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SUBSTANTIVE REVIEW

Impact of Geographic and Transportation-Related Barriers on HIV Outcomes in Sub-Saharan Africa: A Systematic Review

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Abstract Difficulty obtaining reliable transportation to clinic is frequently cited as a barrier to HIV care in sub-Saharan Africa (SSA). Numerous studies have sought to characterize the impact of geographic and transportation-related barriers on HIV outcomes in SSA, but to date there has been no systematic attempt to summarize these findings. In this systematic review, we summarized this body of literature. We searched for studies conducted in SSA examining the following outcomes in the HIV care continuum: (1) voluntary counseling and testing, (2) pre-antiretroviral therapy (ART) linkage to care, (3) loss to follow-up and mortality, and (4) ART adherence and/or viral suppression. We identified 34 studies containing 52 unique estimates of association between a geographic or transportation-related barrier and an HIV outcome. There was an inverse effect in 23 estimates (44 %), a null association in 26 (50 %), and a paradoxical beneficial impact in 3 (6 %). We conclude that geographic and transportation-related barriers are associated with poor outcomes across the continuum of HIV care.

Resúmen Las dificultades para obtener un transporte confiable a la clínica son frecuentemente citadas como una barrera para la atención del VIH en el África subsahariana; sin embargo, la magnitud de este efecto es desconocido. En esta reseña sistemática, resumimos la literatura sobre el impacto de las barreras geográficas y de transporte en los resultados relacionados con el VIH en el África subsahariana. Se buscaron estudios realizados en el África subsahariana examinando los siguientes resultados en el continuo de la atención del VIH: 1) asesoramiento y pruebas voluntarias, 2) vinculo a los servicios antes de empezar el tratamiento antirretroviral (ART), 3) pérdida en el seguimiento y la mortalidad, y 4) adherencia al ART y/o la supresión viral. Se identificaron 34 estudios que contienen 52 estimaciones únicas de asociación entre una barrera geográfica o relacionados al transporte y el resultado de VIH. Se produjo un efecto adverso en 23 estimaciones (44 %), una asociación nula en 26 (50 %), y un impacto paradójico beneficioso en 3 (6 %). Se concluyó que las barreras geográficas y relacionadas con el transporte están asociadas con resultados pobres de todo el continuo de la atención del VIH.

Keywords Transportation barriers · Linkage to care · Retention in care · Adherence · Sub-Saharan Africa

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Introduction

Early treatment of HIV infection with combination antiretroviral therapy (ART) improves health outcomes in infected individuals and reduces transmission [1–4]. Many public health experts advocate for expanding treatment provision through a "test and treat" strategy [5, 6], in which HIV-infected individuals are offered ART regardless of clinical status. Such policies have had beneficial impacts on HIV-related outcomes in resource-rich settings [7]. Yet despite the dramatic expansion of ART in sub-Saharan Africa (SSA) during the last decade [8], the mortality rate in this region continues to exceed that in resource-rich settings [9–13]. In SSA, late presentation to care [14], treatment refusal despite eligibility [15], low rates of pre-ART linkage to care [16, 17], high rates of attrition [18, 19], and interrupted treatment [20] all contribute to poor outcomes and hinder scale-up efforts.

The success of a "test and treat" strategy in SSA will depend on thoughtful consideration of the structural barriers that impede the ability of HIV-infected individuals to get tested, link to HIV care, stay in care, and adhere to ART. "Voltage drops" [21] may occur along the continuum of care, leading to diminishing numbers getting tested, successfully linking to and remaining in care, and achieving sustained adherence to ART. Qualitative studies have found that patients in the region frequently cite difficulty obtaining reliable transportation to clinic as a reason for treatment default, poor ART adherence, and other adverse health outcomes [22–24]. We hypothesized that the presence of geographic and transportation-related barriers would be associated with unfavorable outcomes at all points along the continuum of HIV care, and that this effect would be observed across different sub-continental regions, time periods, and study populations. Guided by these hypotheses, we conducted this review to systematically assess the extent to which—and in what manner—geographic and transportation-related barriers affect HIV outcomes in SSA.

Methods

Search Strategy

All procedures were performed according to the PRISMA guidelines [25]. We searched PubMed and Web of Science for manuscripts that were published prior to August 2011, using title and abstract key words to identify studies that examined associations between geographic or transportation-related barriers and HIV outcomes in SSA (for search terms, see Appendix). We used the "Find Duplicates" function in EndNote X4 (Thomson Reuters, New York, NY, USA) to identify and eliminate duplicates. In addition, we manually searched all abstracts from the International Conference on HIV Treatment and Prevention Adherence of the International Association of Physicians in AIDS Care [now International Association of Providers of AIDS Care (IAPAC)] from 2002–2004 and from 2006–2011.

Study Selection and Eligibility Criteria

Two investigators (AJL and MJS), working independently and in duplicate, screened the first 150 abstracts. Agreement on the selection of studies for full-text review was acceptable ($k = 0.74$), so a single investigator (AJL) completed the remainder of the screening. After the initial screening of abstracts, a single investigator (AJL) obtained full-text journal articles for all records to select studies for inclusion in the final review. We searched PubMed and Google Scholar to identify IAPAC abstracts that had been subsequently published as full-length manuscripts. IAPAC abstracts that had not been subsequently published were also considered for inclusion in the final review. We included all identified manuscripts that were the result of original research that was based at least partially in SSA, described a study population that was either predominantly HIV-infected or prescribed ART for other reasons (e.g. post-exposure prophylaxis), and reported data relating to one of the following four outcomes of interest: (1) voluntary counseling and testing (VCT), (2) pre-ART linkage to care (as defined by Govindasamy et al. [26]), (3) loss to follow-up (LTFU) and/or mortality, and (4) ART adherence and/or viral suppression. Additionally, studies were categorized as eligible during a second round of screening if they described a relationship between at least one of these outcomes and a geographic or transportation-related exposure variable: (1) travel distance, (2) travel time, (3) transportation cost, or (4) rural versus urban setting. In cases where the manuscript or IAPAC abstract contained insufficient information to evaluate estimates of geographic or transportation-related barriers, we contacted the authors to obtain additional information. We also included a limited number of manuscripts and abstracts that were recommended by experts in the field but not identified in our systematic search. There were no language exclusion criteria. In the final compilation of reviewed manuscripts, we only included studies that were conducted in SSA, where the substantial majority of the world's HIV-infected population resides [8], in order to maintain generalizability of our findings to this region.

Data Extraction

Using a standardized extraction form, data from all eligible studies were extracted by a single investigator (AJL). An

initial attempt was made to aggregate study results for meta-analysis; however, substantial heterogeneity in the definition and measurement of study exposures and outcomes precluded this. Therefore, we proceeded with a systematic review. Beyond these quantitative studies, we sorted identified manuscripts into two additional categories of studies—(1) *descriptive*, and (2) *qualitative*. These studies were deemed to be important to understanding the geographic and transportation-related barriers to HIV care, but did not report an inferential statistical relationship. Manuscripts in these categories met all other inclusion criteria and were identified during the same systematic search process. We defined as *descriptive* any study that reported a proportion of respondents indicating a geographic or transportation-related factor to be a barrier to HIV care, but that did *not* estimate an association between this exposure and one of our outcomes of interest. If the authors estimated an association, the study was defined as *quantitative*. We defined as *qualitative* any study that reported general themes regarding geographic or transportation-related barriers to HIV care, but did not report specific proportions.

Data Analysis

In our primary analysis, we examined all eligible *quantitative* studies. One study [27] did not report data in the form of an odds ratio (OR); therefore, we calculated an OR using the data that were presented. Using author-provided definitions, we considered shorter distance, shorter travel time, lower transportation cost, and urban (versus rural) residence as the referent categories. Each estimate of association was categorized as an inverse effect (i.e. increasing distance, time, cost, or rural location was associated with *worsened* HIV outcomes such as lower rate of VCT completion, linkage, or adherence; or, greater rate of LTFU or mortality), a null effect, or a positive effect (i.e. increasing distance, time, cost, or rural location was associated with *improved* HIV outcomes such as higher rate of VCT completion, linkage, or adherence; or, lower rate of LTFU or mortality).

