Supplemental Digital Content - Appendix

1 Statistical analyses

1.1 Description of the dataset

Lighthouse Clinic and Martin Preuss Centre (MPC) are two public-sector ART clinics, run by the Lighthouse Trust and located in Lilongwe, the capital of Malawi. Both clinics use an electronic data system (EDS) to keep record of the patient's progression. The 'Back-to-Care' (B2C) programme was introduced in Lighthouse in July 2006 and in MPC in September 2007 to ascertain the true outcome of patients missing a visit and to improve the long-term retention in care. Patients who start ART at one of these two clinics are asked for consent to be traced in case of a missed visit. If the patient does not attend the clinic within three weeks after the antiretrovirals should have run out, the patient's name will appear on a tracing list. The tracing team will attempt to first call the patient by phone, and if this fails, visit him or her personally. The possible outcomes ascertained at tracing are presented in Table S1. If it is found that the patient has died, is receiving ART from another official ART provider (either because of silent 'self-transfer', or because an official transfer was not ascertained correctly at the original clinic) or has discontinued ART because of clinician's decision, the patient's true outcome in the EDS will be updated. If the patient is found to have discontinued ART independently, to be taking ART less than prescribed or to be taking ART regularly but receiving it outside the official providers (such as from relatives, friends or unlicensed vendors), the tracing clerk will try to bring the patient back to care and, upon agreement of the patient, schedule a new meeting at the clinic.

We included all adult ($\geq$16 years) patients who accessed ART care at either Lighthouse Clinic since July 2006 or MPC since September 2007, until December 2010. A total of 23,137 patients were included in the analyses: 12,702 accessed care at Lighthouse and 10,435 at MPC. Fifty-eight percent of the patients were women and the median age at ART start was 35 years (Table S2). A total of 4851 cases of expected loss to follow-up were observed. After tracing, it was found that in 999 cases the

patient had died, in 741 cases the patient had transferred out, in 976 cases the patient had discontinued (or never started) ART, and in 647 cases the patient was receiving ART irregularly (with gaps and/or from unlicensed sources). The remaining 1470 cases were either not traced or the patient could not be found (Table S3).

1.2 Time to first event

In the first analysis, we estimated the hazard of different events that represent interruption of ART care at the original clinic. The following events were included: death, official transfer to another ART clinic, self-transfer to another ART clinic, ART discontinuation (either independently or officially), missing an appointment due to irregular ART use (ART with gaps or ART without gaps from unofficial sources) and unexplained loss to follow-up. We included only the first event after ART start and censored all events taking place after possible return.

We conducted a competing risk survival analysis using the 'stcompet' function in STATA (version 11.2). All six events were treated as separate competing events, for which the cumulative incidence function was calculated. The cause-specific cumulative incidence functions CI_j and their combined cumulative incidence CI_{TOT} were transferred into cause-specific hazard functions h_j using the following formula:

$$h_j(t_i) = \frac{\frac{d}{dt} CI_j(t_i)}{1 - CI_{TOT}(t_i)}$$

where we approximated the derivative of cumulative incidence as

$$\frac{d}{dt} CI_j(t_i) \approx \frac{CI_j(t_{i+1}) - CI_j(t_i)}{t_{i+1} - t_i}$$

and (t_i) is the sequence of event times.

The remaining LTFU consists in reality of the remaining five outcomes, which could not be ascertained with tracing. We assumed that the proportion of each of these outcomes among the

unascertained cases would be the same as among the ascertained LTFU cases. For each event among the remaining five outcomes, we therefore corrected the cause-specific hazard h_{corr} in the following way:

$$h_{corr}(t) = h_0(t) + ph_{LTFU}(t)$$

where h_0 is the hazard of the event without considering those whose outcomes were not ascertained, p the proportion of the event in question among ascertained LTFU cases and h_{LTFU} the hazard of unascertained LTFU.

In case of mortality, we further split the observed mortality into HIV-related mortality and non-HIV-related background mortality. We used the HIV-free age- and gender-specific background mortality rates for Malawi from the Global Burden of Disease study and calculated the theoretical average hazard of HIV-free mortality in the dataset in the following way:

$$h_{bgmort}(t) = \frac{\sum_i^N I(T_i > t) h_{GBD}(t + a_i; g_i)}{\sum_{i=1}^N I(T_i > t)}$$

where $h_{GBD}(a;g)$ is the HIV-free mortality for a person of age a and sex g, I an indicator function, a_i the baseline age of the patient, g_i the gender of the patient and T_i the time of censoring of the patient. We deducted this from the (corrected) all-cause mortality hazard to obtain the HIV-related mortality.

