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Outcomes of HIV-positive patients lost to follow-up in African treatment programmes

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Abstract

OBJECTIVE—The retention of patients on antiretroviral therapy (ART) is key to achieving global targets in response to the HIV epidemic. Loss to follow-up (LTFU) can be substantial, with unknown outcomes for patients lost to ART programmes. We examined changes in outcomes of patients LTFU over calendar time, assessed associations with other study and programme characteristics and investigated the relative success of different tracing methods.

METHODS—We performed a systematic review and logistic random-effects meta-regression analysis of studies that traced adults or children who started ART and were LTFU in sub-Saharan African treatment programmes. The primary outcome was mortality, and secondary outcomes were undocumented transfer to another programme, treatment interruption and the success of tracing attempts.

RESULTS—We included 32 eligible studies from 12 countries in sub-Saharan Africa: 20 365 patients LTFU were traced, and 15 708 patients (77.1%) were found. Compared to telephone calls, tracing that included home visits increased the probability of success: the adjusted odds ratio (aOR) was 9.35 (95% confidence interval [CI] 1.85–47.31). The risk of death declined over calendar time (aOR per 1-year increase 0.86, 95% CI 0.78–0.95), whereas undocumented transfers (aOR 1.13, 95% CI 0.96–1.34) and treatment interruptions (aOR 1.31, 95% CI 1.18–1.45) tended to increase. Mortality was lower in urban than in rural areas (aOR 0.59, 95% CI 0.36–0.98), but there was no difference in mortality between adults and children. The CD4 cell count at the start of ART increased over time.

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CONCLUSIONS—Mortality among HIV-positive patients who started ART in sub-Saharan Africa, were lost to programmes and were successfully traced has declined substantially during the scale-up of ART, probably driven by less severe immunodeficiency at the start of therapy.

Keywords

HIV; antiretroviral therapy; loss to follow-up; mortality; sub-Saharan Africa

Introduction

Antiretroviral combination therapy (ART) has become more widely available in the low-income and middle-income countries that carry the highest burden of HIV infection and AIDS. By the end of 2015, 17 million people globally received ART, including 12 million persons living with HIV in sub-Saharan Africa [1]. Modelling by UNAIDS and others indicates that there is now a unique opportunity to end the HIV/AIDS epidemic by reaching the 90-90-90 targets by 2020: 90% of HIV infections are diagnosed, 90% of people known to be HIV-positive are on ART and 90% of individuals on ART are virologically suppressed [2, 3].

Retention in care is a key indicator of ART programmes' effectiveness and key to achieving the 90-90-90 targets. Through active tracing by phone calls and home visits or through data linkage to national population registries, it is possible to determine the true outcome of patients lost to follow-up (LTFU) [4–7]. In the last few years, an increasing number of such tracing studies were conducted to examine mortality, treatment interruption and undocumented transfers to other clinics and to link patients back to care. These studies were first systematically reviewed by Brinkhof *et al.* in 2009 [8], who found that mortality among patients LTFU was high (around 40%) and was inversely correlated with the rate of LTFU at the level of the programme. This association was subsequently used in a nomogram to estimate overall programme-level mortality [4].

Since then, additional studies have been published, and evidence has emerged that an increasing number of patients LTFU had self-transferred to other clinics, making the prognosis of patients LTFU to the initial programme better than initially estimated [9–11]. Tracing studies in children have also been published. An updated review is now needed that accounts for undocumented transfers and interruption of ART. We systematically reviewed all tracing studies in adults and children LTFU on ART in sub-Saharan Africa. We examined changes in outcomes of patients LTFU over calendar time, assessed associations with other study and programme characteristics and investigated the relative success of different tracing methods.

Methods

This systematic review was part of the research activities of the Measurement and Surveillance of HIV Epidemics (MeSH; see www.mesh.lshtm.ac.uk) and the International epidemiology Databases to Evaluate AIDS (IeDEA; www.iedea.org) consortia. MeSH develops, tests and implements innovative and efficient methods for routine HIV

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measurement and surveillance among adults and children. IeDEA is a large network of ART programmes in sub-Saharan Africa and other regions [12].

Literature search

We searched three databases (PubMed, EMBASE and LILACS) to identify eligible studies published from 1 January 2009 to 31 December 2015. In PubMed, we used a combination of free text and Medical Subject Headings (MeSH) and then adapted the search to the other data-bases (see Figure S1). The search of LILACS included Spanish, Portuguese and French terms. We also searched conference abstracts to identify studies that we may have missed in the searches of the three literature databases. We covered the Conference on Retroviruses and Opportunistic Infections (CROI, 2014–2015); the Conference on HIV Pathogenesis and Treatment of the International AIDS Society (IAS, 2009–2015) and the International AIDS Conference (AIDS, 2010–2014). We used Google Scholar to identify electronic publications ahead of print of eligible studies presented at CROI, IAS or AIDS. Lastly, we scrutinised the reference lists of previous reviews [8, 9, 13].