We summarized the percentage of studies demonstrating an inverse, null, or positive effect when categorized by study-level variables such as sub-continental region (Eastern Africa, Southern Africa, or Western Africa) as defined by the United Nations (UN); study population [HIV-infected adults, HIV-infected children, HIV/tuberculosis (TB) co-infected individuals receiving anti-TB therapy, or pregnant women receiving services for the prevention of maternal to child transmission of HIV (PMTCT)]; and study time period (pre–2003, 2003–2006, or post–2006). The study time period date ranges were selected based on 2003 being the initial year of the President's Emergency Plan for AIDS Relief, and 2006 being the year in which member states at the UN High Level Meeting on AIDS resolved to scale up access to HIV care with a goal of universal access by 2010.

Assessment of Study Quality

For studies reporting a statistical association between a geographic or transportation-related barrier and an HIV outcome, we designed an assessment tool that accounted for seven parameters within the following four domains: (1) study design and population, (2) exposure measurement, (3) outcome measurement, and (4) data analysis.

Results

Study Selection

We identified 1,008 full-length manuscripts and 763 conference abstracts during our initial search. After excluding 1,487 records on the basis of the initial screen, we reviewed 273 full-length, published manuscripts and 11 IAPAC abstracts that had not yet been published as manuscripts. We also included six studies identified outside of our systematic screening protocol. A total of 66 studies were included in our review: 29 quantitative studies, 17 descriptive studies, 15 qualitative studies, and five studies that contained both descriptive/qualitative and quantitative data (Fig. 1). All studies included in the final review were conducted exclusively in SSA. Excluding two qualitative studies that did not report the number of participants, and accounting for studies that included more than one type of data, these studies involved 131,325 participants from 15 different countries in SSA.

Study Characteristics: Descriptive Studies

In the descriptive studies (Table 1 [28–48]), participants commonly indicated geographic and transportation-related barriers as factors that promoted poor outcomes throughout the continuum of HIV care, including delaying or forgoing HIV testing (percent of study participants ranging from 4.9 to 20.7 %; three studies [28–30]), not successfully linking to HIV care (range 3.8–44 %; two studies [31, 32]), missing clinic visits or dropping out of care (range <5–20.1 %; four studies [33–36]), or failing to adhere to ART (range 5–70 %; 12 studies [37–48]). These studies represented 72,642 subjects in ten countries: Botswana, Cote d'Ivoire, Kenya, Malawi, Nigeria, Tanzania, Togo, Uganda, Zambia, and Zimbabwe.

Study Characteristics: Qualitative Studies

Among the qualitative studies that we identified (Table 2 [24, 49–63]), participants described geographic and

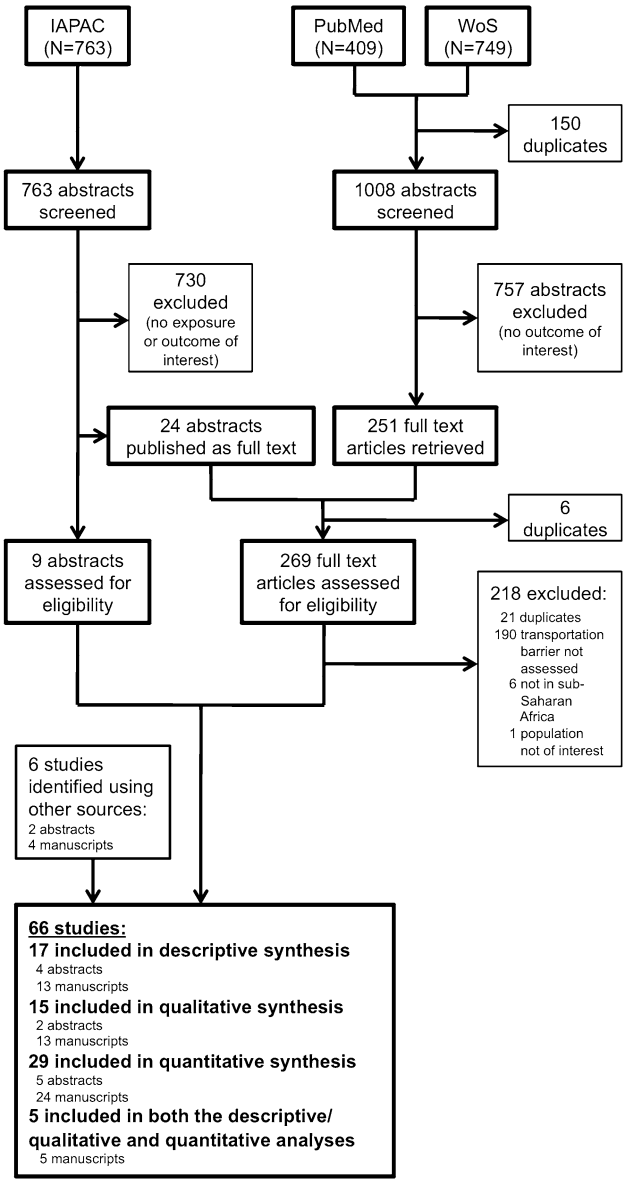

Fig. 1 PRISMA flow diagram of studies identified for review. Studies were identified using a systematic search of PubMed and Web of Science (WoS), as well as manual search of conference abstracts from the International Association of Physicians in AIDS Care (IAPAC) annual meeting from 2002 to 2011

transportation-related barriers as factors that impeded successful navigation of several points along the continuum of HIV care, including pre-ART linkage to care (four studies [49–52]), retention in care once on ART (one study [53]), and maintenance of optimal adherence to ART (11 studies [24, 54–63]). In these studies, prominent themes included lack of money to pay for transportation to clinic [24, 49–54, 57, 59], being forced to decide between paying for transportation to clinic and basic necessities such as feeding one's family or purchasing medications for opportunistic infection prophylaxis [52, 63], and the need to draw on social supports to overcome transportation barriers [62]. Poor road conditions [46], difficulty accessing reliable transportation [24], and the inability to take time off from work to travel long distances to clinic [51], were also described as factors that contributed to transportation difficulties. These studies represented at least 5,373 participants in ten countries: Botswana, Ethiopia, the Gambia, Kenya, Malawi, Namibia, Nigeria, South Africa, Tanzania, and Uganda.

Study Characteristics: Quantitative Studies

In the 34 quantitative studies (Table 3 [27, 36, 42–44, 59, 64–91]), there were 52 estimated associations between geographic or transportation-related barriers and HIV-related outcomes of interest: VCT [two (4 %)], pre-ART linkage to care [eight (15 %)], LTFU or mortality [17 (33 %)], and ART adherence or viral suppression [25 (48 %)]. Geographic or transportation-related barriers had an inverse association with HIV outcomes in 23 estimates (44 %), whereas 26 estimates (50 %) were null and three estimates (6 %) demonstrated a positive effect. When we evaluated these estimates by outcome of interest, we found an inverse association between geographic or transportation-related barriers and HIV outcomes for 2/2 (100 %) VCT estimates, 4/8 (50 %) pre-ART linkage estimates, 8/17 (47 %) LTFU or mortality estimates, and 9/25 (36 %) adherence or viral suppression estimates (Table 4). These studies represented 106,574 participants from nine countries: Ethiopia, Kenya, Malawi, Mozambique, Nigeria, South Africa, Tanzania, Uganda, and Zambia.

