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Intergenerational spillover effects of antiretroviral therapy in sub-Saharan Africa: a scoping review and future directions for research

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ABSTRACT

Background Antiretroviral therapy (ART) may influence individuals who do not receive the intervention but who are connected in some way to the person who does. Relatively little is known, however, about the size and scope of, what we term, spillover effects of ART. We explored intergenerational spillover effects of ART in sub-Saharan Africa (SSA) and identified several directions for future research.

Methods We conducted a scoping review between March and April 2022. We systematically searched PubMed, PsycINFO, EconLit, OTseeker, AIDSInfo, Web of Science, CINHAL, Google Scholar and African Index Medicus. We analysed the distribution of included studies over time and summarised their findings. We examined the intergenerational impact of ART provision to working-age adults living with HIV on children ('downward' spillover effects) and older adults ('upward' spillover effects). We categorised types of intergenerational spillover effects according to broad themes which emerged from our analysis of included studies.

Findings We identified 26 studies published between 2005 and 2022 with 16 studies assessing spillover effects from adults to children (downward), and 1 study explicitly assessing spillover effects from working-age adults to older adults (upward). The remaining studies did not fully specify the direction of spillover effects. Most spillover effects of ART to household and family members were beneficial and included improvements in wealth, labour market outcomes, health outcomes and health services utilisation, schooling, and household composition. Both children and older adults benefited from ART availability among adults. Detrimental spillover effects were only reported in three studies and included financial and opportunity costs associated with health services utilisation and food insecurity in the first year after ART.

Conclusions ART may lead to substantial spillover effects across generations and sectors in SSA. Further research is needed to capitalise on positive spillover effects while mitigating potential negative spillover effects. The returns to investments in large-scale health interventions such as ART may be underestimated without considering these societal benefits.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The expansion of antiretroviral therapy has led to major improvements for treated individuals. Little is known, however, about the impact of antiretroviral therapy on their household and family members (also known as 'spillover effects').

⇒ Indirect impacts of antiretroviral therapy may be particularly large among children and older adults, who depend on the resources of working-age adults, and in the context of Africa, which has the world's largest HIV treatment programme.

WHAT THIS STUDY ADDS

⇒ This review synthesises for the first time empirical evidence on intergenerational spillover effects of antiretroviral therapy in sub-Saharan Africa, using a wide range of databases, and considers quantitative, qualitative and mixed-methods study designs.

⇒ The spillover effects of antiretroviral therapy to household and family members include improvements in financial savings, labour market outcomes, health outcomes and health services utilisation, children's schooling outcomes, and household composition.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We identify directions for future research on intergenerational spillover effects of antiretroviral therapy in sub-Saharan Africa, which is needed to take advantage of positive spillover effects while mitigating potential negative spillover effects.

⇒ Evidence on spillover effects is critical to inform budgets and health policy. As global health organisations are scaling down on HIV funding, spillover effects may further justify ongoing investments in antiretroviral therapy in the region.

INTRODUCTION

Health outcomes have improved substantially in recent decades in sub-Saharan Africa (SSA). Life expectancy at birth, for instance,

increased more than 50% between 1960 and 2020 in SSA, from 40 years to 62 years.[1] In comparison, life expectancy in the USA increased by just 10% during the same period, from 70 years in 1960 to 77 years in 2020. One fundamental reason for these improvements are major innovations in health, such as the advent of antibiotics,[2] childhood immunisation,[3 4] oral rehydration therapy,[5] infection control measures such as sanitation[6] and hygiene,[7] school-based health programmes (such as nutrition fortification and deworming),[8] and, recently, the scale-up of antiretroviral therapy coverage (ART) and the prevention of HIV acquisition[9] and vertical transmission for HIV.[10 11] In addition to reductions in premature mortality among treated individuals, these interventions have led to substantial improvements in several allied sectors, such as educational attainment,[12 13] food security and nutritional status,[14–16] socioeconomic well-being,[17–25] and labour force participation and employment.[26–33]

Little is known, however, about the broader societal effects of these investments in health beyond the person who receives the health intervention. Health interventions may have not only an effect on the treated individuals, but also on those who are somehow connected to these individuals, referring to so-called 'spillover effects' on individuals living in the same household or family members (whether they themselves are on treatment or not). Improvements in health allow treated individuals to return to activities undertaken prior to sickness[34] including (re-)enrolling in school, domestic activities, seeking employment and regaining employment.[26 35] Beyond the direct beneficiary of health interventions, family and household members (eg, children, older adults) who had formerly been occupied by caregiving obligations and/or by compensating for the loss of a working individual in the household, can regain time to pursue other activities including attending school in the case of children and performing income or non-income generating work in the case of adults.[36] There may also be changes in health behaviours and healthcare utilisation among household members once the treated individual's health improves. Conversely, innovations in treatment may also have negative consequences for household or family members. For instance, increased treatment access could result in household-level economic and time losses associated with healthcare utilisation of patients.[37] Health interventions, thus, have the potential to affect the living conditions of people living together with the treatment recipient in multiple ways.

In this study, we assess whether the world's largest HIV treatment programme may have broader effects on households and families of treated individuals. To do so, we review intergenerational spillover effects of ART and collate the diverse effects for individuals living in households or family members exposed to ART. Specifically, the scale-up of ART in SSA in the last two decades has been the largest public-sector health investment, with over US$12.1 billion invested in 2021 alone (constant 2019 US$).[38 39] Over 20 million people living with HIV were on ART in SSA in 2021, which accounted for 70% of individuals on HIV treatment globally.[40] The expansion of ART from, on average, less than 1% in the early 2000s to 78% in 2021 has led to major improvements.[41] This scale-up of treatment has led to massive gains in adult life expectancy and health.[42–46] Moreover, the HIV response frequently serves as a blueprint for other disease-specific interventions in the region, including for non-communicable diseases.[47] Beyond the direct impact on the treated individual, the expansion of ART coverage has led to large 'social exposure' to ART among family and household members affiliated to the treatment recipient.[48]

In our approach, we focus on intergenerational spillover effects of ART provided to working-age adults (typically defined as ages 18–65 years) because the HIV epidemic primarily affected working-age adults. Working-age adults play a central role for household members of both the younger[49] and older generations[50 51] who depend on their income and other resources, particularly in the context of SSA where coresidence between family members is common and public welfare transfers are relatively limited (such as old-age pensions and child-care grants). For example, about 75% of older adults in SSA live with a working-age adult.[52] In the absence of ART, HIV hollows out the middle generation in households, possibly leaving older household members without care.[53] We, therefore, hypothesised that the scale-up of ART in SSA may have large consequences across generations, including potentially both positive and negative consequences.

The aim of this systematic scoping review is to explore spillover effects of ART beyond the treated individual on household and family members in SSA. We aim to explore the breadth of the existing literature on the topic, summarise the key evidence and identify gaps in the literature to inform future directions for research on spillover effects of treatment interventions in the region. To our knowledge, this study is the first systematic scoping review of intergenerational spillover effects of ART in SSA among household and family members of treated individuals.