Inclusion criteria

We included all full-text articles where patients who started ART for their own health in programmes in sub-Saharan Africa were LTFU and then were actively traced to establish their vital status. A range of definitions of LTFU were used and studies were included in the review regardless of how LTFU was defined. We excluded studies from other regions, case reports, studies related to other interventions, such as prevention of mother-to-child transmission (PMTCT), voluntary counselling and testing (VCT) or post-exposure prophylaxis (PEP), and studies in special patient groups such as patients with tuberculosis, or patients considered stable on ART (based on lack of clinical progression, improved CD4 cell counts, suppressed viral load or good adherence to treatment). If several reports from the same ART programme included overlapping study periods, the article on the most recent periods was included. Two reviewers independently assessed the eligibility of articles (A.M. and O.T.). Discrepancies were resolved in consultation with a third reviewer (M.E.).

Data extraction

Data were extracted in duplicate by A.M. and O.T., or K.Z. and M.C., and subsequently checked by N.A. Standardised data extraction sheets covered characteristics of the ART programme and of eligible patients, including location and setting (urban, mostly urban, mostly rural, rural), whether the programme was public or private, the age of patients in care (children, adults, mostly children, mostly adults), CD4 cell count at ART start and time on ART of patients LTFU. We extracted the definition of LTFU used, the number of patients LTFU, the number of patients traced and their outcome: dead, alive but not on ART (treatment interruption), undocumented transfer and not found. We also extracted the start and end date. We defined the calendar year of a study as the mid-study year, calculated to one decimal place. The methods used to trace patients (telephone calls, home visits or linkage with population registry) were also assessed. Data were double-entered into a database, with discrepancies resolved in discussions with a senior reviewer (M.E. or D.N.).

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Statistical analyses

The primary outcome was the proportion of patients who were found to have died among those successfully traced. Secondary outcomes included the proportion of patients LTFU with undocumented transfer to another clinic, the proportion who interrupted treatment among those successfully traced and the proportion of patients LTFU who were successfully traced. We present proportions with exact binomial 95% confidence intervals (95% CIs) in forest plots and calculated the between-study variance (tau-squared).

We explored associations between outcomes and study characteristics using random intercept logistic meta-regression (binomial-normal) models. These models avoid the biases that arise when normal-normal models (which model the within-study variability via normal approximations) are applied to logit- or arcsine-square-root-transformed proportions [14, 15]. We included the calendar year, the study duration, the study setting (urban or mostly urban versus rural or mostly rural) and the study population (adults or mostly adults versus children or mostly children) as covariates in univariable and multivariable analyses. We also examined the effect of the tracing method on the success of tracing with and without adjusting for the covariates used in the main analysis (calendar year, study duration, setting and population). For the latter analysis, we excluded studies from South Africa where the vital status of patients was ascertained via linkage to the national population registry, using the civil identity document (ID) number [16]. We also examined whether in the treatment programmes the proportion of patients lost to follow-up had increased or decreased over calendar time.

Finally, we revisited the previously reported [4, 8] association between the proportion of patients lost in a programme and their mortality. All analyses were carried out in R version 3.2.3 (R Foundation, Vienna, Austria). Results are presented as odds ratios (ORs), adjusted ORs (aORs) and regression lines with 95% CIs.

Results

Selection and characteristics of studies

The searches identified a total of 1152 publications and 467 abstracts. We excluded 1589 items for the reasons detailed in Figure 1. Thirty articles met inclusion criteria [5, 7, 10, 17–44]. Two studies [27, 35] reported results for children and adults separately. A total of 32 cohorts were therefore included in the analyses. The studies were performed in 12 countries in East Africa, West Africa and Southern Africa (Table 1). The median study duration was 3.75 years (range 4 months to 9 years), and the mid-point of the study period ranged from 2003 to 2011. Most settings were urban or predominantly urban; six were rural studies. Most studies included adults only; two studies [32, 37] included mostly adults (over 90%) and four cohorts children [17, 23, 27, 35]. Definitions of LTFU varied from ‘not seen for a few weeks after a missed appointment’ to ‘not seen for over 6 months’. The most common definition was ‘not seen for at least 3 months’.

Three studies used phone calls only to trace patients, 22 studies did home visits and seven South African studies used data linkages (Table 1). Among the 25 studies that used home visits and/or telephone calls to trace patients lost to follow-up, nine used clinic staff (health

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educators, nurses or counsellors), eight employed research assistants for this task, and seven used community health workers or trained outreach workers. Two studies did not report the type of personnel involved [38, 45].

Patients lost and traced

A total of 20 365 patients LTFU were traced (median across studies: 294 patients; range 32–4467). In 30 of the 32 cohorts, the total number of patients LTFU was also given: 31 765 patients (median 588.5, range 68–5780); and in 25 studies, the total number of patients enrolled in the ART programme was reported: 177 890 (median 4674, range 155–34 277). The median percentage of patients LTFU among all patients enrolled was 16.6% (range 2.6–57.4%). Among patients LTFU, the median percentage traced was 81.3% (range 11–100%). The data are summarised in Table 2.

Seventeen studies reported the time from the start of ART to the last patient contact: the median was 5.3 months (range 1.3–14.4). Median CD4 cell counts at the start of ART among patients LTFU were available from 11 studies in adults. The median CD4 cell count increased from 71 cells/μl in the earliest study to 138 cells/μl in the most recent study [5]. Time on ART before LTFU was correlated with study duration, and median CD4 cell count correlated with mid-study calendar year (Figure S1).

