). *The Spectrum of Engagement in HIV Care and its Relevance to Test-and-Treat Strategies for Prevention of HIV Infection*. *52*(6), 793–800. https://doi.org/10.1093/cid/ciq243

Garofalo, R., Kuhns, L. M., Hotton, A., Johnson, A., Muldoon, A., & Rice, D. (2016). A Randomized Controlled Trial of Personalized Text Message Reminders to Promote Medication Adherence Among HIV-Positive Adolescents and Young Adults. *AIDS and Behavior*, *20*(5), 1049–1059. https://doi.org/10.1007/s10461-015-1192-x

Genberg, B. L., Hlavka, Z., Konda, K. A., Maman, S., Chariyalertsak, S., Chingono, A., Mbwambo, J., Modiba, P., Van Rooyen, H., & Celentano, D. D. (2009). A comparison of HIV/AIDS-related stigma in four countries: Negative attitudes and perceived acts of discrimination towards people living with HIV/AIDS. *Social Science and Medicine*, *68*(12), 2279–2287. https://doi.org/10.1016/j.socscimed.2009.04.005

Genberg, B. L., Wilson, I. B., Bangsberg, D. R., Arnsten, J., Goggin, K., Remien, R. H., Simoni, J., Gross, R., Reynolds, N., Rosen, M., & Liu, H. (2012). Patterns of antiretroviral therapy adherence and impact on HIV RNA among patients in North America. *AIDS*, *26*(11), 1415–1423. https://doi.org/10.1097/QAD.0b013e328354bed6

Gerke, D. R., Glotfelty, J., Schlueter, J., Freshman, M., & Plax, K. (2020). E-VOLUTION: A Text Messaging-Powered Intervention-Connection, Support, and HIV Eradication. *Health Promotion Practice*, *21*(5), 716–726.

Gerke, D. R., Step, M. M., Rünger, D., Fletcher, J. B., Brooks, R. A., Davis, N., Kisler, K. A., & Reback, C. J. (2020). Associations Between Social Support and Social

Media Use Among Young Adult Cisgender MSM and Transgender Women Living With HIV. *Health Promotion Practice*, *21*(5), 705–715. https://doi.org/10.1177/1524839920936248

Ghiabi, M. (2019). *Drugs politics : managing disorder in the Islamic Republic of Iran*.

Glasner-Edwards, S., Patrick, K., Ybarra, M. L., Reback, C. J., Rawson, R. A., Chokron Garneau, H., Chavez, K., & Venegas, A. (2016). A Cognitive Behavioral Therapy-Based Text Messaging Intervention Versus Medical Management for HIV-Infected Substance Users: Study Protocol for a Pilot Randomized Trial. *JMIR Research Protocols*, *5*(2), e131. https://doi.org/https://dx.doi.org/10.2196/resprot.5407

Glasziou, P. P., Chalmers, I., Green, S., & Michie, S. (2014). Intervention synthesis: A missing link between a systematic review and practical treatment(s). *PLoS Medicine*, *11*(8), e1001690. https://doi.org/10.1371/journal.pmed.1001690

Global Commission on HIV and the law. (2012). *Risks, Rights, and Health*. https://hivlawcommission.org/wp-content/uploads/2017/06/FinalReport-RisksRightsHealth-EN.pdf

Global Fund. (2020). *Iran HIV Evaluation*.

Goffman, E. (1963). *Stigma: Notes on the management of spoiled identity.* . Simon and schuster.

Gökengin, D., Doroudi, F., Tohme, J., Collins, B., & Madani, N. (2016). HIV/AIDS: Trends in the Middle East and North Africa region. In *International Journal of Infectious Diseases* (Vol. 44, pp. 66–73). Elsevier B.V. https://doi.org/10.1016/j.ijid.2015.11.008

Gonzalez, J. S., Batchelder, A. W., Psaros, C., & Safren, S. A. (2011). Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. *Journal of Acquired Immune Deficiency Syndromes (1999)*, *58*(2), 181–187. https://doi.org/10.1097/QAI.0B013E31822D490A

Goodair, B., & Reeves, A. (2022). Outsourcing health-care services to the private sector and treatable mortality rates in England, 2013–20: an observational study of NHS privatisation. *Lancet Public Health*.

Gourlay, A., Birdthistle, I., Mburu, G., Iorpenda, K., & Wringe, A. (2013). Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: A systematic review. *Journal of the International AIDS Society*, *16*(1). https://doi.org/10.7448/IAS.16.1.18588

Govindasamy, D., Ford, N., & Kranzer, K. (2012). Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. *AIDS (London, England)*, *26*(16), 2059–2067. https://doi.org/10.1097/QAD.0b013e3283578b9b

Graham, S. M., Micheni, M., Chirro, O., Nzioka, J., Secor, A. M., Mugo, P. M., Kombo, B., van der Elst, E. M., Operario, D., Amico, K. R., Sanders, E. J., & Simoni, J. M. (2020). A Randomized Controlled Trial of the Shikamana Intervention to Promote Antiretroviral Therapy Adherence Among Gay, Bisexual, and Other Men Who Have Sex with Men in Kenya: Feasibility, Acceptability, Safety and Initial Effect Size. *AIDS and Behavior*, *24*(7), 2206–2219. https://doi.org/10.1007/s10461-020-02786-5

Graham, S. M., Micheni, M., Kombo, B., Van Der Elst, E. M., Mugo, P. M., Kivaya, E., Aunon, F., Kutner, B., Sanders, E. J., & Simoni, J. M. (2015). Development and pilot testing of an intervention to promote care engagement and adherence among HIV-positive Kenyan MSM. *AIDS (London, England)*, *29*, S241-9.

Greenhalgh, J., & Manzano, A. (2021). Understanding 'context' in realist evaluation and synthesis. *International Journal of Social Research Methodology*. https://doi.org/10.1080/13645579.2021.1918484/SUPPL_FILE/TSRM_A_1918484_SM6637.DOCX

Greenhalgh, T., & Abimbola, S. (2019). The NASSS Framework - A Synthesis of Multiple Theories of Technology Implementation. *Studies in Health Technology and Informatics*, *263*, 193–204. https://doi.org/10.3233/SHTI190123

Greenhalgh, T., & Heath, I. (2010). *Measuring quality in the therapeutic relationship Discussion paper Measuring quality in the therapeutic relationship*.

Greenhalgh, T., & Heath, I. (2010a). Measuring quality in the therapeutic relationship—Part 1: objective approaches. *BMJ Quality & Safety*, *19*(6), 475–478. https://doi.org/10.1136/QSHC.2010.043364

Greenhalgh, T., & Heath, I. (2010b). Measuring quality in the therapeutic relationship—Part 2: subjective approaches. *BMJ Quality & Safety*, *19*(6), 479–483. https://doi.org/10.1136/QSHC.2010.043372

Greenhalgh, T., & Papoutsi, C. (2018). Studying complexity in health services research: Desperately seeking an overdue paradigm shift. *BMC Medicine*, *16*(1), 1–6. https://doi.org/10.1186/S12916-018-1089-4/TABLES/1

Greenhalgh, T., Rosen, R., Shaw, S. E., Byng, R., Faulkner, S., Finlay, T., Grundy, E., Husain, L., Hughes, G., Leone, C., Moore, L., Papoutsi, C., Pope, C., Rybczynska-Bunt, S., Rushforth, A., Wherton, J., Wieringa, S., & Wood, G. W. (2021). Planning and Evaluating Remote Consultation Services: A New Conceptual Framework Incorporating Complexity and Practical Ethics. *Frontiers in Digital Health*, *3*, 726095. https://doi.org/10.3389/FDGTH.2021.726095/BIBTEX

Greenhalgh, T., & Russell, J. (2010). Why do evaluations of eHealth programs fail? An alternative set of guiding principles. *PLoS Medicine*, *7*(11). https://doi.org/10.1371/JOURNAL.PMED.1000360

Greenhalgh, T., Russell, J., Ashcroft, R. E., & Parsons, W. (2011). Why national eHealth programs need dead philosophers: Wittgensteinian reflections on policymakers' reluctance to learn from history. *The Milbank Quarterly*, *89*(4), 533–563. https://doi.org/https://dx.doi.org/10.1111/j.1468-0009.2011.00642.x

Greenhalgh, T., & Stones, R. (2010). Theorising big IT programmes in healthcare: Strong structuration theory meets actor-network theory. *Social Science & Medicine*, *70*(9), 1285–1294. https://doi.org/10.1016/J.SOCSCIMED.2009.12.034

Greenhalgh, T., & Swinglehurst, D. (2011). Studying technology use as social practice: The untapped potential of ethnography. *BMC Medicine*, *9*(1), 1–7. https://doi.org/10.1186/1741-7015-9-45/PEER-REVIEW

Greenhalgh, T., Wherton, J., Papoutsi, C., Lynch, J., Hughes, G., A'Court, C., Hinder, S., Fahy, N., Procter, R., & Shaw, S. (2017). Beyond adoption: A new framework for theorizing and evaluating nonadoption, abandonment, and challenges to the scale-up, spread, and sustainability of health and care technologies. *Journal of Medical Internet Research*, *19*(11). https://doi.org/10.2196/jmir.8775

Grimsrud, A., Bygrave, H., Doherty, M., Ehrenkranz, P., Ellman, T., Ferris, R., Ford, N., Killingo, B., Mabote, L., Mansell, T., Reinisch, A., Zulu, I., & Bekker, L. G. (2016). Reimagining HIV service delivery: The role of differentiated care from prevention to suppression: The. In *Journal of the International AIDS Society* (Vol. 19, Issue 1). Wiley Blackwell. https://doi.org/10.7448/IAS.19.1.21484

Gross, R., Ritz, J., Hughes, M. D., Salata, R., Mugyenyi, P., Hogg, E., Wieclaw, L., Godfrey, C., Wallis, C. L., Mellors, J. W., Mudhune, V. O., Badal-Faesen, S., Grinsztejn, B., & Collier, A. C. (2019). Two-way mobile phone intervention compared with standard-of-care adherence support after second-line antiretroviral therapy failure: a multinational, randomised controlled trial. *The Lancet Digital Health*, *1*(1), e26–e34. https://doi.org/10.1016/S2589-7500(19)30006-8

Gupta, G. R., Parkhurst, J. O., Ogden, J. A., Aggleton, P., & Mahal, A. (2008). Structural approaches to HIV prevention. *Lancet (London, England)*, *372*(9640), 764–775. https://doi.org/10.1016/S0140-6736(08)60887-9

Gupta, R. K., Gregson, J., Parkin, N., Haile-Selassie, H., Tanuri, A., Andrade Forero, L., Kaleebu, P., Watera, C., Aghokeng, A., Mutenda, N., Dzangare, J., Hone, S., Hang, Z. Z., Garcia, J., Garcia, Z., Marchorro, P., Beteta, E., Giron, A., Hamers, R., … Bertagnolio, S. (2018). HIV-1 drug resistance before initiation or re-initiation of first-line antiretroviral therapy in low-income and middle-income countries: a systematic review and meta-regression analysis. *The Lancet. Infectious Diseases*, *18*(3), 346–355. https://doi.org/10.1016/S1473-3099(17)30702-8

Haberer, J. E., Kahane, J., Kigozi, I., Emenyonu, N., Hunt, P., Martin, J., & Bangsberg, D. R. (2010). Real-time adherence monitoring for HIV antiretroviral therapy. *AIDS and Behavior*, *14*(6), 1340–1346. https://doi.org/10.1007/s10461-010-9799-4

Haberer, J. E., Musiimenta, A., Atukunda, E. C., Musinguzi, N., Wyatt, M. A., Ware, N. C., & Bangsberg, D. R. (2016). Short message service (SMS) reminders and real-time adherence monitoring improve antiretroviral therapy adherence in rural

Uganda. *AIDS (London, England)*, *30*(8), 1295–1300. https://doi.org/https://dx.doi.org/10.1097/QAD.0000000000001021

Haberer, J. E., Musinguzi, N., Boum, Y., Siedner, M. J., Mocello, A. R., Hunt, P. W., Martin, J. N., & Bangsberg, D. R. (2015). Duration of Antiretroviral Therapy Adherence Interruption Is Associated With Risk of Virologic Rebound as Determined by Real-Time Adherence Monitoring in Rural Uganda. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *70*(4), 386–392. https://doi.org/10.1097/QAI.0000000000000737