METHODS

We conducted a systematic scoping review of all empirical publications that report on the impact of ART on family and household members who are indirectly affected by ART due to their coresidence or affiliation with a recipient of ART. We define spillover effects of ART broadly as any change that ART induces to the health, development, socioeconomic situation, well-being or living arrangements of household or family members of ART recipients. This scoping review maps the broad range of the topic, assesses heterogeneity in study designs and their key findings, determines the direction and types of intergenerational spillover effects, and identifies gaps in the existing literature.[54] Our methodological framework is based on Arksey and O'Malley 2005[55] and its

elaborations by Levac *et al*[56] and Peters *et al*.[57] Specifically, the framework includes the following six major steps: (1) identifying the research question; (2) identifying relevant studies; (3) selecting the studies; (4) sifting, charting and sorting material according to key issues and themes[58]; (5) collating, summarising and reporting the results; and, lastly, (6) consulting with individuals with relevant expertise and topical knowledge who may suggest additional references and provide insights beyond those available in the existing literature.[56 59]

Research question

We used the PEO mnemonic (Population, Exposure and Outcome)[60 61] to design our research question: 'How does ART indirectly affect household or family members who coreside or are affiliated with at least one person living with HIV on ART in SSA?' Based on the research question, we then developed three main concepts for the search strategy, namely: (1) ART, (2) intergenerational, household, family and (3) SSA.

Data sources and search strategy

In accordance with our search concepts, we used keywords and controlled vocabulary to search a wide range of databases spanning several fields and the general sciences. First, we conducted a limited search to identify all relevant text words and Medical Subject Headings in PubMed. Second, we searched the electronic databases of PubMed, PsycINFO, EconLit, OTseeker, AIDSInfo, Web of Science, CINHAL, Google Scholar and African Index Medicus. The search query was in English with no additional limitations on language or publication date. We present the complete search query in online supplemental texts S1–S9. The search query was reviewed by a librarian of the University of Heidelberg. Second, we searched abstract databases of conferences, including the Conference on Retroviruses and Opportunistic Infections (2014–2022) and the International AIDS conference (2019–2020). We also searched the grey literature, including Google Scholar and the websites of UNAIDS, WHO and the UNESCO Health and Education Resource Centre. Third, all articles identified as relevant in the search process were included in citation searching, including three reviews.[17 19 24] We screened reference lists of all included articles to search for additional eligible studies. Fourth, we supplemented our search results with several relevant publications previously known to the study team, including previous reviews[17 19 62] and seminal works on the effects of health interventions in SSA.[26 63 64]

Study selection

We considered all empirical studies (quantitative and qualitative) which report on the outcomes of individuals who coreside or are affiliated with a person living with HIV on ART in SSA. To include a wide variety of studies, we considered papers on individuals living with HIV who are on ART regardless of their adherence to ART or viral load. The HIV status of household and family members was not always reported in all articles, and we can, therefore, not always specify if they themselves were on HIV treatment or not. We included a wide range of individual-level and household-level outcomes among family and household members, including the health, socioeconomic situation, living arrangements and well-being of the recipients of the spillover effect. First, all articles found in the database search were screened based on title. The following criteria led to the exclusion of articles: exclusively using aggregated data (eg, changes in national-level life expectancy); exclusively reporting outcomes of the ART recipient but not of other household or family members; study location outside SSA; systematic review (reference lists of systematic reviews, however, were included in citation searching); case study; commentary and unrelated to humans. We did not include reports on the prevention of vertical HIV transmission because these represent intended effects of prenatal services as opposed to unintended spillover effects to a different recipient in the household or family. Second, we assessed identified studies for eligibility based on title and abstract and decided on the final inclusion of studies based on a full-text analysis. The screening process and study selection was conducted by the first author and verified by the last author. In case of doubt, articles were reviewed by additional study team members until a consensus was reached. Identified records were added to the citation manager EndNote V.20.

Data collation and reporting

Our analysis proceeded in the following four steps. First, study characteristics were extracted from all included studies, including author names, year, geographical region (urban or rural), design, sample, outcomes, key findings and effect sizes when reported in the article. Second, we reviewed all studies to determine the reported direction of intergenerational spillover effect between household and family members. Specifically, we included (1) 'downward' spillovers (eg, from parents and/or grandparents to offspring); (2) 'upward' spillovers (eg, from offspring to their parents and/or grandparents) and (3) not specified (spillover effects within households or families but without clear indication of intergenerational spillover recipient).[62] We did not include 'horizontal' spillovers in our analysis (eg, between partners or siblings) because the focus of our paper is on intergenerational spillovers as opposed to intragenerational spillovers, under the assumption that the bulk of horizontal spillovers occur within generations (the median age gap between spouses, eg, is about 5 years suggesting that most partners in SSA are of the same generation).[65] In this scoping review, we hypothesise that there may be large spillover effects of ART among children and older adults who depend on the resources and care of working-age adults. Third, we assessed the type of spillover effect and then categorised these effects a posteriori using broad themes which emerged from our analysis of included

studies. Fourth, we assessed whether studies measured spillover effects to household or family members at the individual level (eg, individual healthcare utilisation) or household level (eg, household assets).

Consultation with experts

Results were presented to experts with relevant expertise, including infectious disease physicians, academic experts and research managers in SSA, to seek additional references and to obtain consultation on the study's approach and findings. Selection criteria for experts included peer-reviewed publications related to HIV and ART, health intervention experience in SSA, local contextual knowledge, expertise in the methodology of systematic reviews and sociodemographic characteristics (such as an expert's gender and country of residence). To do so, we purposively selected six experts, all of whom responded positively to our request.

Conceptual framework

In online supplemental figure S2, we present a conceptual framework underpinning our analysis. ART affects the morbidity and premature mortality of treated individuals (direct impact). In turn, improved health may allow individuals to, at least partially, return to activities undertaken prior to illness. Given this effect on people on ART, treatment can also have so-called spillover effects within the household and social environment of the ART recipient. As a result, ART leads to an unintended (indirect) impact beyond the treated individual on household and family members. These spillover effects can be intragenerational between partners or siblings (horizontal) but also intergenerational between working-age adults and children (downward) or between working-age adults and older household and family members (upward).[62] Although spillover effects within a household seem most likely since household members may interact more closely with the ART recipient, children and older adults living elsewhere may also be affected. For example, in contexts where circular migration is common for the purpose of employment, ART may allow working-age adults to regain employment and send remittances back home to their family members.[66 67]

Empirical analyses are needed, however, because these spillover effects on household and family members are theoretically ambiguous. Spillover effects could be positive or negative and direct observation is needed to validate or disprove hypotheses.[68] For example, ART can reduce the burden on household members who are dependent on the treated individual or have been involved in caregiving for the sick or had to compensate for the loss of a working adult in their household. Conversely, ART may also have negative consequences for non-treated household or family members. For instance, due to the financial and opportunity costs associated with healthcare utilisation for patients receiving 'free' nominal care,[37] or the recovery of appetite among patients leading to food insecurity and household resource strain.[69] Moreover, empirical analyses of spillover effects of health interventions are needed to estimate the total economic returns and inform cost–benefit analyses of large-scale health investments such as ART.[70]

Patient and public involvement

As this research represents a review of previously published literature, patients were not directly involved in any aspect of the study.