Exposure and Outcome Heterogeneity

The frequency with which geographic and transportation-related barriers were estimated to have an inverse effect on HIV outcomes varied according to the method of exposure measurement, sub-continental region, time period, study population, number of study participants, and number of study sites (Table 5). Among the three estimates based on an objective measure of distance, two (67 %) demonstrated an inverse effect. Among the 12 estimates where the exposure was residence in a rural area, nine (75 %) demonstrated an inverse effect. In contrast, an inverse effect was shown in only 3/15 (20 %) estimates based on self-reported distance, 5/13 (38 %) based on self-reported travel time, and 0/4 (0 %) based on self-reported transportation cost. When analyzed by sub-continental region, an inverse effect was demonstrated in 13/35 (37 %) studies conducted in Eastern Africa, 3/8 (38 %) in Western Africa, and 7/9 (78 %) in Southern Africa. There was limited variability in the percentage of estimates demonstrating an inverse association when categorized by time period, with 5/8 (63 %) studies conducted prior to 2003, 17/36 (47 %)

Table 1 Descriptive studies

Reference	Duration; country	Population (# of participants)	Setting	Findings related to geographic or transportation-related barriers
Primary outcome: VCT completion				
Kaawa-Mafigiri et al. [28]	2008–2009; Uganda	HIV-infected adults ($n = 889$)	2 Public hospital-based clinics	23/470 (4.9 %) men and 32/466 (6.9 %) women reported that lack of transportation was a reason for delaying HIV testing
Morin et al. [29]	2002–2003; Zimbabwe	Adults participating in a mobile VCT program ($n = 350$)	Mobile VCT vans in public marketplaces	Among those testing for HIV for the first time, 72/348 (20.7 %) reported that "location is not convenient" was a reason for not seeking prior HIV testing
Uganda Ministry of Health and ORC Macro [30]	2004–2005; Uganda	Adults participating in a national survey ($n = 15,497$)	National survey	Among individuals who reported never having been tested for HIV, 2.7 % of women and 4.6 % of men reported that this was due to the testing center being too far away
Primary outcome: linkage to care[a]				
Amuron et al. [31]	2007; Uganda	HIV-infected, ART-eligible adults undergoing pre-ART counseling and assessment ($n = 2,483$)	NGO-based clinic	Among subjects who were eligible and alive at study follow-up but did not initiate ART, 70/158 (44 %) reported that inability to afford transportation costs was a reason for not initiating ART; this was the most common reason given for failure to initiate ART
Parkes-Ratanshi et al. [32]	2007; Uganda	HIV-infected adults with CD4 count 200 in a trial of fluconazole prophylaxis for cryptococcal disease, who delayed initiation of ART for >3 months ($n = 400$)	2 NGO-based clinics	Among participants who delayed ART for >3 months after enrollment in the study, 15/400 (3.8 %) cited transportation cost as a reason for the delay
Primary outcomes: loss to follow-up (LTFU) & mortality[b]				
Braitstein et al. [33]	2009–2010; Kenya	HIV-infected, HIV-exposed, or HIV status unknown children who were LTFU ($n = 97$)	2 public hospital-based clinics	Among children who were LTFU and later interviewed, 7/97 (7 %) reported that transportation cost was the primary reason.; 23 % of children who were LTFU were on ART at the last visit
Krebs et al. [34]	2005; Zambia	HIV-infected adults enrolled in an ART program ($n = 430$)	12 public clinics	Among the 271/430 (63 %) of patients who provided reasons for missed visits, <5 % cited inability to pay for transportation as an important reason
McGuire et al. [35]	2004–2007; Malawi	HIV-infected adults who were LTFU ($n = 221$)	1 NGO-based district hospital and 10 affiliated health centers	Among respondents, 31/172 (20.1 %) of those who were not on ART and 5/49 (12.8 %) of those on ART reported transportation cost as a reason for defaulting; 49/221 (22 %) of respondents were on ART at the time of LTFU
Ochieng-Ooko et al. [36]	2001–2007; Kenya	HIV-infected adults, including ART-naïve and those on ART ($n = 50,275$)	23 public clinics	Among the subset of participants that were interviewed, 124/1037 (12 %) men and 360/2217 (17 %) women cited high transportation cost as a reason for missing scheduled clinic visits
Primary outcomes: ART adherence & viral suppression				
Adeyemo et al. [37]	Time not reported; Nigeria	HIV-infected adults and adolescents defaulting on ART ($n = 127$)	Not reported	76/127 (59.8 %) of participants attributed poor adherence to financial challenges due to transportation costs or purchasing food
Asiimwe et al. [38]	2005; Uganda	HIV-infected adults and children on ART for >1 year ($n = 84$)	Public clinic	13 % of participants reported transportation problems as a barrier to accessing care

Table 1 continued

Reference	Duration; country	Population (# of participants)	Setting	Findings related to geographic or transportation-related barriers
Bajunirwe et al. [39]	2006; Uganda	HIV-infected adults on ART ($n = 175$)	Public hospital-based clinic	Of patients who were interviewed, 9/47 (19 %) reported an inability to secure money for transportation to the clinic as the reason for running out of ART medicines
Eholie et al. [40]	2002; Cote d'Ivoire	HIV-infected adults on ART ($n = 308$)	3 public clinics	Among participants with incomplete adherence, 14 % reported "trips or weariness" as a reason for missing a dose of ART
Kip et al. [41]	2007; Botswana	HIV-infected adults enrolled in an ART clinic ($n = 400$)	4 randomly selected ART clinics situated throughout the country	180/400 (45 %) respondents reported being unable to pay for transportation to ART clinics
Kirsten et al. [42]	2008–2009; Tanzania	HIV-infected women enrolling in a PMTCT program ($n = 122$)	Public hospital-based antenatal clinic	3/19 (16 %) women who missed drug collection at least once mentioned transportation difficulties as a reason
Munseri et al. [43]	2001–2005; Tanzania	HIV-infected adults initiating treatment for latent TB ($n = 8$)	Clinical trial of TB vaccine	1/8 (13 %) interviewed participants who did not complete latent TB treatment reported travel distance to clinic as a significant factor in the decision to stop therapy
Olowookere et al. [44]	2007; Nigeria	HIV-infected adults on ART ($n = 216$)	Public hospital-based clinic	Of those reporting at least one missed dose, 70/216 (32.4 %) and 54/216 (25 %) indicated that distance to clinic and transportation cost, respectively, were contributing factors
Potchoo et al. [45]	2005; Togo	HIV-infected adults on ART ($n = 99$)	NGO-based pharmacies affiliated with a national HIV treatment program	Among patients who missed at least one ART dose intake, 11/43 (25.6 %) reported travel as a factor in their poor adherence
Van Dijk et al. [46]	2007–2008; Zambia	HIV-infected children and caretakers ($n = 192$)	Public hospital-based clinic	Among the 73 % of caretakers who reported difficulty accessing care, 60 % reported that this was due to lack of money, 54 % reported this was due to lack of transportation, and 32 % reported this was due to poor road conditions
Weiser et al. [47]	2000; Botswana	HIV-infected adults on ART, providers ($n = 169$)	3 private clinics	Of participants who were interviewed, 4/75 (5 %) of respondents indicated that distance from clinic caused them to miss doses of ART; of the 32/108 (30 %) of participants who identified frequency of required clinic visits as a barrier to treatment, 16/32 (50 %) indicated that living too far away was a reason for this
Yahaya et al. [48]	Year not reported; Nigeria	HIV-infected adults who were poorly adherent on ART ($n = 100$)	Public hospital	Among the respondents (all of whom were classified as poorly adherent), 70/100 (70 %) lived >10 km from the treatment facility

NGO non-governmental organization

[a] Including eligibility assessment, enrollment in pre-ART care, ART initiation, and pre-ART retention in care [26]

[b] Including measures of LTFU/retention either while on ART, or a combined measure of pre-ART and on-ART LTFU/retention