Haberer, J. E., Sabin, L., Amico, K. R., Orrell, C., Galárraga, O., Tsai, A. C., Vreeman, R. C., Wilson, I., Sam-Agudu, N. A., Blaschke, T. F., Vrijens, B., Mellins, C. A., Remien, R. H., Weiser, S. D., Lowenthal, E., Stirratt, M. J., Sow, P. S., Thomas, B., Ford, N., … Bangsberg, D. R. (2017). Improving antiretroviral therapy adherence in resource-limited settings at scale: A discussion of interventions and recommendations. *Journal of the International AIDS Society*, *20*(1), 21371. https://doi.org/10.7448/IAS.20.1/21371

Haghighat, R., Steinert, J., & Cluver, L. (2019). The effects of decentralising antiretroviral therapy care delivery on health outcomes for adolescents and young adults in low- and middle-income countries: a systematic review. *Https://Doi.Org/10.1080/16549716.2019.1668596*, *12*(1). https://doi.org/10.1080/16549716.2019.1668596

Hajebi, A., Hashemian, S. S., Abolhassani, M., Hajebi, A., Alizadeh, K., Rahnejat, A. M., Khademi, M., & Taghva, A. (2022). Assessing the impact of stigma reduction interventions in Iran: A qualitative study from the perspective of mental health stakeholders. *Frontiers in Public Health*, *10*, 1027002. https://doi.org/10.3389/FPUBH.2022.1027002/BIBTEX

Hall, A. K., Cole-Lewis, H., & Bernhardt, J. M. (2015a). Mobile text messaging for health: A systematic review of reviews. *Annual Review of Public Health*, *36*, 393–415. https://doi.org/10.1146/annurev-publhealth-031914-122855

Hampanda, K. M. (2016). Intimate Partner Violence and HIV-Positive Women's Non-Adherence to Antiretroviral Medication for the Purpose of Prevention of Mother-

to-Child Transmission in Lusaka, Zambia. *Social Science & Medicine (1982)*, *153*, 123. https://doi.org/10.1016/J.SOCSCIMED.2016.02.011

Hampshire, K., Porter, G., Mariwah, S., Munthali, A., Robson, E., Owusu, S. A., Abane, A., & Milner, J. (2017). Who bears the cost of "informal mhealth"? Health-workers' mobile phone practices and associated political-moral economies of care in Ghana and Malawi. *Health Policy and Planning*, *32*(1), 34–42. https://doi.org/10.1093/heapol/czw095

Hardy, H., Kumar, V., Doros, G., Farmer, E., Drainoni, M. L., Rybin, D., Myung, D., Jackson, J., Backman, E., Stanic, A., & Skolnik, P. R. (2011). Randomized Controlled Trial of a Personalized Cellular Phone Reminder System to Enhance Adherence to Antiretroviral Therapy. *AIDS Patient Care and STDs*, *25*(3), 153. https://doi.org/10.1089/APC.2010.0006

Harris, K. (2017). *A Social Revolution: Politics and the Welfare State in Iran.* . University of California Press.

Harrison, M. I., Koppel, R., & Bar-Lev, S. (2007). Unintended Consequences of Information Technologies in Health Care—An Interactive Sociotechnical Analysis. *Journal of the American Medical Informatics Association : JAMIA*, *14*(5), 542. https://doi.org/10.1197/JAMIA.M2384

Hawe, P., Shiell, A., & Riley, T. (2004). Complex interventions: how "out of control" can a randomised controlled trial be? *BMJ*, *328*(7455), 1561–1563. https://doi.org/10.1136/BMJ.328.7455.1561

Henny, K. D., Wilkes, A. L., McDonald, C. M., Denson, D. J., & Neumann, M. S. (2018). A Rapid Review of eHealth Interventions Addressing the Continuum of HIV Care (2007-2017). *AIDS and Behavior*, *22*(1), 43–63.

Hickel, J. (2016). The true extent of global poverty and hunger: questioning the good news narrative of the Millennium Development Goals. *Https://Doi.Org/10.1080/01436597.2015.1109439*, *37*(5), 749–767. https://doi.org/10.1080/01436597.2015.1109439

Hickel, J. (2018). *The Divide* . Windmill Books. https://www.jasonhickel.org/the-divide

Higgins, E. T. (1987). Self-Discrepancy: A Theory Relating Self and Affect. *Psychological Review*, *94*(3), 319–340. https://doi.org/10.1037/0033-295X.94.3.319

Higgins, E. T. (1989). Self-Discrepancy Theory: What Patterns of Self-Beliefs Cause People to Suffer? *Advances in Experimental Social Psychology*, *22*(C), 93–136. https://doi.org/10.1016/S0065-2601(08)60306-8

HIV Policy Lab. (2021). *Iran (Islamic Republic of) | Overall country policy adoption*. https://www.hivpolicylab.org/ir

Hogg, R. S., Heath, K., Bangsberg, D., Yip, B., Press, N., O'Shaughnessy, M. V, & Montaner, J. S. G. (2002). Intermittent use of triple-combination therapy is predictive of mortality at baseline and after 1 year of follow-up. *AIDS (London, England)*, *16*(7), 1051–1058. https://doi.org/10.1097/00002030-200205030-00012

Holloway, I. W., Winder, T. J., Lea, C. H. I. I. I., Tan, D., Boyd, D., & Novak, D. (2017). Technology Use and Preferences for Mobile Phone-Based HIV Prevention and Treatment Among Black Young Men Who Have Sex With Men: Exploratory Research. *JMIR MHealth and UHealth*, *5*(4), e46. https://doi.org/https://dx.doi.org/10.2196/mhealth.6436

Holstad, M. M., Essien, J. E., Ekong, E., Higgins, M., Teplinskiy, I., & Adewuyi, M. F. (2012). Motivational groups support adherence to antiretroviral therapy and use of risk reduction behaviors in HIV positive Nigerian women: a pilot study. *African Journal of Reproductive Health*, *16*(3), 14–27.

Horne, R., Buick, D., Fisher, M., Leake, H., Cooper, V., & Weinman, J. (2004). Doubts about necessity and concerns about adverse effects: Identifying the types of beliefs that are associated with non-adherence to HAART. *International Journal of STD and AIDS*, *15*(1), 38–44. https://doi.org/10.1258/095646204322637245

Horvath, A. O. (2000). The therapeutic relationship: From transference to alliance. In *Journal of Clinical Psychology* (Vol. 56, Issue 2, pp. 163–173). https://doi.org/10.1002/(SICI)1097-4679(200002)56:2<163::AID-JCLP3>3.0.CO;2-D

Horvath, T., Azman, H., Kennedy, G. E., & Rutherford, G. W. (2012). Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. *The Cochrane Database of Systematic Reviews*, *3*, CD009756–CD009756.

Humeniuk, R., Ali, R., Babor, T. F., Farrell, M., Formigoni, M. L., Jittiwutikarn, J., de Lacerda, R. B., Ling, W., Marsden, J., Monteiro, M., Nhiwatiwa, S., Pal, H., Poznyak, V., & Simon, S. (2008). Validation of the alcohol, smoking and substance involvement screening test (ASSIST). *Addiction*, *103*(6), 1039–1047. https://doi.org/10.1111/j.1360-0443.2007.02114.x

Hwang, B., Shroufi, A., Gils, T., Steele, S. J., Grimsrud, A., Boulle, A., Yawa, A., Stevenson, S., Jankelowitz, L., Versteeg-Mojanaga, M., Govender, I., Stephens, J., Hill, J., Duncan, K., & Van Cutsem, G. (2019). Stock-outs of antiretroviral and tuberculosis medicines in South Africa: A national cross-sectional survey. *PLoS ONE*, *14*(3). https://doi.org/10.1371/JOURNAL.PONE.0212405

Ingersoll, K. S., Dillingham, R. A., Hettema, J. E., Conaway, M., Freeman, J., Reynolds, G., & Hosseinbor, S. (2015). Pilot RCT of bidirectional text messaging for ART adherence among nonurban substance users with HIV. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *34S*(0), 1305–1315. https://doi.org/10.1037/hea0000295

Izadi, N., Gouya, M. M., Akbarpour, S., Zareie, B., Moradi, Y., Kazerooni, P. A., Mahboobi, M., Mohseni, P., & Moradi, G. (2023). HIV prevalence and associated factors among female sex workers in Iran: a bio-behavioral survey in 2020. *AIDS and Behavior*, *27*(3), 909–918. https://doi.org/10.1007/S10461-022-03827-X/FIGURES/1

Jager, A., Wong, G., Papoutsi, C., & Roberts, N. (2023). The usage of data in NHS primary care commissioning: a realist review. *BMC Medicine*, *21*(1), 1–12. https://doi.org/10.1186/S12916-023-02949-W/TABLES/2

Jagosh, J., Bush, P. L., Salsberg, J., Macaulay, A. C., Greenhalgh, T., Wong, G., Cargo, M., Green, L. W., Herbert, C. P., & Pluye, P. (2015). A realist evaluation of

community-based participatory research: Partnership synergy, trust building and related ripple effects. *BMC Public Health*, *15*(1), 1–11. https://doi.org/10.1186/S12889-015-1949-1/TABLES/2

James, H. M., Papoutsi, C., Wherton, J., Greenhalgh, T., & Shaw, S. E. (2021). Spread, Scale-up, and Sustainability of Video Consulting in Health Care: Systematic Review and Synthesis Guided by the NASSS Framework. *Journal of Medical Internet Research*, *23*(1). https://doi.org/10.2196/23775

Jenness, S. M., Myers, J. E., Neaigus, A., Lulek, J., Navejas, M., & Raj-Singh, S. (2012). Delayed entry into HIV medical care after HIV diagnosis: risk factors and research methods. *AIDS Care*, *24*(10), 1240–1248. https://doi.org/10.1080/09540121.2012.656569

Jones, E. E. (1984). *Social stigma: The psychology of marked relationships*. W.H. Freeman.

Jongbloed, K., Parmar, S., van der Kop, M., Spittal, P. M., & Lester, R. T. (2015). Recent Evidence for Emerging Digital Technologies to Support Global HIV Engagement in Care. *Current HIV/AIDS Reports*, *12*(4), 451–461.

Julian, L. J. (2011). Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). *Arthritis Care & Research*, *63 Suppl 11*(0 11), S467-72. https://doi.org/10.1002/acr.20561

Kahol, K. (2014). Mobile phone messaging to improve health. *BMJ (Clinical Research Ed.)*, *349*(8900488), g6158.