RESULTS

Number of included studies and ART coverage in SSA over time

Our database search resulted in 5623 articles, catalogued between December 1987 and April 2022. After the removal of 5554 articles and 24 duplicates, we assessed the remaining 45 articles for eligibility based on title and abstract. We excluded 17 studies that did not consider effects of ART on individuals coresiding or affiliated with the recipient of ART. The remaining 28 articles were then assessed based on the full text which led to the exclusion of 7 additional studies, of which 3 did not consider effects of ART on family or household members, another 3 were literature reviews, and 1 study was a working paper which was included when published. Two full texts of selected articles were not available to us through our institution's library for which we contacted and received a copy of the full text directly from the authors. Our search for grey literature, including Google Scholar, UNAIDS, WHO and several conferences databases, resulted in one eligible record (poster presentation). No reports or policy documents were eligible for inclusion. Lastly, we added 4 studies based on screening the references of studies we identified above via databases, and we obtained 1 study through the expert consultation, yielding a final sample of 26 included articles (21 records identified via databases and registers and 5 records identified via other methods such as citation searching and expert consultation). We illustrate the inclusion process in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (online supplemental figure S1).

We identified a total of 26 studies assessing intergenerational spillover effects of ART, including 25 articles which were published in scientific journals with quality assurance, and 1 poster presented at the 2012 International AIDS Conference.[71] In figure 1, we show the distribution of articles by year over the past 17 years. On the second y-axis, we show how the distribution of included articles relates to the scale-up of ART coverage in SSA during the same period (shown as the red line in the figure). The scale-up of ART was relatively smooth during the period covered by studies included in our review and includes the era of universal HIV testing and treatment which started in several countries in the mid-2010s. Despite substantial investments in ART coverage in SSA, the average number of articles assessing intergenerational

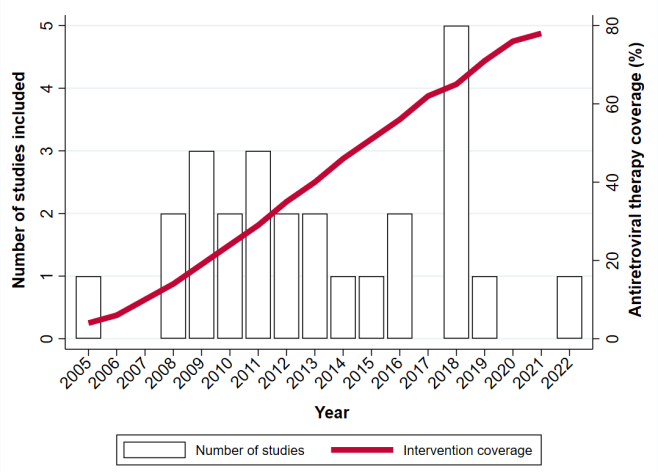

Figure 1 Number of studies and ART coverage in sub-Saharan Africa. Shows the distribution of included studies assessing intergenerational spillover effects and the scale-up of ART coverage (shown as red line) in sub-Saharan Africa by year. ART coverage was defined as the percentage of people living with HIV on ART. Source: data on ART coverage by year was extracted from http://aidsinfo.unaids.org.[41] ART, antiretroviral therapy.

spillover effects per year was about 1.5 articles per year, with a small increase in the late 2000s (2–3 articles per year) and then a decrease in the late 2010s (1–2 articles per year). The first article on intergenerational spillover effects was published in 2005 and assessed the potential influence of access to ART on demand for HIV testing services among household members in South Africa.[72] This study tested the hypothesis that availability of treatment may help motivate others to find out their HIV status.

Study designs, location and direction of intergenerational spillover effects of ART

In table 1 and online supplemental table S1–S6, we show selected characteristics of all studies, including study design and sample; direction, type, and the measurement of spillover effects; key findings as well as estimates of effect size. The vast majority of articles were quantitative (21 out of 26 studies), most of which used longitudinal[34 52 68 71 73–77] or quasi-experimental approaches.[34 63 64 68 69 78–80] Longitudinal approaches included, for instance, prospective cohort studies[73] and individual fixed effects regression models.[68 71] Quasi-experimental designs additionally included difference-in-differences models which exploited spatial and temporal variation in ART availability,[63] and a regression discontinuity design which used the CD4 count-based ART eligibility threshold to examine the impact of ART initiation among household members.[69] We identified one randomised controlled trial which examined the effect of universal HIV testing and treatment on economic outcomes of household members.[81] In figure 2, we map the number of articles by country in SSA. Most single-country studies were from Uganda, South Africa and Kenya, whereas four studies used multicountry data. The largest study used data on over 200 000 individuals from 28 countries.[52] No studies on spillover effects were identified from several high-burden countries such as Eswatini and Botswana, which have among the world's highest HIV prevalence. Over 90% of studies included at least some data from rural settings in SSA, such as rural KwaZulu Natal in South Africa.[69 71 74] Among the 26 included studies, 16 studies explicitly assessed spillover effects from adults to children (downward spillover effects)[34 35 63 64 68 69 76 77 79–86] and 1 study explicitly assessed spillover effects from working-age adults to older adults (upward spillover effects).[52] Several studies reported spillover effects without fully specifying the recipient of the spillover effect (eg, by grouping together all adult ages in their analytical sample), so that we cannot disentangle the direction of intergenerational spillover effects in those studies.[34 63 68 69 71–75 78 83 85–89] The types of spillover effects that emerged from our analysis were related to (1) wealth and labour market outcomes, (2) health and healthcare utilisation, (3) food security and nutrition, (4) schooling outcomes, (5) caregiving responsibilities, and, lastly, (6) coresidency and relationships. All studies measured spillover effects at the individual level, with the exception of two studies which measured spillover effects at the household level[87 89] and three studies which measured spillover effects at both the individual and household levels.[63 71 83]

Types of intergenerational spillover effects of ART

Wealth and labour market outcomes

Variables measured at individual level

The uptake of ART among people living with HIV had substantial economic benefits for their household and family members across several countries in SSA. In Malawi, an increase in ART availability, measured by the distance to an ART facility, increased the savings of household members of people living with HIV. For example, reducing the distance to an ART facility by 5.8 km could increase total savings by 50%.[63] ART also led to a redirection of expenditures from medical expenses for the treated individuals to general household expenses, benefiting all household members.[86] The availability of ART—as indicated by distance between the household and an ART facility—also led to an increase in employment and daily work time of household members who had not been diagnosed with HIV and who had formerly been involved in caregiving for people living with HIV in South Africa[71] and Malawi.[78] Consistent with these findings, higher CD4 counts among ART recipients also led to higher labour force participation of coresiding adults who were not living with HIV[88] and to equal employment outcomes between individuals who had not been diagnosed with HIV in ART

Table 1 Selected characteristics of studies included in review (N=26)

Characteristics	References	N (%)
Study design		
Qualitative	83 84 86 87 89	5 (19)
Modelling	82	1 (4)
Cross-sectional	35 72 85 88	4 (15)
Longitudinal and cohort	34 52 68 71 73–77	9 (35)
Quasi-experimental	34 63 64 68 69 71 78–80	9 (35)
Randomised controlled trial	81	1 (4)
Country		
Kenya	34 68 80	3 (12)
Malawi	63 78	2 (8)
South Africa	69 71 72 74 75	5 (19)
Uganda	35 73 76 77 83 84 86 87 89	9 (35)
Zambia	64 79 88	3 (12)
Multicountry	52 81 82 85	4 (15)
Urban or rural		
Urban	72 88	2 (8)
Rural	34 35 63 68 69 71 73 74 76–78 80 81 85–87	16 (62)
Both	52 64 75 79 82–84 89	8 (31)
Direction of spillover effect		
Downward	34 35 63 64 68 69 76 77 79–86	16 (62)
Upward	52	1 (4)
Not fully specified	34 63 68 69 71–75 78 83 85–89	16 (62)
Type of spillover effect		
Wealth and labour market outcomes	63 68 71 78 85 86 88 89	8 (31)
Health and healthcare utilisation	34 63 72–74 77 78	7 (27)
Food security and nutrition	69 79 80	3 (12)
Schooling outcomes	35 63 64 80 81 83	6 (23)
Caregiving responsibilities	34 75 84 86	4 (15)
Coresidence and relationships	52 76 77 82 83 87	6 (23)
Measurement of spillover effect		
Individual level	34 35 52 63 64 68 69 71–86 88	24 (92)
Household level	63 71 83 87 89	5 (19)