We then transferred all five hazard functions (HIV-related mortality; official transfer out; self-transfer out; ART discontinuation; irregular ART) back to cumulative incidence functions to fit them into distributions. We did this by applying the 'nls' nonlinear least square estimation function in R to each cumulative incidence function. For all other events except death, we fitted the cumulative incidence to a Weibull distribution (see details and definition in Section 3.1 of this appendix), which allows the hazard to either decrease or increase over time. In line with our previous modelling studies, we chose to fit the mortality into a double-Weibull distribution (i.e. weighted sum of two Weibull distributions).

1.3 Success of tracing

In the second analysis, we estimated the success of tracing patients and bringing those outside care back to ART. We used the same dataset as in the previous analysis. We included all episodes where the patient was confirmed to have missed an appointment: we also allowed the same patient to have multiple episodes. A total of 5214 confirmed missing appointments of 4139 patients were included. Of these missed appointments, 3381 cases (70%) were successfully traced and the outcome was ascertained.

We further studied the return rate of the patients who were expected to come back to the clinic. We conducted a survival analysis from being found to returning back to ART care among patients who discontinued ART and patients on irregular ART separately. The results were fitted to a Weibull distribution using the STATA regression analysis 'streg' with parametric Weibull distribution and no covariables.

2 Description of the mathematical model 'gems'

2.1 Disease progression

The mathematical simulation model 'gems' is an R package, which is available on CRAN[1]. The model simulates individual patients starting at a fixed point of time until the maximum follow-up time is reached. The progression of the patients is represented by states and transitions. Let us denote the states S_i and transitions T_{ij} where $i,j = 1,\ldots,n$ and n is the total number of states. The transition T_{ij} represents the patient's progression from state S_i to S_j ($i \neq j$) and is determined in one of the following three ways:

- T_{ij} is *impossible*, if it is not possible to move directly from S_i to S_j
- T_{ij} is defined using a *hazard function* h_{ij}
- T_{ij} is defined by giving the *time to event* t_{ij} explicitly

Backward transitions are always impossible: if $i<j$, it is not allowed to return from S_j back to S_i.

All patients start in state S_1. Let us denote $J_1 = \{j = 2,\ldots,n \mid T_{1j} \text{ is possible}\}$. For each j in J_1 a corresponding transition time t_{1j} is determined, either directly (if T_{1j} is defined by giving the time to event explicitly) or by sampling a time from the distribution determined by h_{1j}. The minimum over j of the times t_{1j} determines the time and next state the patient moves to. At this next state S_j, the process is repeated again. This procedure is repeated as long as the patient reaches an absorbing state (i.e. either the last state S_n or a state S_i where T_{ij} is impossible for all $j>i$) or the given maximum follow-up time is reached.

The main model consists of 113 states. The schematic representation in the main text (Figure 1) is therefore a simplification. Each of the 13 boxes shown in the figure is a group of states, where the status according to retention is common. Most of the groups can be divided further into states according to other properties that are less relevant to the research question. Groups where the patient is receiving ART include 13 states according to ART regimen (1st or 2nd line), presence of

virologic failure as well as presence, reason and observation of immunologic failure. Groups representing death are divided into HIV-related and HIV-unrelated death states according to the cause of death. Table S4 shows a full description of all states and the possible transitions.

2.2 Evaluation of transmission

The package 'gems' produces a cohort table, which includes the times of entering each state for each simulated patient. We created for each patient a continuous viral load trajectory based on the transition times to evaluate the potential for transmission to sexual partners.

We started by defining for each patient four levels of viral load: baseline (at the beginning of the simulation), suppressed (on ART without virologic failure), failing (on ART with present virologic failure) and off-ART. Suppressed viral load was assumed to be 10 copies/ml in all cases; all other viral load values were sampled from distributions. When an event affecting the patient's viral load status happened, the viral load decreased or increased linearly on the $\log_{10}$ scale within the next 1 to 2 months to the new level. The only exception was a rapid treatment failure: if the patient's virologic failure time was within 6 months of ART start (1st line) or switching (2nd line), we assumed that the viral load did not decrease to suppressed in the meantime, but remained on the previous level (baseline or failing). The aim of this was to represent non-response. We assumed that patients on irregular ART had also suppressed viral load, since the majority of these patients were reported to be on ART without gaps. The role of this assumption on the outcomes of the study was tested in a sensitivity analysis.