Table 2 Qualitative studies

Reference	Year(s); country	Population (# of participants)	Setting	Findings related to geographic or transportation-related barriers
Primary outcome: linkage to care[a]				
Assefa et al. [49]	2005–2008; Ethiopia	HIV/AIDS program managers, care providers, and HIV-infected patients on ART (n = not reported)	Various NGO- and public hospital-based clinics	Semi-structured interviews with program managers, care providers, and patients revealed that distance to treatment sites and high transportation costs were among the main reasons described for poor linkage to care
Bowie et al. [50]	2003–2008; Malawi	HIV-infected adults (n = 1,266)	Home-based care administered by a public hospital	Among 131 WHO Stage III or IV patients not receiving ART, many cited difficulty obtaining transportation to the clinic as a barrier to receiving ART
Chan et al. [51]	2004–2008; Malawi	HIV-infected HCWs, HIV care providers, and hospital administrators (n = 306)	Public hospital-based clinic providing care specifically for HIV-infected HCWs	Several of the respondents who participated in in-depth interviews or focus group discussions indicated that distance from the rural health centers and transportation cost were barriers to uptake of services at the HCW HIV clinic
Lubega et al. [52]	2008; Uganda	HIV-infected, ART-naïve adults, health center staff, and community members (n = 74)	Public pre-ART clinic	Transportation difficulties were often mentioned as a reason for dropping out of pre-ART care
Primary outcomes: loss to follow-up (LTFU) & mortality[b]				
Bwirire et al. [53]	2004; Malawi	HIV-infected pregnant women; nurse midwives (n = 25)	Public hospital	Focus groups identified transportation costs as a barrier to attending PMTCT visits
Primary outcomes: ART adherence & viral suppression				
Abrahams et al. [54]	2005–2006; South Africa	HIV-uninfected female adult rape victims initiating ART for PEP (n = 29)	2 hospital-based public health facilities	High transportation costs were identified as a barrier to PEP adherence among some women from the more rural of the 2 sites, which had a larger catchment area and primarily served patients with low socioeconomic status
Byakika-Tusiime et al. [55]	2004–2005; Uganda	HIV-infected adults and children on ART (n = 177)	Public hospital-based clinic	Of patients who were interviewed, one of the reasons given for poor adherence was lack of money for transportation to clinic to refill their prescriptions
Hardon et al. [24]	2005; Uganda, Tanzania, Botswana	Health care workers; HIV-infected adults on ART (n = 272)	12 public or private clinics across 3 countries	Transportation cost was reported by patients and health care workers as an important reason for failure to follow-up at health facilities to refill medications
Nam et al. [56]	Year not reported; Botswana	HIV-infected adults on ART (n = 32)	1 public and 1 private clinic located in the capital city	Transportation cost was not specifically enumerated by participants as a barrier to adherence; however, transportation cost is referenced in the theoretical framework put forth by the authors
Nassali et al. [57]	2006–2007; Uganda	HIV-infected women discharged from a hospital post-natal ward (n = 289)	Public hospital	Among women who did not return for post-natal PMTCT, transportation cost to the health unit was identified as a hindrance to returning
Peterson et al. [58]	Year not reported; The Gambia	HIV-infected adults initiating ART (n = 64)	Public clinic	Among all participants, travel was the most commonly reported barrier to adherence
Pyne-Mercier et al. [59]	2007–2008; Kenya	HIV-infected adults on ART (n = 2,534)	Public clinic	Among participants who were interviewed, transportation was cited as an important barrier to receiving treatment during a period of post-election violence

Table 2 continued

Reference	Year(s); country	Population (# of participants)	Setting	Findings related to geographic or transportation-related barriers
Rowe et al. [60]	2001; South Africa	HIV-infected adults enrolled in a TB prophylaxis program who did not complete a 6-month course of isoniazid ($n = 6$)	Public hospital-based clinic	Participants who were unable to complete a 6-month course of TB prophylaxis therapy cited the cost of obtaining transportation to clinic as an obstacle to completing therapy
Thobias et al. [61]	Year not reported; Namibia	HIV-infected individuals on ART (n = not reported)	Public hospital	Participants identified long distances to health facilities as an important factor influencing adherence
Ware et al. [62]	Year not reported; Nigeria, Tanzania, Uganda	HIV-infected adults on ART, treatment partners, and providers ($n = 252$)	3 public clinics	Participants reported that obtaining transportation to clinic was a significant barrier to optimal adherence and that they often had to rely on social supports to overcome these difficulties
Weiser et al. [63]	2007; Uganda	HIV-infected adults ($n = 47$)	Public hospital-based clinic	Participants reported that often times they were forced to decide between spending money on transportation to clinic and taking care of other essential needs, such as securing food for their families or purchasing medications to treat opportunistic infections

NGO non-governmental organization, *WHO* World Health Organization, *HCW* health care worker, *PEP* post exposure prophylaxis

[a] Including eligibility assessment, enrollment in pre-ART care, ART initiation, and pre-ART retention in care [26]

[b] Including measures of LTFU/retention either while on ART, or a combined measure of pre-ART and on-ART LTFU/retention

conducted from 2003 to 2006, and 15/32 (47 %) conducted after 2006 demonstrating an inverse effect. Similarly, there was limited variability in these findings between studies conducted in different patient populations, with the exception of studies of women enrolled in PMTCT care, where 0/3 (0 %) of studies found an inverse effect. An inverse effect was demonstrated with greater frequency in larger studies, with 2/15 (13 %) studies with $n < 200$, 8/19 (42 %) studies with $n = 201$–$1{,}000$, and 12/17 (72 %) studies with $n > 1{,}000$ demonstrating an inverse effect. Furthermore, multi-site studies [13/18 (72 %)] were more likely than single site studies [7/30 (23 %)] to demonstrate an inverse effect. Additionally, there was significant heterogeneity in the definition and measurement of both exposure and outcomes between studies (Table 6).

Assessment of Study Quality and Risk for Bias

Of the 34 quantitative studies that we identified, 25 (74 %) involved a longitudinal cohort, four (12 %) were specifically designed to measure an association between a geographic or transportation-related barrier and an HIV outcome, five (15 %) reported an objectively measured exposure variable, 28 (82 %) reported an objectively measured outcome variable, 20 (59 %) performed a multivariable analysis to adjust for potential confounders, and six (18 %) adjusted for a marker of wealth in the multivariable analysis (Table 7). Among the 25 cohort studies in which accounting for LTFU, censoring, or missing data would be relevant to potential bias, 14 (56 %) adequately did so. Of the four studies that were specifically designed to measure an association between a geographic or transportation-related barrier and an HIV outcome, three (75 %) demonstrated an inverse effect. Of the ten studies that included a multivariable analysis, used an objectively measured outcome variable, and adequately accounted for LTFU, censoring, and missing data, seven (70 %) found an inverse effect.

Discussion

In this systematic review of 66 studies representing over 130,000 persons receiving HIV care across 15 countries in SSA, we found that geographic and transportation-related barriers were associated with worse outcomes throughout the continuum of HIV care. These inverse associations were observed with variable frequency across different regions, different time periods, and among several subpopulations of HIV-infected individuals. In addition, geographic and transportation-related barriers were characterized as important by a large proportion of participants in descriptive and qualitative studies. This substantial body of

Table 3 Quantitative Studies

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
Primary outcome: VCT completion								
SA1	Hutchinson et al. [27]	2002–2003; South Africa	Adults participating in a cross-sectional survey ($n = 3{,}520$)	Regional community-based survey	Urban versus rural residence	Use of VCT service	Urban individuals were more likely to use VCT services than rural individuals (OR 3.15; 95 % CI 2.59–3.82)	Univariable analysis only
TA1	Wringe et al. [64]	2003–2004; Tanzania	Adult women participating in a longitudinal serologic surveillance study ($n = 4{,}990$)	Community-based cohort	Urban versus peri-urban versus rural residence	Return to testing site in 1 week to receive result and complete VCT	Peri-urban women were more likely to complete testing than rural women (AOR = 1.50; 95 % CI 1.12–2.02); however, urban women were not significantly more likely to complete testing than rural women	Age, marital status, marital change, education, ethnicity, religion, HIV status, spouse HIV status and VCT use, risky partner in last year, perceived HIV risk, heard of VCT, prior VCT
Primary outcome: linkage to care[a]								
MO1	Cook et al. [65]	2007–2008; Mozambique	HIV-infected pregnant women receiving PMTCT who followed up for adult HIV care ($n = 227$)	Public hospital-based clinic	Self-reported distance to clinic	Linkage from PMTCT to EID services	Mother-infant pairs that were successfully linked to EID care were more likely to live farther from clinic (OR 2.14; 95 % CI 1.01–4.51)	Not reported
SA2	Ingle et al. [66]	2004–2007; South Africa	HIV-infected individuals eligible for ART ($n = 22{,}083$)	Public clinics (28 free-standing and 8 hospital-based)	Distance to treatment site; urban/peri-urban versus rural assessment site	Initiation of ART; pre-ART mortality	Participants with initial assessment site >15 km from treatment site were less likely to initiate ART (HR 0.72; 95 % CI 0.66–0.78) and had higher pre-ART mortality (HR 1.65; 95 % CI 1.45–1.88) than those initially assessed and treated at the same site; participants from rural assessment sites were less likely to initiate ART (HR 0.89; 95 % CI 0.83–0.96) and had higher pre-ART mortality (HR 1.42; 95 % CI 1.23–1.64) than those from urban or peri-urban assessment sites	Age, sex, weight, CD4 count at time of ART eligibility, enrollment year, staffing levels of treatment facility, urban vs rural