Shows key characteristics of all included studies (N=26). 'Downward' spillover effects were defined as spillover effects from parents or grandparents to their offspring, whereas 'upward' spillover effects were defined as spillover effects from children to their parents or grandparents. Some studies reported multiple (non-mutually exclusive) characteristics, so that the total number of studies (or percentage) in a category may add up to more than 26 studies (>100%).

and non-ART households.[85] In Kenya, male children coresiding with adults on ART also experienced a decrease in labour force participation.[68] These effects on the labour supply of children are important since they suggest, among other things, potential spillover effects on schooling outcomes (discussed in more detail below).

Variables measured at household level

ART also played an important role in household-level indicators of welfare, including household assets (eg, bed, car, cattle) and property ownership. In South Africa, ART prevented asset loss in households affected by HIV.[71] In Uganda, ART led to a regain of economic self-sufficiency among people living with HIV which generally decreased economic dependency on their household and family members.[89] ART did not, however, lead to a substantial regain of household assets that were sold following HIV infection (but prior to ART). People living with HIV who had sold assets after contracting HIV, reported that they

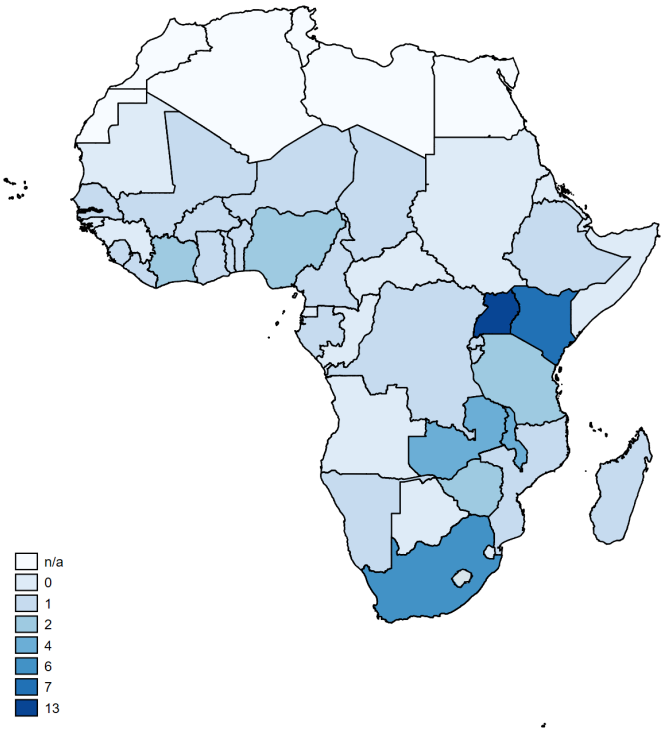

Figure 2 Map of number of studies identified by country. Shows the number of identified articles which assessed intergenerational spillover effects of antiretroviral therapy to household and family members, separately by country in sub-Saharan Africa. For multicountry studies, each country was considered individually. n/a, not applicable.

were unable to buy back these assets when they were on ART, including after their own health improved and returning to work.[89]

Health and healthcare utilisation

Variables measured at individual level

In Malawi, ART among people living with HIV increased the subjective life expectancy of individuals who had not been diagnosed with HIV through a reduction of perceived mortality risk.[63] Proximity to an ART facility also improved the mental health of individuals not living with HIV.[78] In Uganda, home-based ART programmes were associated with a reduction in mortality of 81% among children who had not been diagnosed with HIV.[77] Another study from Uganda examined the sexual behaviour of individuals not living with HIV but who were exposed to ART in their households. The study found that risky sexual behaviour decreased from 29% at baseline to 15% at 24 months.[73] These findings suggest that coresiding with non-spousal adults on ART was not associated with an increase in risky sexual behaviour (or 'behavioural disinhibition') due to ART derived from observing the positive impact of ART on the household index participant. In addition to health outcomes, ART also had spillover effects on healthcare utilisation among household and family members. In South Africa, knowing someone on ART, including family members, increased the likelihood to seek voluntary HIV counselling and testing among women, although this result did not reach conventional benchmarks for statistical significance among men.[72] In addition, ART affected other healthcare seeking behaviour (beyond HIV-related care) of individuals who had not been diagnosed with HIV. The scale-up of ART was associated with a decrease in hospitalisation and a shift from attending private to public sector healthcare.[74] In contrast, young men living in households with members taking ART were more likely to seek healthcare, which could either be a result of caregiving responsibilities for their household members diagnosed with HIV or because they themselves were in greater need for healthcare.[34]

Food security and nutrition

Variables measured at individual level

Food security, broadly defined as consistent access to enough food for an active, healthy life, is a common concern among people living with HIV and their households.[15] In South Africa, ART initiation initially caused a decrease in the probability of food security in the first year of ART, which subsequently diminished within 1–3 years after ART initiation.[69] Specifically, the probability of 'missing a meal' in the past month among adults and children coresiding with individuals living with HIV who had initiated ART increased by 15.2 and 8.9 percentage points, respectively. This initial increase applied to households with limited resources available and was attributed to a regain of appetite of the ART recipient and additional expenditures on HIV treatment, such as transportation costs to the clinics.[37 69] As the ART recipient was likely to regain employment over time, the probability of household food insecurity then decreased to 0 within 1–3 years. In Zambia, the expansion of ART availability also improved anthropometric measurements of children in a household with an adult diagnosed with HIV.[79] Children living in ART-exposed households had higher weight-for-age and weight-for-height. In Kenya, ART was associated with an increase in weight-for-age of 0.60 SD in 6 months and a reduction in the likelihood of extreme malnutrition among children under 5 years old.[80]

Schooling outcomes

Variables measured at individual level

The positive relationship between ART availability and improved schooling outcomes was consistent across several contexts and methodological approaches.[35 63 64 80 81 83] In a randomised controlled trial in Kenya, universal HIV testing and treatment increased primary school completion by 7% among children in households with adults diagnosed with HIV after 3 years of intervention.[81] In another Kenyan study, weekly hours of children's school attendance increased by over 20% within 6 months after ART initiation by the adult person living with HIV.[80] Similarly, in Malawi, ART availability increased expenditures on education and schooling outcomes, including among individuals not living with HIV who did not directly benefit from ART. Specifically, halving the distance of a household to an ART facility increased expenditures on

children's education by US$2.5 and increased years of schooling completed by 0.33. These results appeared to be not driven by the direct health effects of treatment or reductions in caregiving responsibilities, but rather by the reduced perception of mortality risk after ART became available.[63] In addition, in Zambia, the availability of ART increased the probability of being in the appropriate grade for age for primary school-aged children by nearly 50%.[64] These findings were confirmed in qualitative studies. Parents who reported that their children had dropped out of school since the parents' HIV diagnosis noted that these children had at least partially returned to school after ART initiation.[83]