Outcomes

The total number of patients successfully traced, that is the number of patients whose outcome could be ascertained, was 15 708. The median percentage of successfully traced patients was 73.4% across the 32 cohorts (range 20.2–100%). A total of 5380 (34.2% of patients successfully traced) had died (Table 2). Furthermore, 18 studies reported 1663 undocumented transfers of patients to another clinic. The median percentage of patients transferred among those successfully traced was 23.9% (range 2.1–54.4%). Thirteen studies reported on patients who had interrupted ART.

Meta-regression analyses

The tracing method used in the different studies was strongly associated with the probability of successful tracing of patients: compared to telephone calls only, tracing that included home visits substantially increased the probability of success. The univariable regression model predicted an increase in the proportion successfully traced from about 20% to 60% if home visits were included in the tracing strategy. The OR of successful tracing, comparing home visits with telephone calls, was 5.71 (95% CI 1.23–26.42), and the aOR was 9.35 (1.85–47.31).

For mortality, the forest plot indicated that deaths among patients successfully traced declined over calendar time (Figure 2). Meta-regression analyses confirmed this association: in univariable analysis, predicted mortality declined from around 56% in 2003 to 24% in 2011 (Figure 3, panel a). In multivariable analysis, the adjusted odds ratio (aOR) of death per 1-year increase in calendar year was 0.86 (95% CI 0.78–0.95) (Table 3). Mortality also decreased with longer study duration (aOR per 1-year increase 0.84, 95% CI 0.77–0.92) and

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was lower in urban than in rural areas (aOR 0.59, 95% CI 0.36–0.98). There was no evidence that mortality differed between adults and children (Table 3).

The proportion of undocumented transfers among those successfully traced increased with calendar time (Figure 3, panel b), but the association failed to reach statistical significance (aOR 1.13, 95% CI 0.96–1.34). Undocumented transfers were associated with longer study duration and tended to be more common in adults than in children. The proportion of patients who had interrupted ART increased both with calendar time (Figure 3, panel c) and with longer study duration.

Interruptions of ART were also more common in rural settings than in urban settings (Table 3). The variables included in the multivariable meta-regression models explained substantial proportions of the between-study heterogeneity. The model for mortality reduced tau-squared from 0.6279 to 0.2765 (a reduction by 56%). For undocumented transfer, the corresponding reductions were from 0.5852 to 0.3706 (a 37% reduction), and for interruption of ART from 0.3409 to 0.0597 (an 82% reduction).

There was no evidence of a change in the proportion lost to follow-up over calendar years ($P = 0.76$). Finally, as in the previous analysis [4,8], the proportion of patients LTFU in a programme was negatively associated with their mortality, with the regression line shifted towards lower mortality (Figure S4).

Discussion

We systematically reviewed studies of adult and paediatric patients who started ART in clinics and treatment programmes in sub-Saharan Africa, were LTFU and were subsequently traced. We analysed trends over calendar years in mortality, rates of undocumented transfers to other clinics and rates of ART interruption. We found that mortality in these patients decreased substantially over time, with a corresponding increase in undocumented transfers to other clinics and in the rate of interrupting therapy. We also examined the determinants of successful tracing of patients LTFU and found that home visits were more effective than tracing through phone calls alone. Finally, we updated a previous analysis [4,8] and confirmed the negative association between the proportion of patients LTFU in a treatment programme and their mortality.

Strengths of our study include the comprehensive literature search, which identified many studies from sub-Saharan Africa and the inclusion of studies both in adults and in children. In our study and previous reviews [8, 9], the results from individual studies were highly heterogeneous. We therefore focussed on identifying possible sources of heterogeneity, using state-of-the-art metaregression models, rather than on calculating potentially misleading combined estimates [45]. We excluded studies of selected patients on stable ART [46–48]: mortality in these patients will by definition be lower than in other patients LTFU.

Calendar year, study duration and study setting explained some of the heterogeneity in mortality across studies. Unfortunately, the CD4 cell count at the start of ART was not reported consistently and could therefore not be included in the analyses. Nevertheless, the decline in mortality over time may be explained by the increase in CD4 cell counts and

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reduction in severe immunodeficiency observed over time in adults and children starting ART [49, 50], which in turn is likely attributable to changes in HIV treatment guidelines [51], and earlier HIV diagnosis and enrolment into care associated with wider HIV testing [52, 53]. Calendar year may thus be seen as a proxy variable that captured the changes at the individual and health system levels associated with the scaling up of ART. We acknowledge that all outcomes in our study occurred conditional on LTFU, and changes in the determinants of LTFU could therefore also explain the trends observed. Of note, although the proportion of patients LTFU in a treatment programme was associated with mortality, the proportion lost remained fairly constant over time.

We reviewed the abstracts of major conferences to identify studies that we may have missed in our literature searches but did not include abstracts because the data from abstracts were generally incomplete. Missing data were also a problem in the published reports: only 18 of 32 cohorts reported on transfers to other clinics, 13 studies reported on the proportion of patients who interrupted ART and 11 studies gave the CD4 cell count of adults at the start of ART. Studies in children and in rural settings were rare and the statistical power of comparisons therefore limited. Another limitation is the definition of LTFU that was not standardised across studies. Although our search was comprehensive, we may have missed studies that remained unpublished, or studies that were published in reports or in journals not indexed in the databases searched, thus potentially introducing publication bias [54]. Few African journals are indexed in major databases: a survey of 158 African medical journals found that only 18 were indexed on Medline and 10 in EMBASE [55].