Table 3 continued

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
SA3	Lessells et al. [67]	2007; South Africa	HIV-infected adults not yet eligible for ART (CD4 > 200) ($n = 930$)	Public clinic	Distance to clinic (methodology not reported)	Pre-ART retention in care	Distance to clinic not significantly associated with pre-ART retention in care (OR not reported)	Multivariable analysis performed, but variables not reported
ZA1	Sutcliffe et al. [68]	2005–2008; Zambia	HIV-infected children receiving care ($n = 835$)	Public clinics (1 urban and 2 rural)	Self-reported distance to clinic; GIS-mapped straight line distance to clinic; attendance at urban versus rural clinic	Default prior to ART initiation; time to ART initiation	Living farther from clinic was significantly associated with a higher rate of default on ART ($p = 0.05$), but not with initiating ART; compared to children attending an urban clinic, those attending a rural clinic were less likely to initiate ART (AHR = 0.38; 95 % CI 0.29–0.48 among children initially eligible for ART, and AHR 0.59; 95 % CI 0.37–0.95 among children initially ineligible for ART)	For ART default, univariable analysis only; for ART initiation, adjusted for location, time, and any variables either found to be associated with $p < 0.05$ or a priori known to be associated with the outcome
Primary outcomes: loss to follow-up (LTFU) & mortality[b]								
UG1	Elbireer et al. [69]	2006–2008; Uganda	HIV/TB co-infected adults receiving TB therapy ($n = 344$)	Public clinic	Self-reported distance to clinic	LTFU on TB therapy	Those living >10 km from the TB treatment facility were significantly more like to default on TB therapy (AOR = 2.22; 95 % CI 1.21–4.06)	Any variable found to be significant at the level of $p < 0.25$ on univariable analysis (variables not specified)
UG2	Geng et al. [70]	2004–2007; Uganda	HIV-infected adults initiating ART who became LTFU from initial clinic ($n = 48$)	Public hospital-based clinic	Self-reported distance to clinic	Retention in care at a different clinic among patients initially LTFU	Those living farther from the initial clinic were more likely to be connected to care at a different clinic (AOR = 1.45 per every 10 km; 95 % CI 1.11–1.90)	Age, years since last clinic visit
KE1	Karcher et al. [71]	2004–2005; Kenya	HIV-infected adults who either previously received PMTCT care or whose wife or mother received PMTCT care ($n = 153$)	Public hospital-based clinic	Self-reported distance to clinic	Initiation of ART; LTFU (excluding mortality); mortality	Distance to clinic was not significantly associated with initiating ART (OR 0.78; 95 % CI 0.34–1.79), LTFU (OR 0.41, 95 % CI 0.14–1.22), or mortality (OR 0.39, 95 % CI 0.11–1.37)	Univariable analysis only

Table 3 continued

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
ZA2	Kempf et al. [72]	1994–1998; Zambia	HIV sero-discordant couples enrolling in a clinical trial of VCT ($n = 1,771$ couples)	VCT clinic	Patient perception of living "near" or "far" from clinic	LTFU	Among M+F- serodiscordant couples, living "far" from clinic was significantly associated with LTFU (OR 1.7; 95 % CI 1.0–2.8) from the study cohort	Any variable found to be significant at the level of $p < 0.05$ in univariable analysis (variables not specified)
MA1	Massaquoi et al. [73]	2006–2007; Malawi	HIV-infected adults initiating ART ($n = 4,074$)	Public district hospital and nine rural clinics	Enrollment at central hospital versus rural health center	ART default; mortality	Patients treated at a rural health center were less likely to default on ART (HR 0.22; 95 % CI 0.13–0.35) but had higher mortality (HR 2.02; 95 % CI 1.63–2.49) than those treated at the district hospital	Univariable analysis only
TA2	Mossdorf et al. [74]	2005–2008; Tanzania	HIV-infected adults initiating ART ($n = 1,463$)	Public hospital	Self-reported distance to clinic	12-month LTFU/ mortality composite	Distance to clinic was not significantly associated with mortality/LTFU composite ($p = 0.561$)	Univariable analysis only
ET1	Mulissa et al. [75]	2003–2008; Ethiopia	HIV-infected adults initiating ART ($n = 1,428$)	Public hospital	Rural versus urban residence	LTFU (analysis only includes those on ART); mortality	Urban patients were less likely than rural patients to be LTFU (AHR = 0.5; 95 % CI 0.3–0.6), but there was no significant difference in mortality; also, authors did not make a distinction of whether before or after decentralization in this analysis, although separate analyses were performed looking at outcomes by pre- or post- decentralization)	Multivariable analysis performed (variables not specified)

Table 3 continued

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
KE2	Ochieng-Ooko et al. [36]	2001–2007; Kenya	HIV-infected adults ($n = 50,275$)	2 public clinics	Self-reported travel time to clinic; urban versus rural clinic	LTFU	Among patients on ART, longer travel time to clinic was significantly associated with LTFU (HR 1.11, 95 % CI 1.04–1.19); attending a rural clinic was associated with a lower rate of pre-ART retention (HR 0.82, 95 % CI 0.77–0.88), but there was no significant association between rural clinic site and retention in patients already on ART	Sex, other variables found to be significant at the level of $p < 0.05$ on univariable analysis (variables not specified)
Primary outcomes: ART adherence & viral suppression								
NI1	Adeyemi et al. [76]	2009; Nigeria	HIV-infected adults on ART ($n = 320$)	Not reported	Self-reported travel time to clinic	Adherence, as defined by late or missed clinic visit > 7 days	Those living >3 h from clinic were more likely to have poor adherence than those <3 h away (OR 1.9; 95 % CI 1.4–2.8)	Not reported
UG3	Bagenda et al. [77]	2004–2007; Uganda	HIV-infected children initiating ART ($n = 129$)	Public hospital-based clinic	Self-reported distance to clinic	>95 % adherence by pharmacy refill records	There was no significant association between distance to clinic and adherence ($p = 0.74$)	Univariable analysis only
SA4	Barth et al. [78]	2003–2007; South Africa	HIV-infected children who have been on ART for at least one year ($n = 81$)	Public clinic	Self-reported distance to clinic	Viral suppression	Among children who had a good initial virologic response to ART, there was no significant association between distance to clinic and sustained viral suppression (OR not reported)	Multivariable analysis performed (variables not specified)
UG4	Byakika-Tusiime et al. [79]	2002; Uganda	HIV-infected adults purchasing ART who have been on ART for at least one month ($n = 304$)	2 public and 1 private clinic	Self-reported distance to clinic	Adherence >95 % by 3-day self-report	Travel distance to clinic was not associated with adherence (AOR = 1.01; 95 % CI 0.45–1.25)	Not reported