Caregiving responsibilities

Variables measured at individual level

Several studies assessed the impact of ART on the time allocation of household members of an ART recipient.[34 75 84 86] In Kenya, adults living with HIV with poor health pursued fewer household chores, such as collecting firewood or water, while the children (aged 14–18 years) in their households now performed more household tasks instead.[34] Young men spent more time collecting firewood whereas young women spent more time collecting water. The differences in time allocation on household chores diminished over time, which was likely a result of ART leading to a recovery of health among the treated individual. Specifically, treatment initiation in ART households reduced the time spent on household chores among young men by 2.5 hours per week. Coresiding adults were also able to dedicate less time on caregiving support for sick household members and spend more time on other activities.[34] These results were supported by a South African cohort study which investigated the amount of assistance that individuals living with HIV received from their family members, as measured by 'instrumental activities of daily living', such as cooking, cleaning, washing and dressing self, taking medicines, walking around the house and going to other places. ART was associated with a large reduction in assistance with these activities (by up to 41% in the urban cohort) and likely reduced the caregiving responsibilities of household and family members of ART recipients.[75] Family members who had primarily been occupied by caregiving activities for the sick were now available to perform other activities, such as income-generating work.[86] ART also led to a shift in the type of caregiving responsibilities among family members. Children, for instance, now reminded their parents living with HIV to adhere to ART, accompanied them to clinical appointments, or provided their parents money to purchase medication, food, as well as housing.[84]

Coresidence and relationships

Variables measured at individual level

The HIV epidemic and availability of ART have influenced demographic and household structures for several generations in SSA.[50 52] For the younger generation, ART among adults living with HIV reduced the number of HIV-related orphans.[63 76 77 82] For the older generation, the availability of ART was associated with increased coresidence with working-age adults (aged 18–59 years).[52] In a multicountry study in SSA, including individual-level data on over 200 000 older adults aged 60 years or more, an increase in national ART coverage was associated with a higher number of working-age adults living in households with at least one older adult. An increase in ART coverage of 1% was associated with a 0.7 percentage point reduction in the probability of an older adult living without a working-age adult and a 0.2 percentage point reduction in the probability of an older adult living with only dependent children (ie, 'missing generation' households).[52] Conversely, in non-HIV-endemic countries in SSA, where the national roll-out of ART was unlikely to have affected the living conditions of older individuals, no significant relationship was found across several measures of living arrangements of older adults.

Variables measured at household level

People living with HIV also reported that the initiation of ART partially restored previously disrupted relationships at the household level.[83] In Uganda, people living with HIV reported improved social interactions after having commenced ART. Men living with HIV also reported that ART led to a recovery of 'masculine identities', improving the relationship between household members.[87] Prior to ART initiation, men had reported a loss of authority. For example, because men living with HIV had failed to provide for household members by not working and instead depended on the resources of others. However, since starting ART, men living with HIV engaged in productive activities again that brought income to the household, regained their original provider roles and restored their respectability in the domestic sphere.

DISCUSSION

We systematically reviewed the published and grey literature and identified 26 studies that report on intergenerational spillover effects of ART among individuals who are indirectly affected by ART based on their coresidence or affiliation with an ART recipient in SSA. We identified fewer than two studies per year over more than 15 years of HIV research suggesting that the focus of research efforts has largely remained on the impact of ART on the treated individual (figure 1). Out of 26 included studies, most studies assessed intergenerational spillover effects from adults to children (downward spillover effects) or did not specify the recipient of spillover effects (table 1). Even though coresidence with older adults is common in SSA, spillover effects to older adults were relatively understudied (upward spillover effects). Only 1 out of 26 studies explicitly assessed upward spillover effects of ART.[52] In terms of types of spillover effects, ART affected the economic situation and labour market participation,[63 68 71 78 85 86 88 89] health and healthcare seeking

Box 1 Research areas for assessing intergenerational spillovers of antiretroviral therapy (ART)

- ⇒ ART has substantially increased life expectancy in sub-Saharan Africa, but little remains known about its impact on household and family members.
- ⇒ Greater clarity is warranted in disentangling the relationship between the recipient of the treatment (index case) and the recipient of the spillover effect.
- ⇒ Only one study was identified which explicitly assessed spillover effects of ART from working-age adults to older adults ('upward' spillover effects).
- ⇒ Few studies clearly defined ART, such as treatment duration, treatment response, and time between treatment and the observed spillover effect.
- ⇒ More research is needed to identify possible strategies to capitalise on positive spillover effects while mitigating potential negative spillover effects.
- ⇒ No studies assessed intergenerational spillover effects of ART in countries with the world's highest HIV prevalence (eg, Botswana and Eswatini).
- ⇒ There is a need to quantify the economic value of spillover effects of ART to household and family members to inform cost–benefit analyses.

behaviour,[34 63 72–74 77 78] nutrition and food security,[69 79 80] schooling outcomes,[35 63 64 80 81 83] and caregiving responsibilities of household and family members.[34 75 84 86] In addition, ART affected household composition and the relationship between household members.[52 76 77 82 83 87]

The most common source of spillover effects was likely rooted in improved health conditions of the treated individual and a subsequent improvement in the individual's economic outcomes. The recovery of health following treatment led to more economic resources in households[63] and a reallocation of time of household members.[34] Less caregiving responsibilities for sick household members allowed coresiding children to perform less domestic[34] and income generating work[68] whereas coresiding adults were able to increase their labour participation.[26 78 85 88] Household expenditures were redirected from health-related costs (such as clinic stays and transportation to the health facilities) to other household expenses.[86] Treatment also increased household income and savings, including the prevention of further asset loss.[63 71] In turn, improvements to the household's economic situation were a likely source of further beneficial spillover effects downstream, such as reduced children's malnutrition[79 80] as well as increased expenditures on education,[63] with substantial benefits for schooling outcomes of children.[35 64 80 81 83] ART also led to important changes in demographic and household structures, with fewer orphans[76 77 82] and increases in coresidence with older adults.[52] These changes likely increased support from working-age adults for coresiding dependent younger children and older adults. The availability of ART also improved subjective life expectancy and mental health, which may have further contributed to additional savings and investments in human capital.[63 78]

In addition to beneficial spillover effects, we also identified several potential negative spillover effects. Not all caregiving responsibilities among household members, for instance, were eliminated with the initiation of ART.[86] ART does not restore health immediately and necessarily completely, so that ART recipients may remain dependent on some form of household support. The initiation of ART comes with possible constraints such as adherence to therapy (eg, taking medication and attending hospital appointments),[90] regular clinic visits and consequent financial costs (eg, transportation costs to and from health facilities and time losses associated with healthcare utilisation).[37] Out-of-pocket payments and time losses due to ART could amount cumulatively to large sums as treatment is taken lifelong. Family members continued to play an important role in households with individuals on ART, reminding them to adhere to treatment and providing substantial resources such as money, food, as well as housing.[84] Similarly, in South Africa, ART initially increased household food insecurity, which was likely a result of recovery of appetite among people living with HIV or the use of household resources to cover treatment expenses.[69] Our review supports the hypothesis of 'therapeutic citizenship', whereby household members contribute to treatment adherence among people living with HIV.[90]