Kalichman, S. C., Grebler, T., Amaral, C. M., McNerey, M., White, D., Kalichman, M. O., Cherry, C., & Eaton, L. (2013). Intentional Non-Adherence to Medications among HIV Positive Alcohol Drinkers: Prospective Study of Interactive Toxicity Beliefs. *Journal of General Internal Medicine*, *28*(3), 399–405. https://doi.org/10.1007/s11606-012-2231-1

Kalichman, S. C., Katner, H., Banas, E., Hill, M., & Kalichman, M. O. (2020). Intersecting alcohol use and depression impedes HIV treatment in the rural South, USA. *Behavioral Medicine*. https://doi.org/10.1080/08964289.2020.1809336

Kalichman, S. C., Mathews, C., Banas, E., & Kalichman, M. O. (2019). Stigma management intervention to improve antiretroviral therapy adherence: Phase-I test of concept trial, Cape Town South Africa. *Global Public Health*, *14*(8), 1059–1074. https://doi.org/https://dx.doi.org/10.1080/17441692.2018.1552307

Kamarulzaman, A. (2013). Fighting the HIV epidemic in the Islamic world. In *The Lancet* (Vol. 381, Issue 9883, pp. 2058–2060). Lancet Publishing Group. https://doi.org/10.1016/S0140-6736(13)61033-8

Kanters, S., Park, J. H., Chan, K., Ford, N., Forrest, J., Thorlund, K., Nachega, J. B., & Mills, E. J. (2016). Use of peers to improve adherence to antiretroviral therapy: A global network meta-analysis: A. *Journal of the International AIDS Society*, *19*(1). https://doi.org/10.7448/IAS.19.1.21141

Kanters, S., Park, J. J. H., Chan, K., Socias, M. E., Ford, N., Forrest, J. I., Thorlund, K., Nachega, J. B., & Mills, E. J. (2017). Interventions to improve adherence to antiretroviral therapy: a systematic review and network meta-analysis. *The Lancet. HIV*, *4*(1), e31–e40. https://doi.org/10.1016/S2352-3018(16)30206-5

Kaplan, L., Kuhnt, J., & Steinert, J. I. (2020). Do no harm? Field research in the Global South: Ethical challenges faced by research staff. *World Development*, *127*, 104810. https://doi.org/10.1016/J.WORLDDEV.2019.104810

Kaptchuk, T. J., Kelley, J. M., Conboy, L. A., Davis, R. B., Kerr, C. E., Jacobson, E. E., Kirsch, I., Schyner, R. N., Bong, H. N., Nguyen, L. T., Park, M., Rivers, A. L., McManus, C., Kokkotou, E., Drossman, D. A., Goldman, P., & Lembo, A. J. (2008). Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome. *BMJ*, *336*(7651), 999–1003. https://doi.org/10.1136/BMJ.39524.439618.25

Karamouzian, M., Akbari, M., Haghdoost, A.-A., Setayesh, H., & Zolala, F. (2014). "'I Am Dead to Them'": HIV-related Stigma Experienced by People Living With HIV in Kerman, Iran. *Journal of the Association of Nurses in AIDS Care*, *26*, 46–56. https://doi.org/10.1016/j.jana.2014.04.005

Kates, J., Dawson, L., Horn, T. H., Killelea, A., McCann, N. C., Crowley, J. S., & Walensky, R. P. (2021). Insurance coverage and financing landscape for HIV

treatment and prevention in the USA. *The Lancet*, *397*(10279), 1127–1138. https://doi.org/10.1016/S0140-6736(21)00397-4

Katz, I. T., Ryu, A. E., Onuegbu, A. G., Psaros, C., Weiser, S. D., Bangsberg, D. R., & Tsai, A. C. (2013). Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. *Journal of the International AIDS Society*, *16*, 18640. https://doi.org/10.7448/IAS.16.3.18640

Kaufman, M. R., Cornish, F., Zimmerman, R. S., & Johnson, B. T. (2014). Health behavior change models for HIV prevention and AIDS care: Practical recommendations for a multi-level approach. *Journal of Acquired Immune Deficiency Syndromes*, *66*(SUPPL.3). https://doi.org/10.1097/QAI.0000000000000236

Kavanagh, M. M., Agbla, S. C., Joy, M., Aneja, K., Pillinger, M., Case, A., Erondu, N. A., Erkkola, T., & Graeden, E. (2021). Law, criminalisation and HIV in the world: have countries that criminalise achieved more or less successful pandemic response? *BMJ Global Health*, *6*(8), e006315. https://doi.org/10.1136/BMJGH-2021-006315

Kavanagh, M. M., Graeden, E., Pillinger, M., Singh, R., Eaneff, S., Bendaud, V., Gustav, R., & Erkkola, T. (2020). Understanding and comparing HIV-related law and policy environments: cross-national data and accountability for the global AIDS response. *BMJ Global Health*, *5*(9), e003695. https://doi.org/10.1136/BMJGH-2020-003695

Kew Kayleigh, M., & Cates Christopher, J. (2016). Home telemonitoring and remote feedback between clinic visits for asthma. In *Cochrane Database of Systematic Reviews* (Issue 8). John Wiley & Sons, Ltd. https://doi.org/10.1002/14651858.CD011714.pub2

Khalili, H., Rohani, R., Seyedalinaghi, S., Hajiabdolbaghi, M., Dashti-Khavidaki, S., & Talasaz, A. H. (2012). Adherence to antiretroviral therapy among Iranian HIV/AIDS patients. *Current Clinical Pharmacology*, *7*(2), 111–115. http://www.ncbi.nlm.nih.gov/pubmed/22432842

King, E., Kinvig, K., Steif, J., Qiu, A. Q., Maan, E. J., Albert, A. Y., Pick, N., Alimenti, A., Kestler, M. H., Money, D. M., Lester, R. T., & Murray, M. C. M. (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. *Journal of Medical Internet Research*, *19*(6), e190.

Kredo, T., Ford, N., Adeniyi, F. B., & Garner, P. (2013). Decentralising HIV treatment in lower- and middle-income countries. In T. Kredo (Ed.), *Cochrane Database of Systematic Reviews* (Issue 6, p. CD009987). John Wiley & Sons, Ltd. https://doi.org/10.1002/14651858.CD009987.pub2

Kruse, C., Betancourt, J., Ortiz, S., Valdes Luna, S. M., Bamrah, I. K., & Segovia, N. (2019). Barriers to the Use of Mobile Health in Improving Health Outcomes in Developing Countries: Systematic Review. *Journal of Medical Internet Research*, *21*(10), e13263.

Kruse, G. R., Park, E., Haberer, J. E., Abroms, L., Shahid, N. N., Howard, S. E., Chang, Y., Haas, J. S., & Rigotti, N. A. (2019). Proactive text messaging (GetReady2Quit) and nicotine replacement therapy to promote smoking cessation among smokers in primary care: A pilot randomized trial protocol. *Contemporary Clinical Trials*, *80*, 48–54. https://doi.org/10.1016/j.cct.2019.03.006

Kübler-Ross, E. (1969). *On Death and Dying* (1st ed.). Routledge. https://doi.org/10.4324/9780203010495

Labrique, A. B., Kirk, G. D., Westergaard, R. P., & Merritt, M. W. (2013). Ethical issues in mHealth research involving persons living with HIV/AIDS and substance abuse. *AIDS Research and Treatment*, *2013*, 189645. https://doi.org/10.1155/2013/189645

Lai, H., Li, R., Li, Z., Zhang, B., Li, C., Song, C., Zhao, Q., Huang, J., Zhu, Q., Liang, S., Chen, H., Li, J., Liao, L., Shao, Y., Xing, H., Ruan, Y., Lan, G., Zhang, L., & Shen, M. (2023). Modelling the impact of treatment adherence on the transmission of HIV drug resistance. *Journal of Antimicrobial Chemotherapy*. https://doi.org/10.1093/JAC/DKAD186

Lawson, Tony. (1997). *Economics and reality*. Routledge. https://www.routledge.com/Economics-and-Reality/Lawson/p/book/9780415154215

Lee, K., & Zwi, A. B. (2007). A global political economy approach to AIDS: Ideology, interests and implications. *Http://Dx.Doi.Org/10.1080/13563469608406267*, *1*(3), 355–373. https://doi.org/10.1080/13563469608406267

Lee, R., Kochman, A., & Sikkema, K. (2002). Internalized stigma among people living with HIV-AIDS. *AIDS and Behavior*, *6*(4), 309–319. https://doi.org/10.1023/A:1021144511957/METRICS

Lee, S. B., & Valerius, J. (2020). mHealth interventions to promote anti-retroviral adherence in HIV: Narrative review. *JMIR MHealth and UHealth*, *8*(8), 1–16. https://doi.org/10.2196/14739

Leonardi, P. M. (2012). Car Crashes without Cars: Lessons about Simulation Technology and Organizational Change from Automotive Design. In *Car Crashes without Cars*. The MIT Press. https://doi.org/10.7551/MITPRESS/9294.001.0001

Lester, R. T. (2013). Ask, don't tell - mobile phones to improve HIV care. *The New England Journal of Medicine*, *369*(19), 1867–1868.

Lester, R. T., Mills, E. J., Kariri, A., Ritvo, P., Chung, M., Jack, W., Habyarimana, J., Karanja, S., Barasa, S., Nguti, R., Estambale, B., Ngugi, E., Ball, T. B., Thabane, L., Kimani, J., Gelmon, L., Ackers, M., & Plummer, F. A. (2009). The HAART cell phone adherence trial (WelTel Kenya1): a randomized controlled trial protocol. *Trials*, *10*(101263253), 87.

Lester, R. T., Ritvo, P., Mills, E. J., Kariri, A., Karanja, S., Chung, M. H., Jack, W., Habyarimana, J., Sadatsafavi, M., Najafzadeh, M., Marra, C. A., Estambale, B., Ngugi, E., Ball, T. B., Thabane, L., Gelmon, L. J., Kimani, J., Ackers, M., & Plummer, F. A. (2010). Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): A randomised trial. *The Lancet*, *376*(9755), 1838–1845. https://doi.org/doi: 10.1016/S0140-6736(10)61997-6.

Leylabadlo, H. E., Baghi, H. B., Fallahi, L., & Kafil, H. S. (2016). From sharing needles to unprotected sex: a new wave of HIV infections in Iran? *The Lancet. HIV*, *3*(10), e461-2. https://doi.org/10.1016/S2352-3018(16)30158-8

Lima, I. C. V. de, Galvão, M. T. G., Alexandre, H. de O., Lima, F. E. T., & Araújo, T. L. de. (2016). Information and communication technologies for adherence to antiretroviral treatment in adults with HIV/AIDS. *International Journal of Medical Informatics*, *92*, 54–61. https://doi.org/10.1016/j.ijmedinf.2016.04.013

Lima, I. C. V. de, Galvao, M. T. G., Pedrosa, S. C., Farias, O. O., Silva, C. A. C., & Cunha, G. H. da. (2019). Instant messaging application for the care of people living with HIV/aids. *Revista Brasileira de Enfermagem*, *72*(5), 1161–1166.

Lu, M., Barlow, J., Meinck, F., & Neelakantan, L. (2022). Unpacking School-Based Child Sexual Abuse Prevention Programs: A Realist Review. *Trauma, Violence & Abuse*. https://doi.org/10.1177/15248380221082153

Luque-Fernandez, M. A., Van Cutsem, G., Goemaere, E., Hilderbrand, K., Schomaker, M., Mantangana, N., Mathee, S., Dubula, V., Ford, N., Hernán, M. A., & Boulle, A. (2013). Effectiveness of Patient Adherence Groups as a Model of Care for Stable Patients on Antiretroviral Therapy in Khayelitsha, Cape Town, South Africa. *PLoS ONE*, *8*(2), e56088. https://doi.org/10.1371/journal.pone.0056088

Lyons, C. E., Schwartz, S. R., Murray, S. M., Shannon, K., Diouf, D., Mothopeng, T., Kouanda, S., Simplice, A., Kouame, A., Mnisi, Z., Tamoufe, U., Phaswana-Mafuya, N., Cham, B., Drame, F. M., Aliu Djaló, M., & Baral, S. (2020). The role of sex work laws and stigmas in increasing HIV risks among sex workers. *Nature Communications 2020 11:1*, *11*(1), 1–10. https://doi.org/10.1038/s41467-020-14593-6

Lyons, C. E., Twahirwa Rwema, J. O., Makofane, K., Diouf, D., Mfochive Njindam, I., Ba, I., Kouame, A., Tamoufe, U., Cham, B., Aliu Djaló, M., Obodou, E. P., Karita, E., Simplice, A., Nowak, R. G., Crowell, T. A., Matse, S., Kouanda, S., Enama, J. P., Kavanagh, M., … Baral, S. (2023). Associations between punitive policies and legal barriers to consensual same-sex sexual acts and HIV among gay men and other men who have sex with men in sub-Saharan Africa: a multicountry,

respondent-driven sampling survey. *The Lancet. HIV*, *10*(3), e186–e194. https://doi.org/10.1016/S2352-3018(22)00336-8

Maar, M. A., Yeates, K., Perkins, N., Boesch, L., Hua-Stewart, D., Liu, P., Sleeth, J., & Tobe, S. W. (2017). A Framework for the Study of Complex mHealth Interventions in Diverse Cultural Settings. *JMIR MHealth and UHealth*, *5*(4). https://doi.org/10.2196/MHEALTH.7044

Mabachi, N. M., Brown, M., Sandbulte, M., Wexler, C., Goggin, K., Maloba, M., & Finocchario-Kessler, S. (2020). Using a Social Support Framework to Understand How HIV Positive Kenyan Men Engage in PMTCT/EID Care: Qualitative Insights From Male Partners. *AIDS and Behavior*, *24*(1), 18–28. https://doi.org/10.1007/s10461-019-02451-6

MacFarquhar, N. (2002). Condom as a Problem Word: Iran Grapples With a Surge in AIDS - The New York Times. *The New York Times*. https://www.nytimes.com/2002/04/04/world/condom-as-a-problem-word-iran-grapples-with-a-surge-in-aids.html

Mano, M. S., & Morgan, G. (2022). Telehealth, Social Media, Patient Empowerment, and Physician Burnout: Seeking Middle Ground. *American Society of Clinical Oncology Educational Book. American Society of Clinical Oncology. Annual Meeting*, *42*(42), 28–37. https://doi.org/10.1200/EDBK_100030

Marcolino, M. S., Oliveira, J. A. Q., D'Agostino, M., Ribeiro, A. L., Alkmim, M. B. M., & Novillo-Ortiz, D. (2018). The Impact of mHealth Interventions: Systematic Review of Systematic Reviews. *JMIR MHealth and UHealth*, *6*(1), e23.