Both of the previous reviews [8, 9] reported a mortality rate of around 40% among patients LTFU and successfully traced. Similar to the present study, Wilkinson *et al.* [9] found a decline in mortality from 50% to 30% when comparing study periods before and after December 2007. The percentage of patients who transferred to another clinic overall was 19% in their review and the percentage stopping ART 29% [9]. Our study extends their analysis, showing that the decline in mortality was accompanied by an increase in CD4 cell counts, transfers to other clinics and in treatment interruptions. Recent studies have shown that an important proportion of patients who are lost at one clinic remain on ART and in care at another clinic. For example, a study in Lilongwe, Malawi, found that among patients LTFU and found to be alive on tracing, a majority (56%) were still taking ART, sourced from another clinic [40]. Similarly, a study of adults starting ART in Uganda, Tanzania and Kenya found that 59% of patients interviewed had reconnected to care at a different clinic [11]. Recently, an analysis of all public-sector CD4 cell count and viral load test results in South Africa found that systemwide retention in the healthcare system was much higher than retention at the initiating clinic [56].

A study of South African treatment programmes, where the vital status of patients known to have transferred out could be ascertained by linkage to the national population register, reported that mortality in transferred patients was higher than in patients retained in the clinic in the 3 months after transfer, but comparable to or lower than mortality in patients retained in the clinic after 3 months [10]. The higher early mortality probably reflects transfers of patients with advanced disease to better equipped facilities, whereas mortality later on reflects the transfer and self-transfer of stable patients [10].

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Estimations of mortality and life expectancy in HIV-infected populations rely on the complete ascertainment of deaths; however, the proportion of patients lost to follow-up in HIV care programmes is high, especially in sub-Saharan Africa [57]. As patients who are LTFU experience higher mortality than those remaining in care [4, 10, 11], failing to account for deaths of these patients leads to the underestimation of overall programme-level mortality, that is the mortality of all patients who started ART. In the absence of data from tracing studies on mortality of patients LTFU, investigators need to make assumptions on their likely mortality. For example, a study from Uganda [58] assumed that 30% of patients LTFU had died, whereas in Rwanda, investigators assumed that about 50% of patients LTFU had died [59]. Our regression analyses can inform such assumptions, taking into account the proportion of patients LTFU in the treatment programme and calendar year. A nomogram [4] or more sophisticated methods can then be used to obtain estimates of overall mortality that are corrected for LTFU [19].

Only one of the included studies assessed the cost-effectiveness of tracing patients lost to follow-up [47]. In this study, a social worker contacted patients by phone who had initiated antiretroviral therapy (ART) in the Themba Lethu Clinic in Johannesburg and were late for a scheduled visit. The worker could determine the status of 260 of 493 (53%) patients lost to follow-up. Twenty patients returned to care as a result of the intervention, at a cost of $432 per patient returned [47]. Kessler *et al.* simulated the cost-effectiveness of different strategies to retain patients in care in East Africa from a payer's perspective, assessing both interventions that aim to decrease the risk of loss to follow-up and interventions tracing patients lost to follow-up [60]. They found that tracing of patients alone was associated with both minimal costs and minimal benefits, whereas a risk reduction strategy had a greater impact on the quality-adjusted life-years (QALYs) gained. The risk reduction strategy was, however, a more expensive intervention [60].