This review brings together a wide variety of studies using a systematic search strategy and provides a broad overview of the existing evidence. Nevertheless, it has limitations. First, few studies specified the direction of spillover effects between the treatment recipient and recipient of spillover effects. While most studies differentiated between adults and children,[35 63 64 80 81 83] many studies pooled all adult ages in their analytical samples making it difficult to distinguish spillover effects from working-age adults to older adults (upward spillover effects) and spillover effects between partners, spouses or siblings (horizontal spillover effects).[34 63 68 69 71–75 78 83 85–89] Second, studies measured spillover effects in different ways. For example, while some studies take the treated individual (or 'index case') as the unit of analysis,[83] other studies take the recipient of spillover effects as the unit of analysis.[52] Spillover effects can also be measured at the individual or household level. Estimates from measurements at the household level may be difficult to distinguish between the contribution of effects that may be in part direct (a direct effect on the individual undergoing ART) and effects that are 'purely' spillover effects to household members. Third, the purpose of this scoping review was not to assess the quality of included studies or risk of bias but rather to map the existing evidence on spillover effects of ART in SSA and identify gaps for future research.[54] Fourth, as with all literature searches, there is a risk of publication bias. Studies on intergenerational spillover effects of health interventions may be prone to publication bias because spillover effects have

a low perceived prior probability and unexpected findings with large or statistically significant effects may be more appealing to publish. Few included studies on spillover effects explicitly reported null results as their main finding (online supplemental table S1–S6).[68 73] Fifth, our focus on intergenerational spillover effects may underestimate the overall societal impact of investments in ART which would include all other spillover effects but which were beyond the scope of the current review.[91] Similarly, beneficial effects of ART and better population health on other societal outcomes such as regional or national-level political stability and crime were not considered in this review.[92]

Implications for future research and policy

Our findings have several implications for future research and policy (box 1). First, despite the substantial scale-up of ART, few studies have examined its broader societal effects. Possible reasons for this finding is that the identification of causal effects across generations is methodologically complex and spans several life periods which are frequently investigated independently of each other.[93] Second, as noted above, most of the identified studies in our review did not fully specify the recipient of spillover effects (age group or relationship to the treatment recipient) precluding conclusions on the direction of spillover effects. Greater clarity in defining and measuring spillover effects of ART may further reduce conceptual ambiguity. Similarly, future studies could differentiate between spillover effects to household members (intra-household spillover effects) and spillover effects to family members living in different households. Third, among studies which indicated the direction of spillover effects, most studies investigated spillover effects from adults to children (downward spillover effects). However, little is known about potential spillover effects from working-age adults to older adults (upward spillover effects).[62] The older population in SSA is projected to grow with >3% each year between 2022 and 2050 and there will be an increasing need for old-age support.[94] Evidence from Asia, for instance, suggests substantial upward spillover effects of ART to the older generation.[51] Fourth, no studies on spillover effects were identified from countries with a large HIV burden, such as Botswana and Eswatini. ART is likely to have large intergenerational spillovers in these countries. Fifth, we identified only one randomised controlled trial.[81] More research is needed to identify potential causal spillover effects of health interventions. Future research could also identify causal mechanisms to capitalise on the positive spillover effects of treatment while mitigating potential negative spillover effects. Sixth, our review revealed a wide range of spillover effects which are relevant for several non-health sectors, including economic opportunity, food security, education and changes in household composition. One implication of these results is that health investments such as ART have the potential to generate large economic returns, including in sectors other than health and in the form of better health and economic outcomes for future generations. As a result, empirical analyses of spillover effects of ART are needed to estimate the total economic returns and inform cost–benefit analyses of investments in ART.[8 70] Seventh, information on the benefits of ART programmes is critical to inform budgets and health policy. Global health organisations are scaling down on HIV funding and there has been an increasing transition away from HIV.[38] The spillover effects of ART may further justify ongoing investments in ART.

CONCLUSIONS

ART may have large spillover effects on household and family members of treated individuals in SSA. We document substantial spillover effects of ART across several generations and health as well as non-health sectors. Further qualitative, longitudinal and (quasi-)experimental research is warranted to capitalise on these beneficial spillover effects while mitigating potential negative spillover effects. The returns to investments in large-scale health interventions such as ART may be underestimated without considering these broader societal benefits.