Martin, R., Ashimosi, C., Nyandiko, W., Chory, A., Aluoch, J., Scanlon, M., & Vreeman, R. (2022). A systematic review of interventions to reduce HIV-related stigma among primary and secondary school teachers. *AIDS Care*, *34*(1), 1–6. https://doi.org/10.1080/09540121.2021.1960264

Masanjala, W. (2007). The poverty-HIV/AIDS nexus in Africa: a livelihood approach. *Social Science & Medicine (1982)*, *64*(5), 1032–1041. https://doi.org/10.1016/j.socscimed.2006.10.009

Mayer, J. E., & Fontelo, P. (2016). Meta-analysis on the effect of text message reminders for HIV-related compliance. *AIDS Care*, *29*(4), 409–417.

Mayer, J. E., Fontelo, P., J.E., M., Mayer, J. E., Fontelo, P., & J.E., M. (2017). Meta-analysis on the effect of text message reminders for HIV-related compliance. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*, *29*(4), 409–417. http://www.tandf.co.uk/journals/titles/09540121.asp

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*(1), 33. https://doi.org/10.1186/s12913-014-0654-6

Mbuagbaw, L., Sivaramalingam, B., Navarro, T., Hobson, N., Keepanasseril, A., Wilczynski, N. J., Haynes, R. B., & Patient Adherence Review (PAR) Team. (2015). Interventions for Enhancing Adherence to Antiretroviral Therapy (ART): A Systematic Review of High Quality Studies. *AIDS Patient Care and STDs*, *29*(5), 248–266. https://doi.org/10.1089/apc.2014.0308

Mbuagbaw, L., Thabane, L., Ongolo-Zogo, P., Lester, R. T., Mills, E. J., Smieja, M., Dolovich, L., & Kouanfack, C. (2012). The Cameroon Mobile Phone SMS (CAMPS) Trial: A Randomized Trial of Text Messaging versus Usual Care for Adherence to Antiretroviral Therapy. *PLoS ONE*, *7*(12). https://doi.org/10.1371/JOURNAL.PONE.0046909

Mbuagbaw, L., Thabane, L., Ongolo-Zogo, P., Lester, R. T., Mills, E., Volmink, J., Yondo, D., Essi, M. J., Bonono-Momnougui, R.-C., Mba, R., Ndongo, J. S., Nkoa, F. C., & Ondoa, H. A. (2011). The Cameroon mobile phone SMS (CAMPS) trial: a protocol for a randomized controlled trial of mobile phone text messaging versus usual care for improving adherence to highly active anti-retroviral therapy. *Trials*, *12*, 5. https://doi.org/10.1186/1745-6215-12-5

Mbuagbaw, L., van der Kop, M. L., Lester, R. T., Thirumurthy, H., Pop-Eleches, C., Ye, C., Smieja, M., Dolovich, L., Mills, E. J., & Thabane, L. (2013). Mobile phone text messages for improving adherence to antiretroviral therapy (ART): an

individual patient data meta-analysis of randomised trials. *BMJ Open*, *3*(12), e003950.

Meintjes, G., Kerkhoff, A. D., Burton, R., Schutz, C., Boulle, A., Van Wyk, G., Blumenthal, L., Nicol, M. P., & Lawn, S. D. (2015). HIV-Related Medical Admissions to a South African District Hospital Remain Frequent Despite Effective Antiretroviral Therapy Scale-Up. *Medicine*, *94*(50). https://doi.org/10.1097/MD.0000000000002269

Merton, R. K. (1972). Insiders and Outsiders: A Chapter in the Sociology of Knowledge. *American Journal of Sociology*, *78*(1), 9–47. https://doi.org/10.1086/225294

Mills, E. J. , & Lester R.T. (2019). Mobile phone-enabled adherence in HIV/AIDS. *The Lancet Digital Health*, *1*(1), e4–e5. https://www.sciencedirect.com/journal/the-lancet-digital-health

Mills, E. J., Lester, R., & Ford, N. (2012). Adherence to antiretroviral therapy: supervision or support? *The Lancet Infectious Diseases*, *12*(2), 97–98. https://doi.org/10.1016/S1473-3099(11)70354-1

Mills, E. J., Nachega, J. B., Bangsberg, D. R., Singh, S., Rachlis, B., Wu, P., Wilson, K., Buchan, I., Gill, C. J., & Cooper, C. (2006). Adherence to HAART: A Systematic Review of Developed and Developing Nation Patient-Reported Barriers and Facilitators. *PLOS Medicine*, *3*(11), e438. https://doi.org/10.1371/JOURNAL.PMED.0030438

Mills, J. C., Pence, B. W., Edmonds, A., Adedimeji, A., Schwartz, R. M., Kassaye, S., Cocohoba, J., Cohen, M. H., Neigh, G., Fischl, M. A., Kempf, M. C., & Adimora, A. A. (2019). The Impact of Cumulative Depression along the HIV Care Continuum in Women Living with HIV during the Era of Universal Antiretroviral Treatment. *Journal of Acquired Immune Deficiency Syndromes (1999)*, *82*(3), 225. https://doi.org/10.1097/QAI.0000000000002140

Minerva, F., & Giubilini, A. (2023). Is AI the Future of Mental Healthcare? *Topoi*, *42*(3), 809. https://doi.org/10.1007/S11245-023-09932-3

Mir, R., & Watson, A. (2001). Critical Realism and Constructivism in Strategy Research: Toward a Synthesis. *Strategic Management Journal*, *22*(12), 1169–1173. http://www.jstor.org/stable/3094470

Mir-Hosseini, Z. (1999). *Islam and Gender: The Religious Debate in Contemporary Iran.* . Princeton University Press.

Moayed, M. S., Khatiban, M., Nassiri Toosi, M., Khodaveisi, M., Soltanian, A. R., & Ebadi, A. (2019). Barriers to Adherence to Medical Care Programs in Liver Transplant Recipients: A Qualitative Study. *International Journal of Organ Transplantation Medicine*, *10*(3), 115–126.

Mobilizing cell phones to improve antiretroviral adherence and follow-up in Kenya: a randomized controlled trial in progress. (2009). *Essential Medicines Monitor*, *2*, 1–3. http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=105152732&site=ehost-live&authtype=ip,uid

Mohanraj, R., Jeyaseelan, V., Kumar, S., Mani, T., Rao, D., Murray, K. R., & Manhart, L. E. (2015). Cultural Adaptation of the Brief COPE for Persons Living with HIV/AIDS in Southern India. *AIDS and Behavior*, *19*(2), 341–351. https://doi.org/10.1007/s10461-014-0872-2

Mohraz, M., Tayeri, K., Namdari Tabar, H., Bayat Jozani, Z., Sadeghi, L., SeyedAlinaghi, S., Esmaeilzadeh, A., Adl Tabatabai, R., Sajjadipour, M., Gholami, M., & Bayanolhagh, S. (2018). Evaluation of Acquired HIV Drug Resistance among People Living with HIV Who Have Taken Antiretroviral Therapy for 9-15 Months in 14 Triangular Clinics in Iran, 2015-2016. *Intervirology*, *61*(6), 292–300. https://doi.org/10.1159/000497036

Mokri A, & Schottenfeld R. (2008). Drug Abuse and HIV Transmission in Iran - Responding to Public Health Challenges." Public Health Aspects of HIV/AIDS in Low and Middle Income Countries: Epidemiology, Prevention and Care. *Ed. David Celentano and Chris Beyrer. Springer.*, 583–599.

Mol, Annemarie. (2008). *The logic of care : health and the problem of patient choice*. 129.

Moreno, R., Nababan, H. Y., Ota, E., Wariki, W. M. V, Ezoe, S., Gilmour, S., Shibuya, K., R., M., H.Y., N., E., O., W.M., W., S., E., S., G., Moreno, R., Nababan, H. Y., Ota, E., Wariki, W. M. V, Ezoe, S., Gilmour, S., & Shibuya, K. (2014). Structural and community-level interventions for increasing condom use to prevent the transmission of HIV and other sexually transmitted infections. *The Cochrane Database of Systematic Reviews*, *7*(7), CD003363–CD003363. https://doi.org/10.1002/14651858.CD003363.pub3.www.cochranelibrary.com

Morowatisharifabad, M.-A., Movahed, E., Nikooie, R., Farokhzadian, J., Bidaki, R., Askarishahi, M., & Hosseinzadeh, M. (n.d.). Adherence to Medication and Physical Activity among People Living with HIV/AIDS. *Iranian Journal of Nursing and Midwifery Research*, *24*(5), 397–399. https://doi.org/10.4103/ijnmr.IJNMR_205_18

Motazedian, N., Sayadi, M., & Firoozbakhtian, A. (2018). Non-adherence to anti-retroviral medication in Shiraz, 2014: a cross sectional study. *African Health Sciences*, *18*(2), 384–393. https://doi.org/10.4314/ahs.v18i2.24

Muessig, K. E., Nekkanti, M., Bauermeister, J., Bull, S., & Hightow-Weidman, L. B. (2015). A systematic review of recent smartphone, Internet and Web 2.0 interventions to address the HIV continuum of care. *Current HIV/AIDS Reports*, *12*(1), 173–190. https://doi.org/10.1007/s11904-014-0239-3

Mugavero, M. J., Westfall, A. O., Zinski, A., Davila, J., Drainoni, M.-L., Gardner, L. I., Keruly, J. C., Malitz, F., Marks, G., Metsch, L., Wilson, T. E., Giordano, T. P., & Retention in Care (RIC) Study Group. (2012). Measuring Retention in HIV Care. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *61*(5), 574–580. https://doi.org/10.1097/QAI.0b013e318273762f

Mukumbang, F. C., Mwale, J. C., & Van Wyk, B. (2017). Conceptualising the Factors Affecting Retention in Care of Patients on Antiretroviral Treatment in Kabwe District, Zambia, Using the Ecological Framework. *AIDS Research and Treatment*, *2017*. https://doi.org/10.1155/2017/7356362

Murphy, D. A., De Wit, J. B. F., Donohoe, S., & Adam, P. C. G. (2015). The need to know: HIV status disclosure expectations and practices among non-HIV-positive

gay and bisexual men in Australia. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*, *27*, 90–98. https://doi.org/10.1080/09540121.2015.1062077

Murray, M. C. , Borek, N. V. , Graham, R. , Maan, E. J. , Van Der Kop, M. L. , Friesen, K. , Levine, S. , Abaki, J. , Pick, N. , Maginley, J. , Ogilvie, G. , Money, D. M. , & Lester, R. ,. (2013). Weltel BC1: A pilot study exploring feasibility and acceptability of a mhealth intervention to improve care for HIV positive patients on highly active antiretroviral therapy (HAART) in British Columbia (BC), Canada. *Canadian Journal of Infectious Diseases and Medical Microbiology*, *24*, 55A. http://www.pulsus.com/journals/pdf_frameset.jsp?jnlKy=3&atlKy=777&isArt=f&jnlAdvert=Infdis&adverifHCTp=&supKy=516&sTitle=CAHR%20Abstracts%2C%20Pulsus%20Group%20Inc&VisitorType=Consumer

Murray, M. C. M., O'Shaughnessy, S., Smillie, K., Van Borek, N., Graham, R., Maan, E. J., van der Kop, M. L., Friesen, K., Albert, A., Levine, S., Pick, N., Ogilvie, G., Money, D., Lester, R., & Team, W. B. S. (2015). Health care providers' perspectives on a weekly text-messaging intervention to engage HIV-positive persons in care (WelTel BC1). *AIDS and Behavior*, *19*(10), 1875–1887.