We assumed that each patient changed partners at the end of every year and had unprotected sex 100 times a year. The per-act transmission probability at time t, $p(t)$, was calculated using a formula by Wilson *et al*[2]:

$$p(t) = p_0 C^{\log_{10}\frac{V(t)}{V_0}},$$

where p_0 is the risk of transmission with a reference viral load V_0 and C=2.45 a constant. Since each partnership began and ended at the beginning and end of the same year, respectively, the expected number E of transmissions from a patient during a particular year could be calculated

$$E = 1 - \prod_{i=1}^{100} \left(1 - p(t_i)\right)$$

where the time points t_i are distributed evenly across the year.

3 Parameterisation of the model

3.1 Distributions and hazard functions

The key parameters of the model are shown in Table 1 of the main text. Table S5 shows additional parameters that were used in the model but are less relevant for the research question.

Most transitions were parameterised using a Weibull distribution. We used the parameterisation

$$h(t) = \left(\frac{k}{\lambda}\right)\left(\frac{t}{\lambda}\right)^{k-1}$$

where h is the hazard function, k the shape parameter, λ the scale parameter and t the time calculated from a desired origin. Note that the origin of t is often not equal to the time of entry into the state; therefore, in most cases the distribution we used could be more accurately called a shifted Weibull distribution. Exponential distribution is a special case of a Weibull distribution (k = 1). Moreover, we also used a generalization of the Weibull distribution, the double Weibull distribution, which is a weighted sum of two Weibull distributions with different shape and scale parameters.

For all events that could be either registered or not registered, we used the following approach to split the hazard function into separate hazards of the registered and not registered events. Let h be the hazard function of the event and p the probability that the event is immediately registered. Moreover, for simplicity let us assume that the time variable t is counted from the start of the current state. Since the event E itself and its correct registration are assumed to be independent, the probability that the event has happened before time t and that it was correctly registered is

$$P(T_E < t \cap E \text{ registered}) = P(T_E < t)P(E \text{ registered}) = CI_E(t)p = p\left(1 - e^{-\int_0^t h_E(\tau)d\tau}\right)$$

This is by definition the cumulative incidence function of the correctly registered event. Further we can calculate the hazard function for the correctly registered event h_{ER}:

$$h_{ER}(t) = \frac{\frac{d}{dt} p\left(1 - e^{-\int_0^t h_E(\tau) d\tau}\right)}{1 - p\left(1 - e^{-\int_0^t h_E(\tau) d\tau}\right)} = \frac{ph(t)}{1 - p + pe^{-\int_0^t h_E(\tau) d\tau}}$$

3.2 Mortality

Mortality consisted of two components: HIV-related and HIV-unrelated mortality. For HIV-unrelated mortality, we used the age- and gender-specific HIV-free mortality rates for Malawi from the Global Burden of Disease study. HIV-related mortality was parameterised using a double Weibull distribution according to the estimates from the data analyses, described in Section 1.2 of this appendix. Time of ART start was used as the origin of time for HIV-related mortality. In states where the patient was in care, both HIV-related and HIV-free mortality were further split into registered and unregistered according to the approach given in Section 3.1 of this appendix.

In addition to the regular risk, we assumed that the risk of HIV-related death would increase after virologic and immunologic treatment failures. The hazard of HIV-related mortality was multiplied with a constant hazard ratio when a virologic or immunologic failure was present. When the patient was off ART, both hazard ratios (for virologic and immunologic failure) were applied since it could be expected that patients not on ART would have a high viral load and low CD4 cell count.

3.3 ART discontinuation, irregular ART and transfer-out

The remaining events related to retention (official transfer out, self-transfer out, irregular ART, ART discontinuation) were assumed to be Weibull distributed. The parameters were taken directly from the data analyses. We did not assume any association between treatment success and these events.

We were not able to assess the rate of spontaneous return to care without tracing, since the dataset was confounded by tracing. Kranzer *et al* found a return rate of 21.4/100 person-years in a South African cohort study[3]. However, patients returning less than a month after running out of antiretrovirals were excluded from this estimate and we therefore chose a higher rate, 33.3/100 person-years and tested a lower rate (1.0/100 person-years) in a sensitivity analysis.