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REFERENCES

1 The World Bank Group. Life expectancy at birth, total (years). 2022. Available: https://data.worldbank.org/indicator/SP.DYN.LE00.IN [Accessed 21 Aug 2022].
2 Aminov RI. A brief history of the antibiotic era: lessons learned and challenges for the future. *Front Microbiol* 2010;1:134.
3 Aaby P, Benn CS, Flanagan KL, *et al*. The non-specific and sex-differential effects of vaccines. *Nat Rev Immunol* 2020;20:464–70.
4 Akachi Y, Steenland M, Fink G. Associations between key intervention coverage and child mortality: an analysis of 241 sub-national regions of sub-Saharan Africa. *Int J Epidemiol* 2018;47:740–51.
5 Nalin DR, Cash RA. 50 years of oral rehydration therapy: the solution is still simple. *Lancet* 2018;392:536–8.
6 Haller L, Hutton G, Bartram J. Estimating the costs and health benefits of water and sanitation improvements at global level. *J Water Health* 2007;5:467–80.
7 Curtis V, Schmidt W, Luby S, *et al*. Hygiene: new hopes, new horizons. *Lancet Infect Dis* 2011;11:312–21.
8 De Neve J-W, Andriantavison RL, Croke K, *et al*. Health, financial, and education gains of investing in preventive chemotherapy for schistosomiasis, soil-transmitted helminthiases, and lymphatic filariasis in madagascar: a modeling study. *PLOS Negl Trop Dis* 2018;12:e0007002.
9 Tanser F, Bärnighausen T, Grapsa E, *et al*. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science* 2013;339:966–71.
10 Chigwedere P, Seage GR, Lee T-H, *et al*. Efficacy of antiretroviral drugs in reducing mother-to-child transmission of HIV in Africa: a meta-analysis of published clinical trials. *AIDS Res Hum Retroviruses* 2008;24:827–37.
11 Jia Z, Mao Y, Zhang F, *et al*. Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003-11): a national observational cohort study. *Lancet* 2013;382:1195–203.
12 Kombe G, Fieno J, Bhatt P, *et al*. Highly active anti-retroviral treatment as a bridge towards education for all in sub-Saharan Africa. *Int Social Science J* 2005;57:609–20.
13 Risley CL, Drake LJ, Bundy DAP. Economic impact of HIV and antiretroviral therapy on education supply in high prevalence regions. *PLoS One* 2012;7:e42909.
14 Palar K, Wagner G, Ghosh-Dastidar B, *et al*. Role of antiretroviral therapy in improving food security among patients initiating HIV treatment and care. *AIDS* 2012;26:2375–81.
15 Weiser SD, Gupta R, Tsai AC, *et al*. Changes in food insecurity, nutritional status, and physical health status after antiretroviral therapy initiation in rural Uganda. *J Acquir Immune Defic Syndr* 2012;61:179–86.
16 Weiser SD, Palar K, Frongillo EA, *et al*. Longitudinal assessment of associations between food insecurity, antiretroviral adherence and HIV treatment outcomes in rural Uganda. *AIDS* 2014;28:115–20.
17 Beard J, Feeley F, Rosen S. Economic and quality of life outcomes of antiretroviral therapy for HIV/AIDS in developing countries: a systematic literature review. *AIDS Care* 2009;21:1343–56.
18 Chhagan V, Luiz J, Mohapi L, *et al*. The socioeconomic impact of antiretroviral treatment on individuals in Soweto, South Africa. *Health Sociology Review* 2008;17:95–105.
19 Kimou JCA, d'Ivoire C, Kouakou CK, *et al*. A review of the socioeconomic impact of antiretroviral therapy on family wellbeing. 2008. Available: https://hsrc.ac.za/uploads/pageContent/1271/Areviewofthesocioeconomicimpactofantiretrivaltherapyonfamilywellbing.pdf [Accessed 28 Feb 2023].
20 Resch S, Korenromp E, Stover J, *et al*. Economic returns to investment in AIDS treatment in low and middle income countries. *PLoS One* 2011;6:e25310.
21 Rosen S, Larson B, Brennan A, *et al*. Economic outcomes of patients receiving antiretroviral therapy for HIV/AIDS in South Africa are sustained through three years on treatment. *PLoS One* 2010;5:e12731.
22 Rosen S, Larson B, Rohr J, *et al*. Effect of antiretroviral therapy on patients' economic well being: five-year follow-up. *AIDS* 2014;28:417–24.
23 Steinert JI, Khan S, Mlambo K, *et al*. A stepped-wedge randomised trial on the impact of early ART initiation on HIV-patients' economic outcomes in Eswatini. *Elife* 2020;9:e58487.
24 Thirumurthy H, Galárraga O, Larson B, *et al*. HIV treatment produces economic returns through increased work and education, and warrants continued us support. *Health Aff (Millwood)* 2012;31:1470–7.
25 Venkataramani AS, Thirumurthy H, Haberer JE, *et al*. CD4+ cell count at antiretroviral therapy initiation and economic restoration in rural Uganda. *AIDS* 2014;28:1221–6.
26 Bor J, Tanser F, Newell M-L, *et al*. In a study of a population cohort in South Africa, HIV patients on antiretrovirals had nearly full recovery of employment. *Health Aff (Millwood)* 2012;31:1459–69.
27 McLaren Z. The effect of access to AIDS treatment on employment outcomes in South Africa. Baltimore, MD University of Maryland, Baltimore County; 2017. Available: https://mdsoar.org/handle/11603/23511 [Accessed 02 Mar 2023].
28 Coetzee C. The impact of highly active antiretroviral treatment (HAART) on employment in Khayelitsha. *S Afr J Econ* 2008;76:S75–85.
29 French D, Brink J, Bärnighausen T. Early HIV treatment and labour outcomes: a case study of mining workers in South Africa. *Health Econ* 2019;28:204–18.
30 Habyarimana J, Mbakile B, Pop-Eleches C. The impact of HIV/AIDS and ARV treatment on worker absenteeism: implications for African firms. *J Hum Resour* 2010;45:809–39.
31 Larson BA, Fox MP, Rosen S, *et al*. Early effects of antiretroviral therapy on work performance: preliminary results from a cohort study of Kenyan agricultural workers. *AIDS* 2008;22:421–5.
32 Thirumurthy H, Zivin JG. Health and labor supply in the context of HIV/AIDS: the long-run economic impacts on antiretroviral therapy. *Econ Dev Cult Change* 2012;61:73–96.
33 Wagner Z, Barofsky J, Sood N. PEPFAR funding associated with an increase in employment among males in ten sub-Saharan African countries. *Health Aff (Millwood)* 2015;34:946–53.
34 d'Adda G, Goldstein M, Zivin JG, *et al*. ARV treatment and time allocation to household tasks: evidence from Kenya. *Afr Dev Rev* 2009;21:180–208.
35 Thirumurthy H, Chamie G, Jain V, *et al*. Improved employment and education outcomes in households of HIV-infected adults with high CD4 cell counts: evidence from a community health campaign in Uganda. *AIDS* 2013;27:627–34.
36 Skovdal M, Ogutu VO. "I washed and fed my mother before going to school": understanding the psychosocial well-being of children