Mursleen, S. , Khoudigian, S. , Patel, A. R. , Lester, R. T. , & Mbuagbaw, L. ,. (2015). Cost-utility analysis of text messaging interventions for improving antiretroviral therapy adherence in people living with HIV. *Canadian Journal of Infectious Diseases and Medical Microbiology*, *26*, 37B. http://www.pulsus.com/journals/pdf_frameset.jsp?jnlKy=3&atlKy=795&isArt=f&jnlAdvert=Infdis&adverifHCTp=&supKy=526&sTitle=Canadian%20Association%20for%20HIV%20Research%20Abstracts%2C%20Pulsus%20Group%20Inc&VisitorType=Consumer

Müssener, U. (2021). Digital encounters: Human interactions in mHealth behavior change interventions. *Digital Health*. https://doi.org/10.1177/20552076211029776

Mwai, L. ,. (2015). Scaling up WelTel: An evidence-based, patient-centred mHealth intervention. *Annals of Global Health*, *81*(1), 195.

Mykhalovskiy, E. (2011). The problem of "significant risk": Exploring the public health impact of criminalizing HIV non-disclosure. *Social Science & Medicine*, *73*(5), 668–675. https://doi.org/10.1016/J.SOCSCIMED.2011.06.051

Najafi, Z., Taj, L., Dadras, O., Ghadimi, F., Moradmand, B., & SeyedAlinaghi, S. (2020). Epidemiology of HIV in Iran. *Current HIV Research*, *18*(4), 228–236. https://doi.org/10.2174/1570162x18666200605152317

National AIDS Committee, I. (2020). *Country progress report-Iran*.

Newman, J. (2019). *Ontological Social Policy Analysis: An investigation into the ontological assumptions underpinning the social security reforms of the UK Coalition Government 2010-2015*. University of Leeds.

Newzoo. (2019). *Newzoo Global Mobile Market Report 2019 | Light Version | Newzoo*. https://newzoo.com/insights/trend-reports/newzoo-global-mobile-market-report-2019-light-version/

Nhavoto, J. A., Gronlund, A., & Chaquilla, W. P. (2015). SMSaude: Design, Development, and Implementation of a Remote/Mobile Patient Management System to Improve Retention in Care for HIV/AIDS and Tuberculosis Patients. *JMIR MHealth and UHealth*, *3*(1), e26. https://doi.org/https://dx.doi.org/10.2196/mhealth.3854

Nissaramanesh, B., Trace, M., & Roberts, M. (2005). The rise of harm reduction in the Islamic Republic of Iran. *The Berkley Foundation*.

Nittas, V., Ameli, V., Little, M., & Humphreys, D. K. (2020b). Exploring the equity impact of mobile health-based human immunodeficiency virus interventions: A systematic review of reviews and evidence synthesis. *Digital Health*, *6*, 1–11. https://doi.org/10.1177/2055207620942360

Noar, S. M. (2011). Computer technology-based interventions in HIV prevention: state of the evidence and future directions for research. *AIDS Care*, *23*(5), 525–533.

Noar, S. M., Black, H. G., & Pierce, L. B. (2009). Efficacy of computer technology-based HIV prevention interventions: a meta-analysis. *AIDS*, *23*(1), 107–115.

Nolan, C. P., O'Donnell, P. J. M., Desderius, B. M., Mzombwe, M., McNairy, M. L., Peck, R. N., & Kingery, J. R. (2018). Depression screening in HIV-positive

Tanzanian adults: comparing the PHQ-2, PHQ-9 and WHO-5 questionnaires. *Global Mental Health (Cambridge, England)*, *5*, e38. https://doi.org/10.1017/gmh.2018.31

Nordberg, B., Mwangi, W., van der Kop, M. L., Were, E., Kaguiri, E., Kågesten, A. E., Gabriel, E. E., Lester, R. T., Mwangi, J., Ekström, A. M., & Rautiainen, S. (2021). The effect of weekly interactive text-messaging on early infant HIV testing in Kenya: a randomised controlled trial (WelTel PMTCT). *Scientific Reports 2021 11:1*, *11*(1), 1–12. https://doi.org/10.1038/s41598-021-00972-6

Nordberg, B., van der Kop, M. L., Mwangi, W., Mwangi, J., Kaguiri, E., Chamorro de Angeles, K. J., Lester, R. T., Gabriel, E. E., Rautiainen, S., Awiti, P. O., Kågesten, A. E., Were, E., & Ekström, A. M. (2023). The effect of an interactive weekly text-messaging intervention on retention in prevention of mother-to-child transmission of HIV care: a randomised controlled trial (WelTel PMTCT). *Scientific Reports 2023 13:1*, *13*(1), 1–12. https://doi.org/10.1038/s41598-023-35817-x

Nöstlinger, C., Cosaert, T., Landeghem, E. Van, Vanhamel, J., Jones, G., Zenner, D., Jacobi, J., Noori, T., Pharris, A., Smith, A., Hayes, R., Val, E., Waagensen, E., Vovc, E., Sehgal, S., Laga, M., & Van Renterghem, H. (2022). HIV among migrants in precarious circumstances in the EU and European Economic Area. *The Lancet. HIV*, *9*(6), e428–e437. https://doi.org/10.1016/S2352-3018(22)00032-7

Nsagha, D. S., Siysi, V. V., Ekobo, S., Egbe, T. O., & Kibu, O. D. (2020). One-Way and Two-Way Mobile Phone Text Messages for Treatment Adherence Among Patients With HIV: Protocol for a Randomized Controlled Trial. *JMIR Research Protocols*, *9*(9), e16127.

Nyblade, L., Srinivasan, K., Mazur, A., Raj, T., Patil, D. S., Devadass, D., Radhakrishna, K., & Ekstrand, M. L. (2018). HIV Stigma Reduction for Health Facility Staff: Development of a Blended- Learning Intervention. *Frontiers in Public Health*, *6*, 362233. https://doi.org/10.3389/FPUBH.2018.00165/BIBTEX

OHRP. (1993). *United States Department of Health and Human Services, Office of Human Research Protections (OHRP) IRB Guidebook, Part D (Privacy and Confidentiality)*.

Onono, M., Odwar, T., Abuogi, L., Owuor, K., Helova, A., Bukusi, E., Turan, J., & Hampanda, K. (2020). Effects of Depression, Stigma and Intimate Partner Violence on Postpartum Women's Adherence and Engagement in HIV Care in Kenya. *AIDS and Behavior*, *24*(6), 1807–1815. https://doi.org/10.1007/s10461-019-02750-y

Otiso, L., McCollum, R., Mireku, M., Karuga, R., De Koning, K., & Taegtmeyer, M. (2017). Decentralising and integrating HIV services in community-based health systems: a qualitative study of perceptions at macro, meso and micro levels of the health system. *BMJ Global Health*, *2*(1), e000107. https://doi.org/10.1136/BMJGH-2016-000107

Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews*, *5*(1). https://doi.org/10.1186/S13643-016-0384-4

Owusu, M. W., Krankowska, D. C., Lourida, P., & Weis, N. (2023). Late HIV diagnosis among migrant women living in Europe - a systematic review of barriers to HIV testing. *IJID Regions*, *7*, 206–215. https://doi.org/10.1016/J.IJREGI.2023.03.006

Owusu-Addo, E., Renzaho, A. M. N., & Smith, B. J. (2018). The impact of cash transfers on social determinants of health and health inequalities in sub-Saharan Africa: a systematic review. *Health Policy and Planning*, *33*(5), 675–696. https://doi.org/10.1093/HEAPOL/CZY020

Palinkas, L. A., Horwitz, S. M., Green, C. A., Wisdom, J. P., Duan, N., & Hoagwood, K. (2015). Purposeful Sampling for Qualitative Data Collection and Analysis in Mixed Method Implementation Research. *Administration and Policy in Mental Health and Mental Health Services Research*, *42*(5), 533–544. https://doi.org/10.1007/s10488-013-0528-y

Pantelic, M., Boyes, M., Cluver, L., & Meinck, F. (2017). HIV, violence, blame and shame: Pathways of risk to internalized HIV stigma among South African adolescents living with HIV. *Journal of the International AIDS Society*, *20*(1), 21771. https://doi.org/10.7448/IAS.20.1.21771

Pantelic, M., Sprague, L., & Stangl, A. L. (2019). It's not "all in your head": Critical knowledge gaps on internalized HIV stigma and a call for integrating social and structural conceptualizations. *BMC Infectious Diseases*, *19*(1), 1–8. https://doi.org/10.1186/S12879-019-3704-1/PEER-REVIEW

Papoutsi, C., Mattick, K., Pearson, M., Brennan, N., Briscoe, S., & Wong, G. (2017). Social and professional influences on antimicrobial prescribing for doctors-in-training: A realist review. *Journal of Antimicrobial Chemotherapy*, *72*(9), 2418–2430. https://doi.org/10.1093/jac/dkx194

Papoutsi, C., Shaw, J., Paparini, S., & Shaw, S. (2021). We Need to Talk About Complexity in Health Research: Findings From a Focused Ethnography. *Qualitative Health Research*, *31*(2), 338. https://doi.org/10.1177/1049732320968779

Parker, R., & Aggleton, P. (2003). HIV and AIDS-related stigma and discrimination: a conceptual framework and implications for action. *Social Science & Medicine*, *57*(1), 13–24. https://doi.org/10.1016/S0277-9536(02)00304-0

Parker, R. G. (1996). Empowerment, community mobilization and social change in the face of HIV/AIDS. *AIDS (London, England)*, *10 Suppl 3*, S27-31. http://www.ncbi.nlm.nih.gov/pubmed/8970709

Parker, R. G., Easton, D., & Klein, C. H. (2000). Structural barriers and facilitators in HIV prevention: a review of international research. *AIDS (London, England)*, *14 Suppl 1*(11 SUPPL.). https://doi.org/10.1097/00002030-200006001-00004

Pasipanodya, E. C., Montoya, J. L., Watson, C. W.-M., Marquine, M. J., Hoenigl, M., Garcia, R., Kua, J., Gant, V., Trambley, J., & Moore, D. J. (2020). Tailoring a mobile health text-messaging intervention to promote antiretroviral therapy adherence among African Americans: A qualitative study. *PloS One*, *15*(6), e0233217.

Pawson, R. (2006). *Evidence-based policy : a realist perspective*. SAGE.

Pawson, R. (2013). The Science of Evaluation: A Realist Manifesto. *The Science of Evaluation: A Realist Manifesto*. https://doi.org/10.4135/9781473913820

Pawson, R., Greenhalgh, T., Harvey, G., & Walshe, K. (2005). Realist review - A new method of systematic review designed for complex policy interventions. *Journal of Health Services Research and Policy*, *10*(SUPPL. 1), 21–34. https://doi.org/10.1258/1355819054308530

Pawson, R., & Tilley, N. (1997). *Realist Evaluation*. http://www.communitymatters.com.au/RE_chapter.pdf

Pawson, R., & Tilley, N. (2014). An Introduction to Scientific Realist Evaluation. *Evaluation for the 21st Century: A Handbook*, 405–418. https://doi.org/10.4135/9781483348896.N29

Pearson, M. (2010). 'What do we know? What should we do?' Melding research validity and rhetoric in the analysis of policy making. *Evidence & Policy*, *6*(1), 77–90. https://doi.org/10.1332/174426410X483015

Pearson, M., & Coomber, R. (2010). The challenge of external validity in policy-relevant systematic reviews: a case study from the field of substance misuse. *Addiction*, *105*(1), 136–145. https://doi.org/10.1111/J.1360-0443.2009.02713.X

Pecoraro, A., Royer-Malvestuto, C., Rosenwasser, B., Moore, K., Howell, A., Ma, M., & Woody, G. E. (2013). Factors contributing to dropping out from and returning to HIV treatment in an inner city primary care HIV clinic in the United States. *AIDS Care*, *25*(11), 1399–1406. https://doi.org/10.1080/09540121.2013.772273

Pega, F., Liu, S. Y., Walter, S., Pabayo, R., Saith, R., & Lhachimi, S. K. (2017). Unconditional cash transfers for reducing poverty and vulnerabilities: effect on use of health services and health outcomes in low- and middle-income countries. *The Cochrane Database of Systematic Reviews*, *11*(11). https://doi.org/10.1002/14651858.CD011135.PUB2

Pellowski, J. A., & Kalichman, S. C. (2012). Recent advances (2011-2012) in technology-delivered interventions for people living with HIV. *Current HIV/AIDS Reports*, *9*(4), 326–334.