Table 3 continued

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
ZA3	Carlucci et al. [80]	2006; Zambia	HIV-infected adults on ART ($n = 409$)	Public hospital-based clinic	Self-reported cost and travel time to clinic; odometer-tracked distance to clinic; GPS-estimated linear distance from nearest health center to clinic	Adherence >95 % by pill count	There was no significant association between linear distance ($p = 0.1$), actual travel distance ($p = 0.1$), transportation cost (OR 0.7, 95 % CI 0.35–1.4), or travel time (OR 1.0, 95 % CI 0.91–1.0) and adherence	Only travel time and transportation cost were modeled in multivariable analysis (variables not specified)
NI2	Charurat et al. [81]	2005–2006; Nigeria	HIV-infected adults initiating ART ($n = 5{,}760$)	5 tertiary hospitals	Self-reported travel time to clinic	Adherence by pharmacy refill records; LTFU	Those traveling >2 h to reach clinic were significantly more likely to be non-adherent than those traveling <1 h (AOR = 1.11; 95 % CI 1.01–1.23); travel time was not significantly associated with LTFU	Adherence analysis adjusted for age, sex, education, disclosure, employment, baseline CD4, time on ART, and ART regimen; LTFU analysis was univariable only
UG5	Haberer et al. [82]	2008–2010; Uganda	HIV-infected children on ART and living within 20 km of clinic ($n = 121$)	Public hospital-based clinic	Self-reported travel time to clinic; self-reported transport cost to reach clinic	Adherence >90 %; treatment interruption >48 h (by MEMS)	Travel time (AOR = 1.00; 95 % CI 1.00–1.01) and transportation cost (AOR = 1.00; 95 % CI 1.00–1.01) were not significantly associated with adherence	Any variable found to be significant at the level of $p < 0.1$ (variables not specified)
SA5	Hirschhorn et al. [83]	Year not reported; South Africa	HIV-infected adults on ART ($n = 407$)	Not reported	Self-report of "difficult to get to clinic"	Adherence by visual analog scale, last dose missed, and # doses missed in last week	Self-report of "less difficult to get to clinic" was associated with higher adherence (OR not reported)	Not reported
NI3	Iroha et al. [84]	2008; Nigeria	HIV-infected children on ART ($n = 212$)	Public hospital-based clinic	Self-reported distance to clinic	Adherence by 3-day self report of at least 1 missed dose	Travel distance was not significantly associated with adherence (for >20 km, OR 0.69; 95 % CI 0.24–1.99)	Univariable analysis only

Table 3 continued

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
MA2	Kirsten et al. [42]	2008–2009; Tanzania	HIV-infected women enrolling in a PMTCT program ($n = 122$)	Public hospital-based antenatal clinic	Self-reported travel time to clinic; self-reported transportation cost	Acceptance of PMTCT medications; adherence to PMTCT regimen by medication possession ratio	Travel time was not significantly associated with maternal acceptance of PMTCT (OR 0.74; 95 % CI 0.34–1.64) or adherence to PMTCT ($p = 0.788$); transportation cost was not significantly associated with maternal acceptance of PMTCT (OR 0.91; 95 % CI 0.40–2.08) or adherence to PMTCT ($p = 0.728$)	Age, participation in an income-generating activity, gestational age
NI4	Kurlander et al. [85]	2005–2006; Nigeria	HIV-infected adults on ART ($n = 116$)	Public hospital	Self-reported travel time to clinic	>95 % adherence by pharmacy refill records	There was no significant association between travel time to clinic and adherence (OR not reported)	Not reported
SA6	Maqutu et al. [86]	2004–2006; South Africa	HIV-infected adults initiating ART ($n = 688$)	2 public clinics (1 urban and 1 rural)	Urban versus rural treatment site	>95 % adherence by pharmacy refill records	Patients receiving care at the urban treatment site were more likely to achieve >95 % adherence than those at the rural treatment site (AOR = 4.35; 95 % CI 2.26–8.37)	Multivariable analysis performed (variables not specified)
NI5	Mbaezue et al. [87]	2005–2006; Nigeria	HIV-infected adults initiating ART ($n = 228$)	Public hospital	Self-reported travel time to clinic	Failure to pick up medications within 1 week of scheduled appointment	There was no significant association between travel time to clinic and failure to pick up medications within one week of scheduled appointment (OR not reported)	Not reported
TA3	Munseri et al. [43]	2001–2005; Tanzania	HIV-infected adults initiating IPT for latent TB ($n = 117$)	Clinical trial of TB vaccine	Self-reported distance to clinic	Completion of IPT course	Self-reported distance to clinic was not significantly associated with IPT completion ($p = 0.055$); however, patient subjective assessment of "clinic far from home" was associated with non-completion of IPT ($p = 0.04$)	Univariable analysis only

Table 3 continued

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
NI6	Olowookere et al. [44]	2007; Nigeria	HIV-infected adults on ART ($n = 216$)	Public hospital-based clinic	Self-report of "unable to pay for transport"	Adherence>95 % by 1-week self-report	"Unable to pay for transport" was not significantly associated with adherence (OR 1.83; 95 % CI 0.98–3.4)	Multivariable analysis performed (variables not specified)
KE3	Pyne-Mercier et al. [59]	2007–2008; Kenya	HIV-infected adults on ART ($n = 2,534$)	Public clinic (during period of post-election violence)	Self-reported travel time to clinic	Treatment interruption of >48 h	Patients who lived >3 h from clinic were significantly more likely to have at least one treatment interruption than those who lived within 1–2 h of clinic (AOR = 1.86; 95 % CI 1.28–2.71)	Sex, time on ART
TA4	Ramadhani et al. [88]	2005; Tanzania	HIV-infected adults on ART ($n = 150$)	Public hospital-based clinic	Self-reported walking time to clinic	Adherence by self-report of at least one missed dose in last 6 months	Walking time to clinic was not significantly associated with non-adherence (AOR = 1.2; 95 % CI 0.94–1.6)	Multivariable analysis performed (variables not specified)
UG6	Sethi et al. [89]	Year not reported; Uganda	HIV-infected adults ($n = 132$)	Public hospital-based clinic	Self-reported distance to clinic	Adherence by self-report of never having missed a dose of ART	Those living >5 km from clinic were significantly more likely to have ever missed a dose of ART than those living <5 km from clinic (OR 2.6; 95 % CI 1.1–6.0)	Sex
NI7	Taiwo et al. [90]	2006–2007; Nigeria	HIV-infected adults initiating ART ($n = 499$)	Public clinic	Self-reported distance to clinic	Adherence >95 % by pharmacy refill	Those living <20 km from clinic were significantly more likely to have >95 % adherence at 24 weeks (AOR = 2.31; 95 % CI 1.30–4.10) and at 48 weeks (AOR = 2.35; 95 % CI 1.43–3.87) after initiating ART than those living >100 km from clinic	Age, sex, disclosure status, presence of treatment partner

Table 3 continued

Study code	Reference	Year(s); country	Population (# of participants)	Setting	Exposure(s) of interest	Outcome(s) of interest	Findings related to geographic or transportation-related barriers	Potential confounding co-variables included
ZA4	Van Dijk et al. [91]	2007–2010; Zambia	HIV-infected children initiating ART ($n = 267$)	Public hospital-based clinic	Self-reported travel time to clinic	Viral suppression; mortality	Patients who lived >5 h from clinic were significantly less likely to achieve viral suppression at 6 months after ART initiation (OR 0.10; 95 % CI 0.01–0.82) compared to those living <1 h from clinic; travel time to clinic was not significantly associated with mortality (for >5 h, HR 2.93; 95 % CI 0.37–23.48)	Any variable found to be significant at $p < 0.1$ in univariable analysis (variables not specified)

EID early infant diagnosis, *GIS* geographic information system, *GPS* global positioning system, *MEMS* medication event monitoring system, *IPT* isoniazid prophylactic therapy, *OR* odds ratio, *AOR* adjusted odds ratio, *HR* hazard ratio, *AHR* adjusted hazard ratio

[a] Including eligibility assessment, enrollment in pre-ART care, ART initiation, and pre-ART retention in care [26]

[b] Including measures of LTFU/retention either while on ART, or a combined measure of pre-ART and on-ART LTFU/retention

evidence supports our hypothesis that geographic and transportation-related barriers contribute to poor outcomes for HIV-infected individuals in SSA at all points along the continuum of HIV care.

Overall, we found that ~50 % of estimates demonstrated an inverse association between a geographic or transportation-related barrier and an HIV-related outcome. This proportion varied across different study-level parameters, including sub-continental region, time period, study population, number of participants, and number of study sites. It is notable that studies with greater numbers of participants were more likely to report an inverse effect of geographic and transportation barriers on HIV outcomes, suggesting that smaller studies may not have had sufficient statistical power to estimate such an association with precision. Furthermore, in our assessment of study quality and risk for bias, we found that the higher quality studies were more likely than those of lesser quality to have reported an inverse association between geographic or transportation barriers and an HIV outcome.