Our study has important implications. First, patients who started therapy and were lost to follow-up in recent years will likely have better outcomes than patients enrolling in earlier years of the scale-up of ART. Mortality was also lower in urban than in rural areas. Our results thus caution against the simplistic imputation of mortality rates based on older studies, or studies from other settings. Second, although mortality has declined, it is still much higher than mortality among patients retained in care, and efforts to retain patients in care and to bring patients back to care must continue, both to improve outcomes in individuals and to prevent HIV transmissions at the population level. Third, HIV care programmes should collect time-updated contact information on all patients to allow the effective tracing of patients LTFU through home visits, and a system of unique IDs should be introduced at the national level to link patients transferring between clinics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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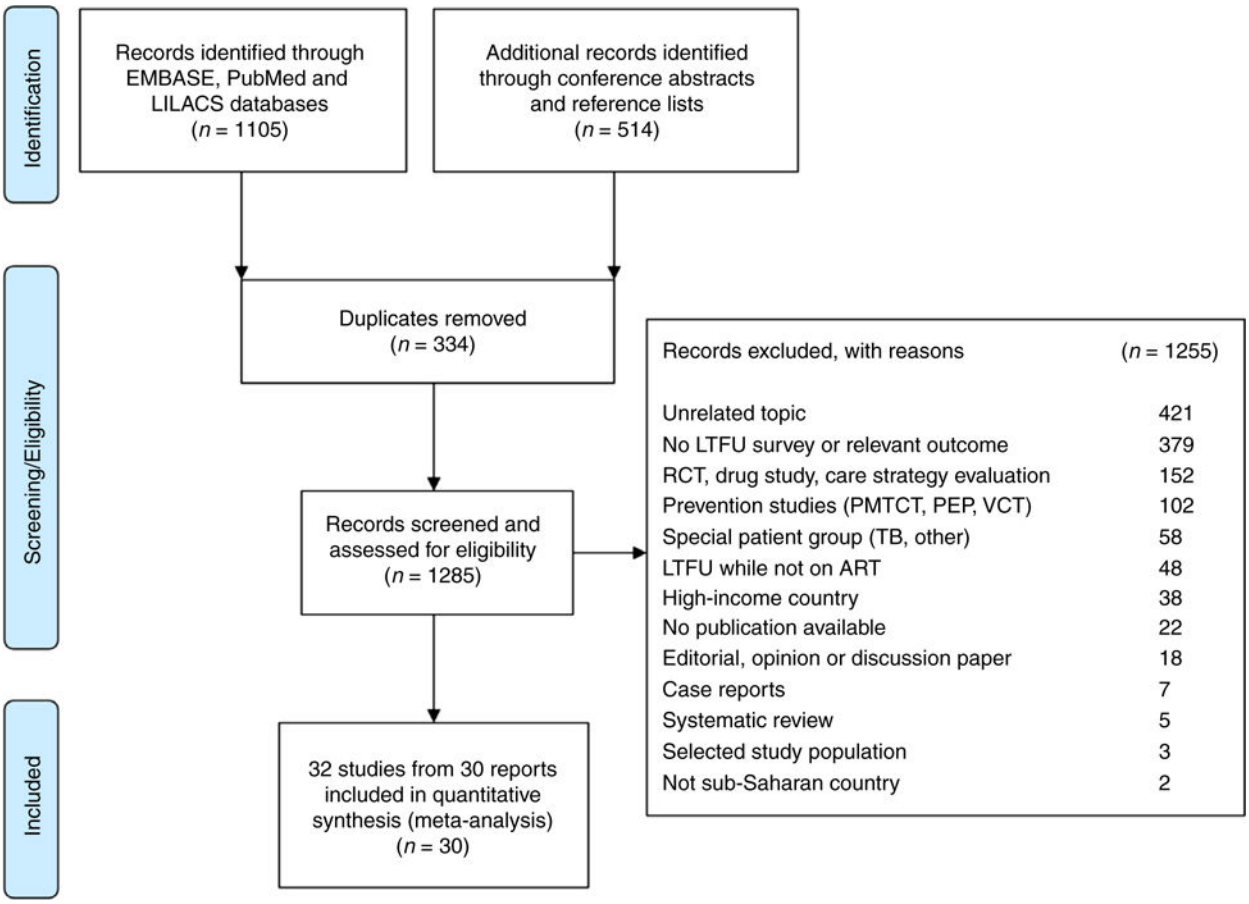

Figure 1.
Identification and selection of eligible studies.

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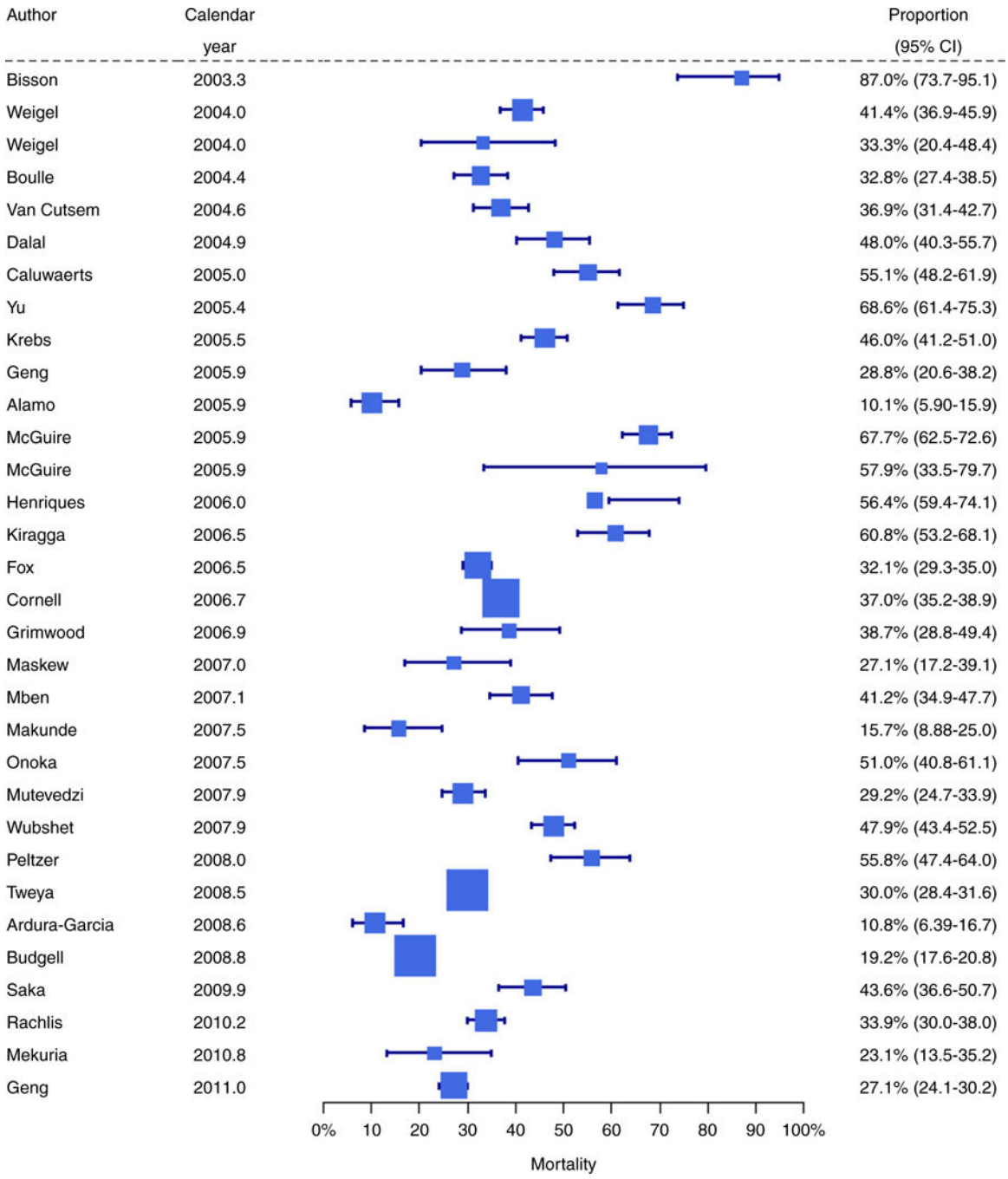