Pellowski, J. A., Kalichman, S. C., Kalichman, M. O., & Cherry, C. (2016). Alcohol-antiretroviral therapy interactive toxicity beliefs and daily medication adherence

and alcohol use among people living with HIV. *AIDS Care*, *28*(8), 963–970. https://doi.org/https://dx.doi.org/10.1080/09540121.2016.1154134

Peng, M. L., Wickersham, J. A., Altice, F. L., Shrestha, R., Azwa, I., Zhou, X., Halim, M. A. A., Ikhtiaruddin, W. M., Tee, V., Kamarulzaman, A., & Ni, Z. (2022). Formative Evaluation of the Acceptance of HIV Prevention Artificial Intelligence Chatbots By Men Who Have Sex With Men in Malaysia: Focus Group Study. *JMIR Form Res 2022;6(10):E42055 Https://Formative.Jmir.Org/2022/10/E42055*, *6*(10), e42055. https://doi.org/10.2196/42055

Perazzo, J., Reyes, D., & Webel, A. (2017). A Systematic Review of Health Literacy Interventions for People Living with HIV. *AIDS and Behavior*, *21*(3), 812–821. https://doi.org/10.1007/s10461-016-1329-6

Pinna Pintor, M., Suhrcke, M., & Hamelmann, C. (2023). The impact of economic sanctions on health and health systems in low-income and middle-income countries: a systematic review and narrative synthesis. *BMJ Global Health*, *8*(2), e010968. https://doi.org/10.1136/BMJGH-2022-010968

Pirnia, B., & Pirnia, K. (2022). Sex Reassignment Surgery in Iran, Re-Birth or Human Rights Violations against Transgender People? *Iranian Journal of Public Health*, *51*(11), 2632. https://doi.org/10.18502/IJPH.V51I11.11183

Pols, J. (2012). Caring devices: About warm hands, cold technology and making things fit. In J. W. Duyvendak (Ed.), *Care at a Distance: On the Closeness of Technology*. Amsterdam University Press.

Pope, C. (2000). Qualitative research in health care: Analysing qualitative data. *BMJ*, *320*(7227), 114–116. https://doi.org/10.1136/bmj.320.7227.114

Pop-Eleches, C., Thirumurthy, H., Habyarimana, J. P., Zivin, J. G., Goldstein, M. P., de Walque, D., MacKeen, L., Haberer, J., Kimaiyo, S., Sidle, J., Ngare, D., & Bangsberg, D. R. (2011). Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. *AIDS*, *25*(6), 825–834. https://doi.org/10.1097/QAD.0b013e32834380c1

Pronyk, P. M., Hargreaves, J. R., Kim, J. C., Morison, L. A., Phetla, G., Watts, C., Busza, J., & Porter, J. D. H. (2016). Effect of a structural intervention for the prevention of intimate-partner violence and HIV in rural South Africa: a cluster randomised trial. *The Lancet*, *368*(9551), 1973–1983. https://doi.org/10.1016/S0140-6736(06)69744-4

Quintana, Y., Gonzalez Martorell, E. A., Fahy, D., & Safran, C. (2018). A Systematic Review on Promoting Adherence to Antiretroviral Therapy in HIV-infected Patients Using Mobile Phone Technology. *Applied Clinical Informatics*, *9*(2), 450–466.

Rahnama, R., Mohraz, M., Mirzazadeh, A., Rutherford, G., McFarland, W., Akbari, G., & Malekinejad, M. (2014). Access to harm reduction programs among persons who inject drugs: Findings from a respondent-driven sampling survey in Tehran, Iran. *The International Journal on Drug Policy*, *25*(4), 717. https://doi.org/10.1016/J.DRUGPO.2014.05.013

Rana, A. I., van den Berg, J. J., Lamy, E., & Beckwith, C. G. (2016). Using a Mobile Health Intervention to Support HIV Treatment Adherence and Retention Among Patients at Risk for Disengaging with Care. *AIDS Patient Care and STDs*, *30*(4), 178–184.

Rasoolinajad, M., Abedinia, N., Noorbala, A. A., Mohraz, M., Badie, B. M., Hamad, A., & Sahebi, L. (2018). Relationship among HIV-related stigma, mental health and quality of life for HIV-positive patients in Tehran. *AIDS and Behavior*, *22*(12), 3773–3782. https://doi.org/10.1007/S10461-017-2023-Z/TABLES/6

Reda, A. A. (2011). Reliability and Validity of the Ethiopian Version of the Hospital Anxiety and Depression Scale (HADS) in HIV Infected Patients. *PLoS ONE*, *6*(1), e16049. https://doi.org/10.1371/journal.pone.0016049

Reeves, A., Steele, S., Stuckler, D., McKee, M., Amato-Gauci, A., & Semenza, J. C. (2017). National sex work policy and HIV prevalence among sex workers: an ecological regression analysis of 27 European countries. *The Lancet. HIV*, *4*(3), e134–e140. https://doi.org/10.1016/S2352-3018(16)30217-X

Reinius, M., Wettergren, L., Wiklander, M., Svedhem, V., Ekström, A. M., & Eriksson, L. E. (2017). Development of a 12-item short version of the HIV stigma scale. *Health and Quality of Life Outcomes*, *15*. https://doi.org/10.1186/s12955-017-0691-z

Reis, H. T., Clark, M. S., Pereira Gray, D. J., Tsai, F. F., Brown, J. B., Stewart, M., & Underwood, L. G. (2008). Measuring responsiveness in the therapeutic relationship: A patient perspective. *Basic and Applied Social Psychology*, *30*(4), 339–348. https://doi.org/10.1080/01973530802502275

Remien, R. H., Mellins, C. A., Robbins, R. N., Kelsey, R., Rowe, J., Warne, P., Chowdhury, J., Lalkhen, N., Hoppe, L., Abrams, E. J., El-Bassel, N., Witte, S., & Stein, D. J. (2013). Masivukeni: Development of a Multimedia Based Antiretroviral Therapy Adherence Intervention for Counselors and Patients in South Africa. *AIDS and Behavior*, *17*(6), 1979–1991. https://doi.org/10.1007/s10461-013-0438-8

Rhodes, T., & Cusick, L. (2000). Love and intimacy in relationship risk management: HIV positive people and their sexual partners. *Sociology of Health and Illness*, *22*(1), 1–26. https://doi.org/10.1111/1467-9566.00189

Rhodes, T., Singer, M., Bourgois, P., Friedman, S. R., & Strathdee, S. A. (2005). The social structural production of HIV risk among injecting drug users. *Social Science & Medicine*, *61*(5), 1026–1044. https://doi.org/10.1016/J.SOCSCIMED.2004.12.024

Richterman, A., & Thirumurthy, H. (2022). The effects of cash transfer programmes on HIV-related outcomes in 42 countries from 1996 to 2019. *Nature Human Behaviour 2022 6:10*, *6*(10), 1362–1371. https://doi.org/10.1038/s41562-022-01414-7

Rittenberg, E., Liebman, J. B., & Rexrode, K. M. (2022). Primary Care Physician Gender and Electronic Health Record Workload. *Journal of General Internal Medicine*, *37*(13), 3295–3301. https://doi.org/10.1007/S11606-021-07298-Z

Rivet Amico, K. (2011). A situated-Information Motivation Behavioral Skills Model of Care Initiation and Maintenance (sIMB-CIM): An IMB model based approach to

understanding and intervening in engagement in care for chronic medical conditions. *Journal of Health Psychology*, *16*(7), 1071–1081. https://doi.org/10.1177/1359105311398727

Robb, N., & Greenhalgh, T. (2006). "You have to cover up the words of the doctor": the mediation of trust in interpreted consultations in primary care. *Journal of Health Organization and Management*, *20*(5), 434–455. https://doi.org/10.1108/14777260610701803

Robbins, R. N., Mellins, C. A., Leu, C.-S., Rowe, J., Warne, P., Abrams, E. J., Witte, S., Stein, D. J., & Remien, R. H. (2015). Enhancing Lay Counselor Capacity to Improve Patient Outcomes with Multimedia Technology. *AIDS and Behavior*, *19 Suppl 2*(0 2), 163–176. https://doi.org/10.1007/s10461-014-0988-4

Rogers, C. (1951). *Client-centered therapy; its current practice, implications, and theory.* . Houghton Mifflin.

Rogers, E. M., Singhal, A., & Quinlan, M. M. (2014). Diffusion of Innovations. In *Taylor & Francis Group* (2nd ed.). Routledge. https://doi.org/10.4324/9780203887011-36

Roos, S. (2013). Chronic Sorrow and Ambiguous Loss: Gestalt Methods for Coping with Grief. *Gestalt Review*, *17*(3), 229–239. https://doi.org/10.5325/GESTALTREVIEW.17.3.0229

Rosenberg, J., Bohrer, M., & Rhatigan, J. (2011). Iran's Triangular Clinic. *The Global Health Delivery Project*. https://www.globalhealthdelivery.org/case-collection/case-studies/asia-and-middle-east/irans-triangular-clinic

Rosenberg, T. (2010a). How Iran Derailed a Health Crisis - The New York Times. *The New York Times*. https://archive.nytimes.com/opinionator.blogs.nytimes.com/2010/12/03/how-iran-derailed-a-health-crisis/

Rosenberg, T. (2010b). Needle Exchange in Iran - The New York Times. *The New York Times*. https://archive.nytimes.com/opinionator.blogs.nytimes.com/2010/11/29/an-enlightened-exchange-in-iran/

Roter, D., & Larson, S. (2002). The Roter interaction analysis system (RIAS): utility and flexibility for analysis of medical interactions. *Patient Education and Counseling*, *46*(4), 243–251. https://doi.org/10.1016/S0738-3991(02)00012-5

Rotheram-Borus, M. J., Swendeman, D., & Chovnick, G. (2009). The past, present, and future of HIV prevention: integrating behavioral, biomedical, and structural intervention strategies for the next generation of HIV prevention. *Annual Review of Clinical Psychology*, *5*, 143–167. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=19327028

Ruan, Y., Xiao, X., Chen, J., Li, X., Williams, A. B., & Wang, H. (2017). Acceptability and efficacy of interactive short message service intervention in improving HIV medication adherence in Chinese antiretroviral treatment-naive individuals. *Patient Preference and Adherence*, *11*(101475748), 221–228.

Rueda, S., Mitra, S., Chen, S., Gogolishvili, D., Globerman, J., Chambers, L., Wilson, M., Logie, C. H., Shi, Q., Morassaei, S., & Rourke, S. B. (2016). Examining the associations between HIV-related stigma and health outcomes in people living with HIV/AIDS: a series of meta-analyses. *BMJ Open*, *6*(7), e011453. https://doi.org/10.1136/BMJOPEN-2016-011453

Sabin, L. L., DeSilva, M. B., Gill, C. J., & Li, Z. (2015). Improving Adherence to Antiretroviral Therapy with Triggered Real Time Text Message Reminders: the China through Technology Study (CATS). *J Acquir Immune Defic Syndr*, *69*(5), 551-559. https://doi.org/10.1002/nbm.3369.Three

Sabin, L. L., DeSilva, M. B., Hamer, D. H., Xu, K., Zhang, J., Li, T., Wilson, I. B., & Gill, C. J. (2010). Using electronic drug monitor feedback to improve adherence to antiretroviral therapy among HIV-positive patients in China. *AIDS and Behavior*, *14*(3), 580–589. https://doi.org/10.1007/s10461-009-9615-1

Sabin, L. L., Mansfield, L., DeSilva, M. B., Vian, T., Li, Z., Wubin, X., Gifford, A. L., Barnoon, Y., & Gill, C. J. (2018). Why it Worked: Participants' Insights into an mHealth Antiretroviral Therapy Adherence Intervention in China. *The Open AIDS*

Journal, *12*, 20–37. https://doi.org/https://dx.doi.org/10.2174/1874613601812010020

Sadeghi, L., Lolaie, M., Tabatabai, R. A., Bayanolhagh, S., Taj, L., Ahmadi, N. E., Abedinzadeh, N., Vakili, F., Ahmadi, G., & Mohraz, M. (2018). HIV-1 Drug Resistance Profiles for the HIV Protease and Reverse Transcriptase Gene in Patients Receiving Combination Therapy in Tehran, Iran. *Infectious Disorders Drug Targets*, *18*(3), 241–248. https://doi.org/10.2174/1871526518666180416110259

Said, E. (1978). *Orientalism*. Pantheon Books.