Interpretation of our findings is subject to several important limitations. First, most of the quantitative observational studies that we identified were not designed to evaluate geographic or transportation-related barriers as the primary exposure of interest. In our analysis of study quality, we did find that studies specifically designed for this purpose were more likely to report an inverse association than those for which such an analysis was a secondary aim. Second, authors often neglected to adjust for potential confounding variables (or did not report the variables that were adjusted for). However, studies that did adjust for potential confounding variables were more likely to report an inverse effect than those that failed to do so. Third, our summary measures are crude relative to the pooled relative risks and odds ratios that would be calculated in a meta-analysis. However, as previously noted, the heterogeneity in study designs among the identified studies precluded a formal meta-analysis. A fourth and related limitation was the significant variability in measurement and definition of both exposure and outcome variables (as demonstrated in Table 6). Self-reported measures of geographic and transportation-related barriers, such as travel time, distance, and cost, are intrinsically subjective measures that may either under- or over-estimate true difficulties in health care access [92]. For example, in one recently published study of people on HIV treatment in rural Uganda, distance measures based on global positioning systems were inversely associated with missed clinic visits, while self-reported distance measures were not [93]. Additionally, most quantitative studies identified in this review defined the exposure variable as categorical or binary, rather than continuous. This resulted in a wide range of cut-off values when comparing relatively

Table 4 Quantitative studies grouped by exposure and outcome of interest

Transportation variable	Outcome of interest										
	VCT			Linkage to care[a]			LTFU & mortality[b]			Adherence & viral suppression		
	Inverse effect	Null effect	Positive effect	Inverse effect	Null effect	Positive effect	Inverse effect	Null effect	Positive effect	Inverse effect	Null effect	Positive effect
Travel distance				SA2	SA3, ZA1, KE1	MO1	SA2, ZA1, UG1, ZA2	KE1[c], KE1[d], TA2	UG2	UG6, NI7, TA3[f]	UG3, SA4, UG4, ZA3, NI3, TA3[e]	
Travel time							KE2	NI2, ZA4		NI1, NI2, KE3, ZA4	ZA3, UG5, MA2, NI4, NI5, TA4	
Transportation Cost										SA5	ZA3, UG5, MA2, NI6	
Rural residence or clinic location	SA1, TA1			SA2, ZA1, KE2			SA2, MA1[d], ET1[c]	ET1[d], KE2	MA1[c]	SA6		
Total estimates	2	0	0	4	3	1	8	7	2	9	16	0

Study codes (from Table 3) populate individual cells

[a] Including eligibility assessment, enrollment in pre-ART care, ART initiation, and pre-ART retention in care [26]

[b] Including measures of LTFU/retention either while on ART, or a combined measure of pre-ART and on-ART LTFU/retention

[c] LTFU outcome

[d] Mortality outcome

[e] Self-reported distance

[f] Self-report of living "far from clinic"

Table 5 Variability in estimates by study parameter

Study parameter[a]	% (n/N) of estimates demonstrating an inverse association between a geographic/transportation-related barrier and an HIV outcome
Geographic/transportation barrier	
Rural	75 % (9/12)
Distance (objective)	67 % (2/3)
Distance (self-reported)	20 % (3/15)
ravel time (self-reported)	38 % (5/13)
Transport cost (self-reported)	0 % (0/4)
Region	
Eastern Africa	37 % (13/35)
Western Africa	38 % (3/8)
Southern Africa	78 % (7/9)
Time period	
Pre–2003	63 % (5/8)
2003–2006	47 % (17/36)
Post–2006	47 % (15/32)
Study population	
HIV-infected adults	50 % (18/36)
HIV-infected children	30 % (3/10)
HIV/TB care	67 % (2/3)
PMTCT care	0 % (0/3)
Number of participants	
$n < 200$	13 % (2/15)
$n = 20$–$1{,}000$	42 % (8/19)
$n > 1{,}000$	72 % (12/17)
Number of study sites	
Single site	23 % (7/30)
Multiple sites	72 % (13/18)

[a] For some estimates, certain study parameters were not reported and therefore not considered in this calculation. For study time period, a single study may be classified in more than one time period if it was reported to span multiple time period categories

"shorter" versus "longer" travel distance and time, or relatively "higher" versus "lower" transportation cost. Finally, the null findings of some studies may have resulted from the design of the study itself. For example, Haberer et al. [82] found that, among HIV-infected children in Uganda, neither travel time nor transportation cost had a statistically significant association with ART adherence. It should be noted that participants living >20 km from clinic were excluded from that study, and that this was the most common reason for exclusion. If the effect of travel time on ART adherence were non-linear (e.g. no association below a certain threshold and an inverse effect at distances above the threshold), then the exclusion criteria of this study would preclude valid estimation of an association between distance and adherence.

Table 6 Heterogeneity in measurement and definition of exposures and outcomes

Exposure measure (# of estimates)	Study codes	Total estimates
Travel distance (20)		
Self-reported integer	MO1, ZA1, UG1, UG2, KE1, TA2, UG3, SA4, UG4, NI3, TA3, UG6, NI7	13
GPS or odometer tracked	ZA3	1
Straight line (approximate)	ZA1, ZA3	2
Patient perception of difficulty	ZA2, SA5	2
Other	SA2, SA3	2
Travel time (11)		
Self-reported integer	KE2, NI1, ZA3, NI2, UG5, MA2, NI4, NI5, KE3, TA4, ZA4	11
Transportation cost (4)		
Self-reported integer	ZA3, UG5, MA2	3
Other	NI6	1
Urban vs. rural (8)		
Urban+rural	SA1, ZA1, ET1, KE2, SA6	5
Urban+peri-urban+rural	TA1, SA2	2
Other	MA1	1
Outcome measure (# of estimates)	Study codes	Total estimates
Linkage to care (6)		
Pre-ART retention in care	SA3, ZA1	2
ART initiation	SA2, ZA1, KE1	3
Other	MO1	1
Retention in care/mortality (12)		
Pre-ART mortality	SA2	1
Post-ART	MA1, ET1, ZA4	3
Without respect to ART status	SA2, UG1, UG2, KE1, ZA2, TA2, KE2, NI2	8
Adherence/viral suppression (20)		
Self-reported	UG4, SA5, NI3, TA4, UG6	5
Pharmacy refill or pill count	UG3, ZA3, NI2, MA2, NI4, SA6, NI7	7
MEMS device	UG5	1
Treatment interruption <1 week	UG5, KE3	2
Treatment interruption at least 1 week	NI5	1
Viral suppression	SA4, ZA4	2
Other	NI1, TA3	2

GPS global positioning system, *MEMS* medication event monitoring system

We were surprised to find a small number of studies that demonstrated a paradoxically beneficial impact of geographic and transportation-related barriers on HIV outcomes [65, 70, 73]. It is notable that none of these three studies was specifically designed to estimate the effect of a geographic or transportation barrier on an HIV outcome. In certain cases, the findings were not fully inconsistent with our hypothesis that geographic and transportation barriers negatively affect HIV outcomes. For example, Geng et al. [70] found that among patients LTFU from clinic, greater distance to clinic was associated with increased likelihood of re-establishing care at different site. The authors hypothesized that this was due to emergence of new clinics as part of treatment decentralization in Uganda. Importantly, the reference clinic was the only ART provider in southwest Uganda in year 2000, while in 2009 (at the time of the study) there were over 60 rural treatment sites in the same region. Although Cook and colleagues found that greater distance to clinic was associated with a higher rate of linkage from PMTCT to early infant diagnosis care, this study excluded mothers who failed to enroll in adult HIV care after their pregnancy, which accounted for nearly half of the total sample [65]. Finally, although Massaquoi and colleagues found that patients treated at a rural health center were significantly less likely to default on ART than those treated at an urban center, the authors also found that