Figure 2.

Forest plot of mortality among patients successfully traced in 32 cohorts of patients LTFU in ART programmes in sub-Saharan Africa. Study-specific mortality estimates are shown with exact binomial 95% confidence intervals. The studies are ordered by the mid-point of the study periods. Mortality among LTFU patients that were successfully traced decreased over time. The size of each square is inversely proportional to the variance of the estimate for that study.

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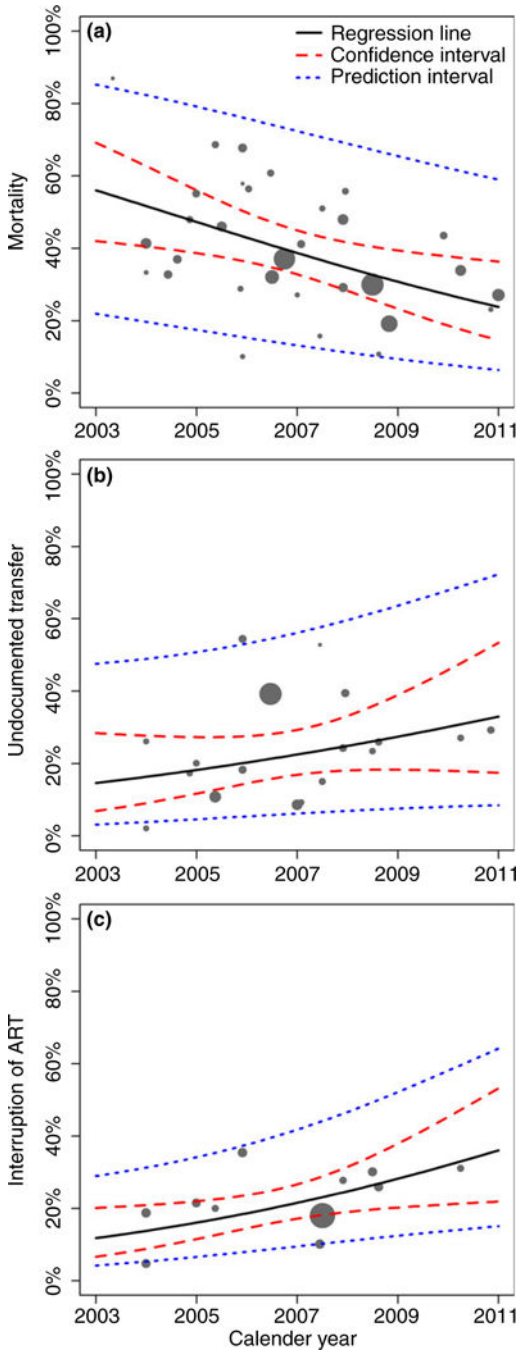

Figure 3.

Estimated change in mortality (a), undocumented transfers (b) and interruption of ART (c) over calendar time among patients LTFU and successfully traced in studies from sub-Saharan Africa. The area of each circle is inversely proportional to the variance of the estimate for that study. Results from univariable random-effects meta-regression analyses.

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Table 1

Characteristics of ART programmes tracing patients lost to follow-up (LTFU) in sub-Saharan Africa