Salehi-Isfahani, D. (2020). *Impact of sanctions on household welfare and employment*. https://www.rethinkingiran.com/iranundersanctions/salehiisfahani

Samarasekera, U. (2021). Minoo Mohraz—Iran's leader in HIV research. *The Lancet Infectious Diseases*, *21*(12), 1640. https://doi.org/10.1016/S1473-3099(21)00718-0

Santos, M., Makofane, K., Arreola, S., & Do, T. (2017). Reductions in access to HIV prevention and care services are associated with arrest and convictions in a global survey of men who have sex with men. *Sexually Transmitted Infections*, *93*(1), 62–64. https://doi.org/http://dx.doi.org/10.1136/sextrans-2015-052386

Seeley, J., Watts, C. H., Kippax, S., Russell, S., Heise, L., & Whiteside, A. (2012). Addressing the structural drivers of HIV: a luxury or necessity for programmes? *Journal of the International AIDS Society*, *15 Suppl 1*, 1–4. https://doi.org/10.7448/IAS.15.3.17397

Seyed Alinaghi, S. A., Farhoudi, B., Mohraz, M., Alipour, A., Golrokhy, R., Hosseini, M., & Miri, J. (2016). Adherence to Antiretroviral Therapy and Tuberculosis Treatment in a Prison of Tehran, Iran. *Infectious Disorders Drug Targets*, *16*(3), 199–203. http://www.ncbi.nlm.nih.gov/pubmed/27311561

Shah, R., Watson, J., & Free, C. (2019). A systematic review and meta-analysis in the effectiveness of mobile phone interventions used to improve adherence to antiretroviral therapy in HIV infection. *BMC Public Health*, *19*(1), 915.

Shahrokni, N. (2021). *Bursting at the Seams Economic Sanctions and Transformation of the Domestic Sphere in Iran*.

Shahrokni, Nazanin. (2020). *Women in Place: The Politics of Gender Segregation in Iran.* University of California Press.

Shanahan, L., Hill, S. N., Gaydosh, L. M., Steinhoff, A., Costello, E. J., Dodge, K. A., Harris, K. M., & Copeland, W. E. (2019). Does despair really kill? A roadmap for an evidence-based answer. In *American Journal of Public Health* (Vol. 109, Issue 6, pp. 854–858). American Public Health Association Inc. https://doi.org/10.2105/AJPH.2019.305016

Sharifi, H., Mirzazadeh, A., Shokoohi, M., Karamouzian, M., Khajehkazemi, R., Navadeh, S., Fahimfar, N., Danesh, A., Osooli, M., McFarland, W., Gouya, M. M., & Haghdoost, A. A. (2018). Estimation of HIV incidence and its trend in three key populations in Iran. *PLOS ONE*, *13*(11), e0207681. https://doi.org/10.1371/journal.pone.0207681

Sidney, K., Antony, J., Rodrigues, R., Arumugam, K., Krishnamurthy, S., D'souza, G., De Costa, A., & Shet, A. (2012). Supporting patient adherence to antiretrovirals using mobile phone reminders: Patient responses from South India. *AIDS Care*, *24*(5), 612–617. https://doi.org/https://dx.doi.org/10.1080/09540121.2011.630357

Siegrist, C. A., Yerly, S., Kaiser, L., Wyler, C. A., & Perrin, L. (1994). Mother to child transmission of zidovudine-resistant HIV-1. *Lancet (London, England)*, *344*(8939–8940), 1771–1772. https://doi.org/10.1016/S0140-6736(94)92911-4

Simoni, J. M., Kutner, B. A., & Horvath, K. J. (2015). Opportunities and Challenges of Digital Technology for HIV Treatment and Prevention. *Current HIV/AIDS Reports*, *12*(4), 437–440. file:///Users/vasilinittas/Library/Application Support/Mendeley Desktop/Downloaded/Simoni, Kutner, Horvath - 2015 - Opportunities and Challenges of Digital Technology for HIV Treatment and Prevention.pdf

Singer, E., & Bossarte, R. M. (2006). Incentives for Survey Participation. *American Journal of Preventive Medicine*, *31*(5), 411–418. https://doi.org/10.1016/j.amepre.2006.07.013

Skivington, K., Matthews, L., Simpson, S. A., Craig, P., Baird, J., Blazeby, J. M., Boyd, K. A., Craig, N., French, D. P., McIntosh, E., Petticrew, M., Rycroft-Malone, J., White, M., & Moore, L. (2021). A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *BMJ*, *374*. https://doi.org/10.1136/BMJ.N2061

Skovdal, M., Campbell, C., Nyamukapa, C., & Gregson, S. (2011). When masculinity interferes with women's treatment of HIV infection: A qualitative study about adherence to antiretroviral therapy in Zimbabwe. *Journal of the International AIDS Society*, *14*(1). https://doi.org/10.1186/1758-2652-14-29

Sligo, J., Gauld, R., Roberts, V., & Villa, L. (2017). A literature review for large-scale health information system project planning, implementation and evaluation. *International Journal of Medical Informatics*, *97*, 86–97. https://doi.org/10.1016/J.IJMEDINF.2016.09.007

Smillie, K., Van Borek, N., Abaki, J., Pick, N., Maan, E. J., Friesen, K., Graham, R., Levine, S., van der Kop, M. L., Lester, R. T., & Murray, M. (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). *The Journal of the Association of Nurses in AIDS Care : JANAC*, *25*(6), 614–625.

Smillie, K., Van Borek, N., van der Kop, M. L., Lukhwaro, A., Li, N., Karanja, S., Patel, A. R., Ojakaa, D., & Lester, R. T. (2014). Mobile health for early retention in HIV care: a qualitative study in Kenya (WelTel Retain). *African Journal of AIDS Research : AJAR*, *13*(4), 331–338.

Smith, C., & van Velthoven, M. H. (2020). Best practices in digital health to improve antiretroviral treatment adherence. *BMJ Health & Care Informatics*, *27*(3).

Soderholm, A. (2020). *Sanctions and illicit drug use in Iran*.

Standing, C., Standing, S., McDermott, M. L., Gururajan, R., & Kiani Mavi, R. (2018). The Paradoxes of Telehealth: a Review of the Literature 2000–2015. *Systems Research and Behavioral Science*, *35*(1), 90–101. https://doi.org/10.1002/SRES.2442

Stangl, A. L., Lloyd, J. K., Brady, L. M., Holland, C. E., & Baral, S. (2013). A systematic review of interventions to reduce HIV-related stigma and discrimination from 2002 to 2013: how far have we come? *Journal of the International AIDS Society*, *16*(3Suppl 2). https://doi.org/10.7448/IAS.16.3.18734

Steinert, J. I., Atika Nyarige, D., Jacobi, M., Kuhnt, J., & Kaplan, L. (2021). A systematic review on ethical challenges of 'field' research in low-income and middle-income countries: respect, justice and beneficence for research staff? *BMJ Global Health*, *6*(7), e005380. https://doi.org/10.1136/BMJGH-2021-005380

Stone, J., Artenie, A., Hickman, M., Martin, N. K., Degenhardt, L., Fraser, H., & Vickerman, P. (2022). The contribution of unstable housing to HIV and hepatitis C virus transmission among people who inject drugs globally, regionally, and at country level: a modelling study. *The Lancet Public Health*, *7*(2), e136–e145. https://doi.org/10.1016/S2468-2667(21)00258-9

Sutcliffe, K., Thomas, J., Stokes, G., Hinds, K., & Bangpan, M. (2015). Intervention Component Analysis (ICA): A pragmatic approach for identifying the critical features of complex interventions. *Systematic Reviews*, *4*(1), 140. https://doi.org/10.1186/s13643-015-0126-z

Tabaar, M. (2018). *Religious Statecraft: The Politics of Islam in Iran.* . Columbia University Press.

Tabrizi, J. S., Pourasghar, F., & Gholamzadeh Nik-Joo, R. (2017). Status of Iran's Primary Health Care System in Terms of Health Systems Control Knobs: A Review Article. *Iranian Journal of Public Health*, *46*(9), 1156. /pmc/articles/PMC5632316/

Taylor, D., Lunny, C., Lolic, P., Warje, O., Geldman, J., Wong, T., Gilbert, M., Lester, R., & Ogilvie, G. (2019). Effectiveness of text messaging interventions on prevention, detection, treatment, and knowledge outcomes for sexually transmitted infections (STIs)/HIV: a systematic review and meta-analysis. *Systematic Reviews*, *8*(1), 12.

The France 24 Observers. (2015). French foreign minister's Iran visit tainted by HIV scandal protests. *France 24*. https://observers.france24.com/en/20150729-blood-scandal-protest-fabius-iran-france

The RAMESES II. (2017). *What realists mean by context*. https://www.ramesesproject.org/media/RAMESES_II_Context.pdf

Tierney, S., Westlake, D., Wong, G., Markham, S., Turk, A., Gorenberg, J., & Mahtani, K. (2023). Fitting in or belonging: emerging findings from a realist evaluation of social prescribing link workers in primary care. *The British Journal of General Practice : The Journal of the Royal College of General Practitioners*, *73*. https://doi.org/10.3399/BJGP23X733521

Tong F, L. R., D'Alfonso S, Berry K, & Bucci S. (2022). Digital Therapeutic Alliance With Fully Automated Mental Health Smartphone Apps: A Narrative Review. . *Front. Psychiatry*, *13*(819623).

Treichler, P. A. (1999). *How to have theory in an epidemic : cultural chronicles of AIDS*. Duke University Press.

Tremain, H., McEnery, C., Fletcher, K., & Murray, G. (2020). The Therapeutic Alliance in Digital Mental Health Interventions for Serious Mental Illnesses: Narrative Review. *JMIR Mental Health*, *7*(8). https://doi.org/10.2196/17204

Tsai, A. C., Bangsberg, D. R., Kegeles, S. M., Katz, I. T., Haberer, J. E., Muzoora, C., Kumbakumba, E., Hunt, P. W., Martin, J. N., & Weiser, S. D. (2013). Internalized stigma, social distance, and disclosure of HIV seropositivity in rural uganda. *Annals of Behavioral Medicine*, *46*(3), 285–294. https://doi.org/10.1007/s12160-013-9514-6

Tsai, Y. T., Sriyani Padmalatha, K. M., Ku, H. C., Wu, Y. L., & Ko, N. Y. (2023). Global overview of suicidal behavior and associated risk factors among people living with human immunodeficiency virus: A scoping review. *PLoS ONE*, *18*(3 March). https://doi.org/10.1371/journal.pone.0269489

Turan, B., Fazeli, P. L., Raper, J. L., Mugavero, M. J., & Johnson, M. O. (2016). Social support and moment-to-moment changes in treatment self-efficacy in men living

with HIV: Psychosocial moderators and clinical outcomes. *Health Psychology*, *35*(10), 1126–1134. https://doi.org/10.1037/hea0000356

UNAIDS. (2015). *Using TRIPS flexibilities to improve access to HIV treatment*. https://www.unaids.org/sites/default/files/media_asset/JC2049_PolicyBrief_TRIPS_en_1.pdf

UNAIDS. (2018). *New HIV Infections*. http://aidsinfo.unaids.org/

UNAIDS. (2020a). *Country progress report-Iran*.

UNAIDS. (2020b). *HIV Criminalization, Human Rights Fact Sheet Series*. https://www.unaids.org/sites/default/files/media_asset/01-hiv-human-rights-factsheet-criminalization_en.pdf

UNAIDS. (2021). *AIDSinfo | UNAIDS*. https://aidsinfo.unaids.org/

UNAIDS. (2022). *In Danger: UNAIDS Global AIDS Update 2022*. https://www.unaids.org/sites/default/files/media_asset/2022-global-aids-update_en.pdf

UNAIDS. (2023). *The path that ends AIDS* . https://www.unaids.org/sites/default/files/media_asset/2023-unaids-global-aids-update_en.pdf

UNDP. (2020). *Focused Country Evaluation - Iran HIV Evaluation* . https://erc.undp.org/evaluation/evaluations/detail/13203

United Nations Iran. (2016). *Tehran Positive Club receives Red Ribbon Award 2016 for its exceptional work in the field of HIV and AIDS*. https://www.un.org.ir/all-stories/item/3522-22-july-2016-tehran-positive-club-receives-red-ribbon-award-2016-for-its-exceptional-work-in-the-field-of-hiv-and-aids

UNODC. (2020). *Compulsory drug treatment and rehabilitation in East and Southeast Asia*.