providing chronic care for adults affected by HIV/AIDS in Western Kenya. *Global Health* 2009;5:8.
37 Chimbindi N, Bor J, Newell M-L, *et al*. Time and money: the true costs of health care utilization for patients receiving "free" HIV/tuberculosis care and treatment in rural Kwazulu-natal. *J Acquir Immune Defic Syndr* 2015;70:e52–60.
38 Dieleman JL, Haakenstad A, Micah A, *et al*. Spending on health and HIV/AIDS: domestic health spending and development assistance in 188 countries, 1995-2015. *Lancet* 2018;391:1799–829.
39 UNAIDS. UNAIDS: financial estimates. 2022. Available: https://hivfinancial.unaids.org/hivfinancialdashboards.html# [Accessed 21 Aug 2022].
40 UNAIDS. Global HIV & AIDS statistics — fact sheet. 2022. Available: https://www.unaids.org/en/resources/fact-sheet [Accessed 31 Aug 2022].
41 UNAIDS. AIDSinfo: global data on HIV epidemiology and response. 2022. Available: https://aidsinfo.unaids.org/ [Accessed 21 Aug 2022].
42 Bor J, Herbst AJ, Newell M-L, *et al*. Increases in adult life expectancy in rural south africa: valuing the scale-up of HIV treatment. *Science* 2013;339:961–5.
43 Payne CF, Kohler H-P. The population-level impact of public-sector antiretroviral therapy rollout on adult mortality in rural Malawi. *Demogr Res* 2017;36:1081–108.
44 Sabin CA. Do people with HIV infection have a normal life expectancy in the era of combination antiretroviral therapy? *BMC Med* 2013;11:1–7.
45 Burger C, Burger R, van Doorslaer E. The health impact of free access to antiretroviral therapy in South Africa. *Soc Sci Med* 2022;299:114832.
46 Forsythe SS, McGreevey W, Whiteside A, *et al*. Twenty years of antiretroviral therapy for people living with HIV: global costs, health achievements, economic benefits. *Health Aff (Millwood)* 2019;38:1163–72.
47 UNAIDS. Feature story: learning lessons from the AIDS response to control NCDs. 2018. Available: https://www.unaids.org/en/resources/presscentre/featurestories/2018/september/learning-lessons-from-the-aids-response-to-control-ncds [Accessed 21 Aug 2022].
48 Bor J, Bärnighausen T, Newell C, *et al*. Social exposure to an antiretroviral treatment programme in rural KwaZulu-Natal. *Trop Med Int Health* 2011;16:988–94.
49 Monasch R, Boerma JT. Orphanhood and childcare patterns in sub-Saharan Africa: an analysis of national surveys from 40 countries. *AIDS* 2004;18 Suppl 2:S55–65.
50 Kautz T, Bendavid E, Bhattacharya J, *et al*. AIDS and declining support for dependent elderly people in Africa: retrospective analysis using demographic and health surveys. *BMJ* 2010;340:c2841.
51 Knodel J. Poverty and the impact of AIDS on older persons: evidence from Cambodia and Thailand. *Econ Dev Cult Change* 2008;56:441–75.
52 De Neve J-W, Karlsson O, Coetzee L, *et al*. Antiretroviral therapy coverage associated with increased co-residence between older and working-age adults in Africa. *AIDS* 2018;32:2051–7.
53 Schatz E, Seeley J. Gender, ageing and carework in East and Southern Africa: a review. *Glob Public Health* 2015;10:1185–200.
54 Munn Z, Peters MDJ, Stern C, *et al*. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol* 2018;18:143.
55 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
56 Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci* 2010;5:69.
57 Peters MDJ, Godfrey CM, Khalil H, *et al*. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc* 2015;13:141–6.
58 Bryman A, Burgess RG. *Qualitative data analysis for applied policy research. Analyzing qualitative data*. Routledge, 1994: 173–94.
59 Oliver DS. Making research more useful: integrating different perspectives. In: *Using research for effective health promotion*. 2001: 167.
60 Munn Z, Stern C, Aromataris E, *et al*. What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. *BMC Med Res Methodol* 2018;18:5.
61 Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for scoping reviews (PRISMA-scr): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
62 De Neve J-W, Kawachi I. Spillovers between siblings and from offspring to parents are understudied: a review and future directions for research. *Soc Sci Med* 2017;183:56–61.
63 Baranov V, Kohler H-P. The impact of AIDS treatment on savings and human capital investment in Malawi. *Am Econ J Appl Econ* 2018;10:266–306.
64 Lucas AM, Chidothe M, Wilson NL. Effects of adult health interventions at scale on children's schooling: evidence from antiretroviral therapy in Zambia. *Economics of Education Review* 2019;72:107–20.
65 Barbieri M, Hertrich V. Écarts d'âge entre conjoints et pratique contraceptive en afrique sub-saharienne. *Population (Paris)* 2005;60:725.
66 Kohler IV, Kohler H-P, Anglewicz P, *et al*. Intergenerational transfers in the era of HIV/AIDS: evidence from rural Malawi. *Demogr Res* 2012;27:775–834.
67 Payne CF, Pesando LM, Kohler HP. Private intergenerational transfers, family structure, and health in a sub-Saharan African context. *Popul Dev Rev* 2019;45:41–80.
68 Thirumurthy H, Zivin JG, Goldstein M. The economic impact of AIDS treatment: labor supply in Western Kenya. *J Hum Resour* 2008;43:511–52.
69 Patenaude BN, Chimbindi N, Pillay D, *et al*. The impact of ART initiation on household food security over time. *Soc Sci Med* 2018;198:175–84.
70 Verguet S, Kim JJ, Jamison DT. Extended cost-effectiveness analysis for health policy assessment: a tutorial. *Pharmacoeconomics* 2016;34:913–23.
71 Bor J, Tanser F, Newell M-L, *et al*. Economic spillover effects of HIV treatment on rural south african households. In: *XIX International AIDS Conference*. Washington D C, 2012.
72 Mfundisi C, Chiranjan N, Rodrigues C, *et al*. Availability of antiretroviral therapy is associated with increased uptake of HIV testing services. *S Afr Med J* 2005;95:483–5.
73 Bechange S, Bunnell R, Awor A, *et al*. Two-year follow-up of sexual behavior among HIV-uninfected household members of adults taking antiretroviral therapy in Uganda: no evidence of disinhibition. *AIDS Behav* 2010;14:816–23.
74 Hontelez JAC, Tanser FC, Naidu KK, *et al*. The effect of antiretroviral treatment on health care utilization in rural South Africa: a population-based cohort study. *PLoS One* 2016;11:e0158015.
75 Kakinami L, de Bruyn G, Pronyk P, *et al*. The impact of highly active antiretroviral therapy on activities of daily living in HIV-infected adults in South Africa. *AIDS Behav* 2011;15:823–31.
76 Makumbi FE, Nakigozi G, Sekasanvu J, *et al*. Incidence of orphanhood before and after implementation of a HIV care programme in Rakai, Uganda: alpha network HIV supplement. *Trop Med Int Health* 2012;17:e94–102.
77 Mermin J, Were W, Ekwaru JP, *et al*. Mortality in HIV-infected Ugandan adults receiving antiretroviral treatment and survival of their HIV-uninfected children: a prospective cohort study. *Lancet* 2008;371:752–9.
78 Baranov V, Bennett D, Kohler HP. The indirect impact of antiretroviral therapy: mortality risk, mental health, and HIV-negative labor supply. *J Health Econ* 2015;44:195–211.
79 Lucas AM, Wilson NL. Adult antiretroviral therapy and child health: evidence from scale-up in Zambia. *Am Econ Rev* 2013;103:456–61.
80 Zivin JG, Thirumurthy H, Goldstein M. AIDS treatment and intrahousehold resource allocation: children's nutrition and schooling in Kenya. *J Public Econ* 2009;93:1008–15.
81 Jakubowski A, Kabami J, Balzer LB, *et al*. Effect of universal HIV testing and treatment on socioeconomic wellbeing in rural Kenya and Uganda: a cluster-randomised controlled trial. *Lancet Glob Health* 2022;10:e96–104.
82 Anema A, Au-Yeung CG, Joffres M, *et al*. Estimating the impact of expanded access to antiretroviral therapy on maternal, paternal and double orphans in sub-Saharan Africa, 2009-2020. *AIDS Res Ther* 2011;8:1–8.
83 Wagner G, Ryan G, Huynh A, *et al*. A qualitative exploration of the impact of HIV and ART on social disruption and household continuity in Uganda. *Afr J AIDS Res* 2011;10:37–42.
84 Nalugya R, Russell S, Zalwango F, *et al*. The role of children in their HIV-positive parents' management of antiretroviral therapy in Uganda. *Afr J AIDS Res* 2018;17:37–46.
85 Jakubowski A, Snyman K, Kwarisiima D, *et al*. High CD4 counts associated with better economic outcomes for HIV-positive adults and their HIV-negative household members in the search trial. *PLoS One* 2018;13:e0198912.
86 Kaler A, Alibhai A, Kipp W, *et al*. "Living by the hoe" in the age of treatment: perceptions of household well-being after antiretroviral treatment among family members of persons with AIDS. *AIDS Care* 2010;22:509–19.
87 Siu GE, Wight D, Seeley J. "Dented" and "resuscitated" masculinities: the impact of HIV diagnosis and/or enrolment on

antiretroviral treatment on masculine identities in rural Eastern Uganda. *SAHARA J* 2014;11:211–21.
88 Tirivayi N, Koethe JR. The economic benefits of high CD4 counts among people living with HIV/AIDS in Zambia. *J Public Health (Oxf)* 2016;38:704–11.
89 Wagner G, Ryan G, Huynh A, *et al*. A qualitative analysis of the economic impact of HIV and antiretroviral therapy on individuals and households in Uganda. *AIDS Patient Care STDS* 2009;23:793–8.
90 Nguyen V-K, Ako CY, Niamba P, *et al*. Adherence as therapeutic citizenship: impact of the history of access to antiretroviral drugs on adherence to treatment. *AIDS* 2007;21 Suppl 5:S31–5.
91 Cohen MS, Chen YQ, McCauley M, *et al*. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011;365:493–505.
92 Berlanda A, Cervellati M, Esposito E, *et al*. Medication against conflict. *SSRN Journal* 2022.
93 Kuh D, Ben-Shlomo Y, Lynch J, *et al*. Life course epidemiology. *J Epidemiol Community Health* 2003;57:778–83.
94 United Nations, Department of Economic and Social Affairs Population Division. World population prospects 2022: summary of results 2022. 2022. Available: https://population.un.org/wpp/Publications/ [Accessed 22 Aug 2022].