Study/Region	Location	Country	Setting	Study population	LTFU definition	Tracing method	Study period
East Africa							
Geng (2008) [29]	Mbarara	Uganda	Rural	Adults	No visit for >6 months	Home visit	2004–2007
Alamo (2012) [44, 61]	Kampala	Uganda	Urban	Adults	No visit for >90 days	Home visit, buddy contact	2001–2010
Makunde (2012) [26]	Tanga City	Tanzania	Urban	Adults	No visit for >3 months	Home visit	2006–2008
Kiragga (2013) [19]	Kampala	Uganda	Urban	Adults	No visit for >3 months	Telephone, home visit	2005–2007
Wubshet (2013) [42]	Gondar	Ethiopia	Urban	Adults	Missed appointment >3 months	Home visit	2005–2010
Geng (2015) [5]	–	Kenya, Uganda, Tanzania	Urban	Adults	Missed appointment >90 days	Home visit	2009–2012
Mekuria (2015) [39]	Addis Ababa	Ethiopia	Urban	Adults	No visit for >1 month,	Telephone	2009–2012
Rachlis (2015) [37]	Nyanza	Kenya	Urban	Mostly adults	No visit >3 months	Home visit	2009–2011
West Africa							
Mben (2012) [34]	Yaounde	Cameroon	Urban	Adults	Missed appointment >1 month	Telephone, home visit, relatives	2006–2007
Onoka (2012) [20]	Emuga State	Nigeria	Mostly urban	Adults	Missed ≥3 appointments	Telephone, home visit	2007–2007
Saka (2013) [41]	Lome	Togo	Mostly urban	Adults	–	Telephone	2008–2011
Southern Africa							
Maskew (2007) [38]	Johannesburg	South Africa	Urban	Adults	Missed appointment	Telephone	2006–2007
Yu (2007) [32]	Four facilities	Malawi	Rural	Mostly adults	No visit for >3 months	Home visit	2004–2006
Bisson (2008) [31]	Gaborone	Botswana	Urban	Adults	Missed appointment >1 month	Telephone, home visit	2003–2003
Dalai (2008) [24]	Johannesburg	South Africa	Urban	Adults	Missed appointment for ≥6 weeks	Telephone, home visit	2004–2005
Krebs (2008) [25]	Lusaka	Zambia	Urban	Adults	Missed appointment	Home visit	2005–2005
Caluwaerts (2009) [36]	Tete	Mozambique	Urban	Adults	No visit for >60 days	Home visit	2002–2007
Boulle (2010) [7]	Khayelitsha	South Africa	Urban	Adults	No visit for > 6 months	Linkage	2001–2007
Fox (2010) [18]	Johannesburg	South Africa	Urban	Adults	Missed appointment ≥3 months	Linkage	2004–2008
McGuire (2010) [27]	Chiradzulu	Malawi	Rural	Adults	Missed appointment >1 month	Home visit	2004–2007
McGuire (2010) [27]	Chiradzulu	Malawi	Rural	Children	Missed appointment >1 month	Home visit	2004–2007
Peltzer (2011) [28]	Uthukela	South Africa	Mostly urban	Adults	Missed appointment ≥2 months	Telephone, home visit	2007–2008
Van Cutsem (2011) [21]	Cape Town	South Africa	Urban	Adults	No visit for >6 months	Linkage	2001–2008
Weigel (2011) [35]	Lilongwe	Malawi	Urban	Adults	Missed appointment >2 weeks	Telephone, home visit	2002–2005
Weigel (2011) [35]	Lilongwe	Malawi	Urban	Children	Missed appointment >2 weeks	Telephone, home visit	2002–2005

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Study/Region	Location	Country	Setting	Study population	LTFU definition	Tracing method	Study period
Grimwood (2012) [17]	4 provinces	South Africa	Mostly urban	Children	No visit for ≥3 months	Linkage	2004–2009
Henriques (2012) [30]	Chiradzulu	Malawi	Rural	Adults	Missed appointment >1 month	Home visit	2004–2007
Mutevedzi (2013) [22]	Hlabisa	South Africa	Rural	Adults	No visit for 180 days	Linkage	2004–2011
Tweya (2013) [40]	Lilongwe	Malawi	Urban	Adults	Missed appointment >3 weeks	Telephone, home visit	2006–2010
Cornell (2014) [10]	4 provinces	South Africa	Mostly urban	Adults	No visit for ≥6 months	Linkage	2004–2009
Ardura-Garcia (2015) [23]	Lilongwe	Malawi	Urban	Children	Missed appointment ≥3 weeks	Home visit	2006–2010
Budgell (2015) [33]	Johannesburg	South Africa	Urban	Adults	Missed appointment ≥3 months	Linkage	2004–2013

–, not reported.

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Table 2

Outcomes of HIV-positive patients lost to follow-up (LTFU) in ART programmes in sub-Saharan Africa