Uthman, O. A., Magidson, J. F., Safren, S. A., & Nachega, J. B. (2014). Depression and adherence to antiretroviral therapy in low-, middle- and high-income countries: a systematic review and meta-analysis. *Current HIV/AIDS Reports*, *11*(3), 291. https://doi.org/10.1007/S11904-014-0220-1

Van Der Kop, M. L., Karanja, S., Thabane, L., Marra, C., Chung, M. H., Gelmon, L., Kimani, J., & Lester, R. T. (2012). In-Depth Analysis of Patient-Clinician Cell Phone Communication during the WelTel Kenya1 Antiretroviral Adherence Trial. *PLoS ONE*, *7*(9), e46033. https://doi.org/10.1371/journal.pone.0046033

Van Der Kop, M. L., Muhula, S., Ekstrom, A. M., Jongbloed, K., Smillie, K., Abunah, B., Kinagwi, K., Kyomuhangi, L. B., Gelmon, L., Ojakaa, D. I., Lester, R. T., & Awiti, P. O. (2017). Participation in a mobile health intervention trial to improve retention in HIV care: does gender matter?. *Journal of Telemedicine and Telecare*, *23*(2), 314–320.

Van Der Kop, M. L., Muhula, S., Nagide, P. I., Thabane, L., Gelmon, L., Awiti, P. O., Abunah, B., Kyomuhangi, L. B., Budd, M. A., Marra, C., Patel, A., Karanja, S., Ojakaa, D. I., Mills, E. J., Ekstrom, A. M., & Lester, R. T. (2018). Effect of an interactive text-messaging service on patient retention during the first year of HIV care in Kenya (WelTel Retain): an open-label, randomised parallel-group study. *The Lancet. Public Health*, *3*(3), e143–e152. https://doi.org/https://dx.doi.org/10.1016/S2468-2667(17)30239-6

Van Der Kop, M. L., Ojakaa, D. I., Patel, A., Thabane, L., Kinagwi, K., Ekstrom, A. M., Smillie, K., Karanja, S., Awiti, P., Mills, E., Marra, C., Kyomuhangi, L. B., & Lester, R. T. (2013). The effect of weekly short message service communication on patient retention in care in the first year after HIV diagnosis: study protocol for a randomised controlled trial (WelTel Retain). *BMJ Open*, *3*(6).

Venables, E., Ndlovu, Z., Munyaradzi, D., Martínez-Pérez, G., Mbofana, E., Nyika, P., Chidawanyika, H., Garone, D. B., & Bygrave, H. (2019). Patient and health-care worker experiences of an HIV viral load intervention using SMS: A qualitative study. *PLoS ONE*, *14*(4), 1–13. https://doi.org/10.1371/journal.pone.0215236

Verhoeks, C., Teunissen, D., van der Stelt-Steenbergen, A., & Lagro-Janssen, A. (2019). Women's expectations and experiences regarding e-health treatment: A systematic review. *Health Informatics Journal*, *25*(3), 771–787. https://doi.org/10.1177/1460458217720394

Von Wyl, V., Yerly, S., Böni, J., Bürgisser, P., Klimkait, T., Battegay, M., Bernasconi, E., Cavassini, M., Furrer, H., Hirschel, B., Vernazza, P. L., Francioli, P., Bonhoeffer, S., Ledergerber, B., & Günthard, H. F. (2009). Long-Term Trends of HIV Type 1 Drug Resistance Prevalence among Antiretroviral Treatment–Experienced Patients in Switzerland. *Clinical Infectious Diseases*, *48*(7), 979–987. https://doi.org/10.1086/597352

Wald, D. S., Butt, S., & Bestwick, J. P. (2015). One-way Versus Two-way Text Messaging on Improving Medication Adherence: Meta-analysis of Randomized Trials. *The American Journal of Medicine*, *128*(10), 1139.e1-1139.e5. https://doi.org/10.1016/J.AMJMED.2015.05.035

Walsh, R. (2003). The methods of reflexivity. *Humanistic Psychologist*, *31*(4), 51–66. https://doi.org/10.1080/08873267.2003.9986934

Wang, Z., Zhu, Y., Cui, L., & Qu, B. (2019). Electronic Health Interventions to Improve Adherence to Antiretroviral Therapy in People Living With HIV: Systematic Review and Meta-Analysis. *JMIR MHealth and UHealth*, *7*(10), e14404.

Ware, N. C., Pisarski, E. E., Tam, M., Wyatt, M. A., Atukunda, E., Musiimenta, A., Bangsberg, D. R., & Haberer, J. E. (2016). The Meanings in the messages: How SMS reminders and real-time adherence monitoring improve antiretroviral therapy adherence in rural Uganda. *AIDS (London, England)*, *30*(8), 1287–1294. https://doi.org/https://dx.doi.org/10.1097/QAD.0000000000001035

Watkins, J. A., Goudge, J., Gomez-Olive, F. X., Huxley, C., Dodd, K., & Griffiths, F. (2018). mHealth text and voice communication for monitoring people with chronic diseases in low-resource settings: a realist review. *Bmj Global Health*, *3*(2), e000543.

Weingarten, K. (2012). Sorrow: A Therapist's Reflection on the Inevitable and the Unknowable. *Family Process*, *51*(4), 440–455. https://doi.org/10.1111/J.1545-5300.2012.01412.X

Westergaard, R. P., Genz, A., Panico, K., Surkan, P. J., Keruly, J., Hutton, H. E., Chang, L. W., & Kirk, G. D. (2017). Acceptability of a mobile health intervention to enhance HIV care coordination for patients with substance use disorders.

Addiction Science & Clinical Practice, *12*(1), 11. https://doi.org/https://dx.doi.org/10.1186/s13722-017-0076-y

Westergaard, R. P., Hess, T., Astemborski, J., Mehta, S. H., & Kirk, G. D. (2013). Longitudinal changes in engagement in care and viral suppression for HIV-infected injection drug users. *AIDS (London, England)*, *27*(16), 2559–2566. https://doi.org/10.1097/QAD.0b013e328363bff2

WHO. (2003). *Adherence to Long-term Therapies - Evidence for action*. http://www.who.int/chp/knowledge/publications/adherence_full_report.pdf?ua=1

WHO. (2010). *A strategy for addressing the key determinants of health in the African Region*. https://apps.who.int/iris/handle/10665/1670

WHO. (2014). WHO | The implementation of ethical guidelines for research on HIV. *WHO*.

WHO. (2015a). *Consolidated Guidelines On The Use Of Antiretroviral Drugs for Treating and Preventing HIV Infection* (Issue 2). www.who.int/about/licensing/copyright_form/en/index.html

WHO. (2015b). *Guideline on When to Start Antiretroviral Therapy and on Pre-exposure Prophylaxis for HIV*. http://apps.who.int/iris/bitstream/10665/186275/1/9789241509565_eng.pdf?ua=1

WHO. (2019a). *Recommendations on digital interventions for health system strengthening*. https://apps.who.int/iris/bitstream/handle/10665/311941/9789241550505-eng.pdf?ua=1

WHO. (2019b). *WHO HIV policy adoption and implementation status in countries*. https://apps.who.int/iris/bitstream/handle/10665/326035/WHO-CDS-HIV-19.20-eng.pdf?ua=1

WHO. (2023). *Providing care to people with advanced HIV disease who are seriously ill*. https://www.who.int/publications/i/item/9789240068650

Wilson, I. B., Lee, Y., Michaud, J., Fowler, F. J., & Rogers, W. H. (2016). Validation of a New Three-Item Self-Report Measure for Medication Adherence. *AIDS and Behavior*, *20*(11), 2700–2708. https://doi.org/10.1007/s10461-016-1406-x

Wilson, I. B., Tie, Y., Padilla, M., Rogers, W. H., & Beer, L. (2020). Performance of a short, self-report adherence scale in a probability sample of persons using HIV antiretroviral therapy in the United States. *AIDS (London, England)*, *34*(15), 2239–2247. https://doi.org/10.1097/QAD.0000000000002689

WMA. (2013). *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects – WMA – The World Medical Association*. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

Wong, G. (2017). *The RAMESES II Project. 2017. Realist evaluation, realist synthesis, realist research - what's in a name?* http://www.ramesesproject.org/media/RAMESES_II_RE_RS_RR_whats_in_a_name.pdf

Wong, G., Greenhalgh, T., & Pawson, R. (2010). Internet-based medical education: A realist review of what works, for whom and in what circumstances. *BMC Medical Education*, *10*(1), 1–10. https://doi.org/10.1186/1472-6920-10-12/FIGURES/2

World Bank. (2021). *Antiretroviral Therapy Coverage (% of People Living with HIV)*. https://data.worldbank.org/indicator/SH.HIV.ARTC.ZS

World Health Organization. (2013). *Consolidated Guidelines on The Use of Antiretroviral Drugs for Treating and Preventing HIV Infection* (Issue June).

World Health Organization. (2016). *Consolidated Guidelines on The Use of Antiretroviral Drugs for Treating and Preventing HIV infection*. https://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684_eng.pdf

World Health Organization. (2021). *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring : recommendations for a public health approach.Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.* 548.

World Health Organization (WHO). (2019). WHO guideline: recommendations on digital interventions for health system strengthening: evidence and recommendations. *Documentos Técnicos*, *WHO/RHR/19*(1), 13. https://www.ncbi.nlm.nih.gov/books/NBK541902/

WTO. (2001). *TRIPS declaration*. Ministerial Conferences - Doha 4th Ministerial . https://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm

Yah, C. S., Tambo, E., Khayeka-Wandabwa, C., & Ngogang, J. Y. (2017). Impact of telemonitoring approaches on integrated HIV and TB diagnosis and treatment interventions in sub-Saharan Africa: a scoping review. *Health Promotion Perspectives*, *7*(2), 60–65. https://doi.org/https://dx.doi.org/10.15171/hpp.2017.12

Yakob, B., & Ncama, B. P. (2016). A socio-ecological perspective of access to and acceptability of HIV/AIDS treatment and care services: a qualitative case study research. *BMC Public Health 2016 16:1*, *16*(1), 1–15. https://doi.org/10.1186/S12889-016-2830-6

You, W. X., Comins, C. A., Jarrett, B. A., Young, K., Guddera, V., Phetlhu, D. R., Mulumba, N., McIngana, M., Hausler, H., Baral, S., & Schwartz, S. (2020). Facilitators and barriers to incorporating digital technologies into HIV care among cisgender female sex workers living with HIV in South Africa. *MHealth*, *6*. https://doi.org/10.21037/MHEALTH.2019.12.07

Zakumumpa, H., Kiweewa, F. M., Khuluza, F., & Kitutu, F. E. (2019). "The number of clients is increasing but the supplies are reducing": provider strategies for responding to chronic antiretroviral (ARV) medicines stock-outs in resource-limited settings: a qualitative study from Uganda. *BMC Health Services Research*, *19*(1). https://doi.org/10.1186/S12913-019-4137-7

Zang, C., Guida, J., Sun, Y., & Liu, H. (2014). Collectivism culture, HIV stigma and social network support in Anhui, China: a path analytic model. *AIDS Patient Care and STDs*, *28*(8), 452–458. https://doi.org/10.1089/APC.2014.0015

Zeligman, M., & Wood, A. W. (2017). Conceptualizing an HIV Diagnosis Through a Model of Grief and Bereavement. *Adultspan Journal*, *16*(1), 18–30. https://doi.org/10.1002/ADSP.12031

Zimet, G. D., Powell, S. S., Farley, G. K., Werkman, S., & Berkoff, K. A. (1990). Psychometric Characteristics of the Multidimensional Scale of Perceived Social Support. *Journal of Personality Assessment*, *55*(3–4), 610–617. https://doi.org/10.1080/00223891.1990.9674095