Table 7 Assessment of study quality and risk of bias

Reference	Study design and population		Exposure measurement	Outcome measurement		Analysis	
	Cross-sectional, case control, or cohort?	Specifically designed to assess geographic or transportation barriers ?	Objective or self-reported?	Accounted for LTFU, censoring, and/or missing data?	Objective or self-reported?	Included multivariable analysis?	Adjusted for marker of wealth?
Hutchinson et al. [27]	Cross-sectional	No	Objective	n/a	Self-reported	No	No
Wringe et al. [64]	Cohort	No	Unclear	No	Objective	Yes	No
Cook et al. [65]	Cohort	No	Self-reported	No (excluded 226 mothers who did not enroll in adult HIV care after PMTCT)	Objective	Yes	Yes
Ingle et al. [66]	Cohort	No	Unclear	Yes	Objective	Yes	No
Lessells et al. [67]	Cohort	No	Unclear	Yes	Objective	Yes	No
Sutcliffe et al. [68]	Cohort	Yes	Objective	Yes	Objective	Yes	No
Elbireer et al. [69]	Case control	No	Self-reported	n/a	Objective	Yes	No
Geng et al. [70]	Cohort	No	Self-reported	Yes	Objective	Yes	No
Karcher et al. [71]	Cohort	No	Self-reported	Yes	Objective	No	No
Kempf et al. [72]	Cohort	No	Self-reported	Yes	Objective	Yes	Yes
Massaquoi et al. [73]	Cohort	No	Objective	No	Objective	No	No
Mossdorf et al. [74]	Cohort	No	Self-reported	Yes	Objective	No	No
Mulissa et al. [75]	Cohort	No	Unclear	No	Objective	Yes	No
Ochieng-Ooko et al. [36]	Cohort	No	Unclear	Yes	Objective	Yes	No
Adeyemi et al. [76]	Cross-sectional	No	Unclear	n/a	Objective	No	No
Bagenda et al. [77]	Cohort	No	Self-reported	Yes	Objective	No	No
Barth et al. [78]	Cohort	No	Self-reported	Yes	Objective	Yes	Yes

Table 7 continued

Reference	Study design and population		Exposure measurement	Outcome measurement		Analysis	
	Cross-sectional, case control, or cohort?	Specifically designed to assess geographic or transportation barriers ?	Objective or self-reported?	Accounted for LTFU, censoring, and/or missing data?	Objective or self-reported?	Included multivariable analysis?	Adjusted for marker of wealth?
Byakika-Tusiime et al. [79]	Cross-sectional	No	Self-reported	n/a	Self-reported	No	No
Carlucci et al. [80]	Cohort	Yes	Objective	No (excluded 75 subjects who were LTFU or died prior to study)	Objective	No	No
Charurat et al. [81]	Cohort	No	Self-reported	Yes	Objective	Yes	Yes
Haberer et al. [82]	Cohort	No	Self-reported	No (excluded subjects living > 20 km from clinic)	Objective	Yes	Unclear
Hirschhorn et al. [83]	Cohort	No	Self-reported	Unclear	Self-reported	No	No
Iroha et al. [84]	Cross-sectional	No	Self-reported	n/a	Self-reported	No	No
Kirsten et al. [42]	Cohort	No	Self-reported	No	Objective	No	No
Kurlander et al. [85]	Cohort	No	Self-reported	No (excluded 14 subjects who were LTFU)	Objective	No	No
Maqutu et al. [86]	Cohort	No	Objective	No	Objective	Yes	Yes
Mbaezue et al. [87]	Case control	No	Self-reported	n/a	Objective	No	No
Munseri et al. [43]	Cohort	No	Self-reported	No	Objective	No	No
Olowookere et al. [44]	Cross-sectional	No	Self-reported	n/a	Self-reported	Yes	No
Pyne-Mercier et al. [59]	Cohort	No	Self-reported	No	Objective	Yes	No
Ramadhani et al. [88]	Cross-sectional	No	Self-reported	n/a	Self-reported	Yes	No
Sethi et al. [89]	Cross-sectional	Yes	Self-reported	n/a	Self-reported	Yes	No
Taiwo et al. [90]	Cohort	No	Self-reported	Yes	Objective	Yes	No
Van Dijk et al. [91]	Cohort	Yes	Self-reported	Yes	Objective	Yes	Yes

rural patients had a significantly higher mortality rate compared to their urban counterparts [73]. Furthermore, this analysis was not adjusted to account for potential confounding variables.

Alternatively, these paradoxical findings may be explained in part by HIV-related stigma. HIV is highly stigmatized throughout SSA [94], with increasing evidence suggesting that the stigma of HIV is an important determinant of health-related behaviors, such as HIV testing [95], disclosure of sero-positivity to sexual partners or other social supports [96], retention in care [97], and HIV treatment adherence [98]. It is also possible that in certain settings some people may prefer to travel longer distances for their HIV care in order to maintain their anonymity, a phenomenon that has been discussed in HIV-related studies conducted in various African settings [99–101]. Thus a highly motivated population of patients who intentionally travel long distances to minimize stigma could account for a paradoxically positive association between distance and HIV-related outcomes.

Conclusions

We found that geographic and transportation-related barriers impede access to care at all points in the HIV care continuum. This systematic review has important implications for HIV policy and programming in SSA. The provision of HIV care across large rural catchment areas in many parts of SSA presents a significant challenge to scaling up services for HIV-infected individuals and retaining patients in care with optimal and durable adherence. Although the distance one lives from their HIV clinic is not a readily modifiable risk factor, geographic and transportation-related barriers could be attenuated by public health interventions that seek to improve the accessibility of HIV care facilities. Recommended measures to mitigate these effects have included strengthening investment in rural health care infrastructure [102], decentralization of HIV treatment services [103–105], adoption of simplified management protocols that can be administered at the level of the primary health clinic [106], decreasing visit frequency [107], implementation of mobile clinics [108], point-of-care testing [109], immediate referral [110], improving patient-provider communication of test results and other information [111], and provision of transportation stipends [112, 113].

Additionally, identification of standardized and validated measures of geographic and transportation-related barriers might improve risk-stratification and resource allocation to patients in the region. To optimize and expand HIV care delivery in SSA, it will be important to standardize the measurement of geographic and transportation-related barriers and to develop, evaluate, and scale up interventions to mitigate them. Different interventions will likely need to be designed to address different points in the continuum of HIV care. For example, point-of-care CD4 testing and immediate referral for treatment initiation are likely to be effective interventions for improving pre-ART linkage to care, whereas decreasing visit frequency may be a more effective intervention to help patients overcome geographic and transportation-related barriers to maintaining optimal ART adherence. Decentralization of treatment facilities will diminish the transportation time and cost for patients seeking regular and sustained HIV care. In areas where HIV care decentralization is underway, these efforts should be continued. We also urge policy-makers to aggressively pursue service decentralization, and to prioritize investment in the necessary rural health care infrastructure. Finally, interventions that seek to better monitor ART adherence in real time may help to overcome geographic and transportation-related barriers by identifying and allowing for targeting of patients who are at high risk for viral rebound and other poor outcomes. Such interventions are actively being explored [114–117].

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Appendix

Search Terms Used in PubMed and Web of Science

1. PubMed search performed 8/14/11.
("mortality"[MH] or "survival"[TIAB] or "patient dropouts"[MH] or "lost to follow up"[MH] or retention[TIAB] or default[TIAB] or interruption[TIAB] or "linkage"[TIAB] or "medication adherence"[MH] OR "patient compliance"[MH] or "adherence"[TIAB] or "non-adherence"[TIAB] or "compliance"[TIAB] OR "non-compliance"[TIAB]) AND "africa south of the sahara"[MH] AND ("acquired immunodeficiency syndrome"[MH] OR "HIV"[TIAB] OR "AIDS"[TIAB]) AND (distance[TIAB] or "health services accessibility"[MH] or travel[TIAB] or barriers[TIAB] or structural[TIAB] or rural[TIAB] or "rural health services"[MH] or "rural population"[MH] or "hospitals, rural"[MH]).
2. Web of Science search performed 8/14/11.
TS = ("SSA" OR Africa) AND TS = ("loss to follow up" OR mortality OR survival OR default OR

interruption OR linkage OR "non-compliance" OR compliance OR adherence OR "non-adherence") AND TS = ("human immunodeficiency virus" OR HIV OR "acquired immunodeficiency syndrome" OR "acquired immune deficiency syndrome" OR AIDS) AND TS = (distance or "health services accessibility" or travel or barriers or structural or rural or "rural health services" or "rural population" or "hospitals, rural").

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