	Number of patients				Vital status among successfully traced patients (%)			
	Enrolled in programme	Lost to programme	Tracing attempted	Successfully traced (100%)	Died	Alive and undocumented transfer	Alive and interruption of ART	Alive total
East Africa								
Geng (2008) [29]	3628	829	128	111	32 (28.8%)	–	13/67 (19.4%)†	79 (71.2%)
Alamo (2012) [44, 61]	2713	1502	164	158	16 (10.1%)	86 (54.4%)	56 (35.4%)	142 (89.9%)
Makunde (2012) [26]	155	89	89	89	14 (15.7%)	47 (52.8%)	9 (10.1%)	75 (84.3%)
Kiragga (2013) [19]	5633	806	406	176	107 (60.8%)	69 (39.2%)	–	69 (39.2%)
Wubshet (2013) [42]	3012	551	551	486	233 (47.9%)	118 (24.3%)	135 (27.8%)	253 (52.1%)
Geng (2015) [5]	34 277	5780	991	860	233 (27.1%)	–	–	627 (72.9%)
Mekuria (2015) [39]	836	116	116	65	15 (23.1%)	19 (29.2%)	–	50 (76.9%)
Rachlis (2015) [37]	–	1071	851	569	193 (33.9%)	154 (27.1%)	177 (31.1%)	376 (66.1%)
Western Africa								
Mben (2012) [34]	–	238	238	238	98 (41.2%)	22 (9.2%)	–	140 (58.8%)
Onoka (2012) [20]	1034	219	150	100	51 (51.0%)	15 (15.0%)	18 (18.0%)	49 (49.0%)
Saka (2013) [41]	16 617	1216	1004	202	88 (43.6%)	–	–	114 (56.4%)
Southern Africa								
Maskew (2007) [38]	5849	154	154	70	19 (27.1%)	6 (8.6%)	–	51 (72.9%)
Yu (2007) [32]	5009	253	253	185	127 (68.6%)	20 (10.8%)	37 (20.0%)	58 (31.4%)
Bisson (2008) [31]	410	68	68	46	40 (87.0%)	–	–	6 (13.0%)
Dalai (2008) [24]	1631	267	267	173	83 (48.0%)	30 (17.3%)	–	90 (52.0%)
Krebs (2008) [25]	–	–	654	417	192 (46.0%)	–	–	225 (54.0%)
Caluwaerts (2009) [36]	2818	594	594	214	118 (55.1%)	43 (20.1%)	46 (21.5%)	96 (44.9%)
Boulle (2010) [7]	6402	628	293	293	96 (32.8%)	–	–	197 (67.2%)
Fox (2010) [18]	11 694	2435	1037	1037	333 (32.1%)	–	–	704 (67.9%)
McGuire (2010) [27] *	–	75	32	19	11 (57.9%)	–	–	8 (42.1%)
McGuire (2010) [27]	–	1186	624	344	233 (67.7%)	63 (18.3%)	34/152 (22.3%)†	111 (32.3%)
Peltzer (2011) [28]	727	169	169	147	82 (55.8%)	58 (39.5%)	–	65 (44.2%)
Van Cutsem (2011) [21]	6411	627	295	295	109 (36.9%)	–	–	186 (63.1%)

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	Number of patients				Vital status among successfully traced patients (%)			
	Enrolled in programme	Lost to programme	Tracing attempted	Successfully traced (100%)	Died	Alive and undocumented transfer	Alive and interruption of ART	Alive total
Weigel (2011) [35]	–	1840	659	486	201 (41.4%)	127 (26.1%)	23 (4.7%)	285 (58.6%)
Weigel (2011) [35] *	–	–	65	48	16 (33.3%)	1 (2.1%)	9 (18.8%)	32 (66.7%)
Grimwood (2012) [17] *	3563	211	93	93	36 (38.7%)	–	–	57 (61.3%)
Henriques (2012) [30]	6727	583	305	170	114 (56.4%)	–	–	88 (43.6%)
Mutevedzi (2013) [22]	4674	558	558	394	115 (29.2%)	–	–	279 (70.8%)
Tweya (2013) [40]	21 382	4560	4467	3176	952 (30.0%)	744 (23.4%)	957 (30.1%)	2224 (70.0%)
Cornell (2014) [10]	19 481	2624	2624	2624	972 (37.0%)	–	–	1652 (63.0%)
Ardura-Garcia (2015) [23] *	985	251	201	158	17 (10.8%)	41 (25.9%)	41 (25.9%)	141 (89.2%)
Budgell (2015) [33]	12 222	2265	2265	2265	434 (19.2%)	–	–	1831 (80.8%)
Overall	177 890	31 765	20 365	15 708	5380 (34.1%)	1663	1555	10360 (65.9%)

–, not reported.

*Study or study subgroup of children.

†Only a subsample of patients found to be alive was interviewed.

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Table 3

Meta-regression analyses for mortality, undocumented transfer and ART interruption

Outcome	Variable		Crude OR (95% CI)	Adjusted* aOR (95% CI)
Mortality	Calendar year	Per 1-year increase	0.84 (0.74–0.96)	0.86 (0.78–0.95)
	Study duration	Per 1-year increase	0.82 (0.74–0.92)	0.84 (0.77–0.92)
	Setting	Rural	1	1
		Urban	0.51 (0.25–1.01)	0.59 (0.36–0.98)
	Population	Children	1	1
		Adults	1.51 (0.63–3.62)	1.47 (0.78–2.78)
Undocumented transfer	Calendar year	Per 1-year increase	1.14 (0.94–1.38)	1.13 (0.96–1.34)
	Study duration	Per 1-year increase	1.13 (0.96–1.34)	1.17 (1.01–1.36)
	Setting	Rural	1	1
		Urban	1.89 (0.63–5.73)	1.57 (0.59–4.24)
	Population	Children	1	1
		Adults	2.38 (0.67–8.39)	2.78 (0.93–8.30)
Interruption of ART	Calendar year	Per 1-year increase	1.20 (1.03–1.39)	1.31 (1.18–1.45)
	Study duration	Per 1-year increase	1.13 (0.97–1.33)	1.22 (1.11–1.34)
	Setting	Rural	1	1
		Urban	1.02 (0.45–2.28)	0.51 (0.31–0.84)
	Population	Children	1	1
		Adults	0.89 (0.34–2.34)	0.90 (0.51–1.58)

*Adjusted for all variables listed.