3.4 Treatment failures and their consequences

We used estimates from a previous modelling study to evaluate the virologic and immunologic success of therapy. Time to virologic failure was assumed to be Weibull distributed starting 3 months after ART start (1st-line) or switch (2nd-line). In addition, a resistance penalty factor was applied if the patient had previously been on failing ART or off ART. We used an estimate based on Kimmel *et al*[4] for the resistance penalty due to time spent on failing ART and assumed that the penalty would be twice as high if the patient was completely off ART. The resistance penalty reduces the time from ART start to first-line treatment failure and from switch to second-line ART to second-line virologic failure. If *t'* is the time from 3 months after starting the current regimen to failure sampled without taking into account resistance penalty, the corrected time *t* is calculated

$$t = e^{-p_S \Delta t_S - p_F \Delta t_F} t'$$

where p_S and p_F are the resistance penalty coefficients and Δt_S and Δt_F the times spent off ART and on failing ART, respectively.

Immunologic failure was split into two events: immunologic failure as a consequence of virologic failure, and immunologic failure independent of virologic failure. The former was assumed to follow an exponential distribution after virologic failure, and the latter a Weibull distribution from 3 months after ART start. Immunologic failure as a consequence of 1st-line virologic failure remained only until switching, whereas independent immunologic failure remained for the rest of the follow-up time.

3.5 Transmission

We assumed an exponential relationship between individual $\log_{10}$ viral load at time of sex act and the probability of transmission. The parameters for the risk were adapted from Wilson *et al*[2], using the results of the Rakai study from Uganda[5]. Parameters related to sexual behaviour (one-year partnership, 100 sex acts per year) were based on our assumptions and chosen to correspond to

those of our previous study[6]. In addition, we assumed that a fraction of the partners would be already infected at the beginning of the partnership. Based on reported estimates from Malawi[7], we assumed a prevalence of 15% for all partners except for the first one. For the first partnership, we assumed that 30% of the partners would be already infected.

References

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Table S1. Possible outcomes of tracing patients lost to follow-up. "Outcome in dataset" refers to the name of the outcome used by the tracing team and recorded in the data. "Outcome in paper" is the name of the corresponding outcomes that is used in this paper (see Table 1 of the main text).

Code	Outcome in dataset	Outcome in paper	Explanation
Not found, outcome not ascertained			
4	Not traced	n/a	Patient is not found
5	Tracing rejected	n/a	Patient lives outside Lilongwe urban area and is therefore not traced
6	No FU attempt	n/a	Patient is not traced because of lack of time and/or resources
12	Refused	n/a	Patient has not given permission to be traced
Found, outcome ascertained			
7	Dead	Death	Patient has died
8	TFO silent	Self-transfer	Patient is found on another ART clinic without informing the original clinic
9	TFO official	Official transfer	Patient is found on another ART clinic
10	Stop ARV self	ART discontinuation	Patient has discontinued taking ARVs himself/herself
11	Stop ARV official	ART discontinuation	Patient has discontinued taking ARVs due to clinician's decision
13	Never started ARVs	ART discontinuation	Patient has never started taking ARVs
14	On ARV gaps	Irregular ART	Patient takes ARVs less than prescribed (the drugs last longer)
15	On ARV no gaps	Irregular ART	Patient receives ARVs from unofficial sources (friends, relatives, unlicensed vendors)

n/a, not applicable; FU, follow-up; TFO, transfer out; ART, antiretroviral therapy; ARV, antiretroviral drug

Table S2. Baseline characteristics of 'Back-to-Care' cohort (n=23,137)

	n (%)
Sex	
Male	9820 (42.4%)
Female	13317 (57.6%)
Age	
16 - <20	324 (1.4)
20 - <25	1620 (7.0)
25 - <30	4247 (18.4)
30 - <35	5463 (23.6)
35 - <40	4565 (19.7)
40 - <45	3001 (13.0)
45 - <50	1877 (8.1)
50 - <55	1047 (4.5)
55 - <60	600 (2.6)
≥60	393 (1.7)
Clinic	
Lighthouse Clinic	12703 (54.9)
Martin Preuss Centre	10434 (45.1)
Reason to start ART	
CD4 below threshold	6089 (26.3)
WHO stage 3	12678 (54.8)
WHO stage 4	4148 (17.9)
Pregnancy	2 (0.0)
Information missing	220 (1.0)

ART, antiretroviral therapy; WHO, World Health Organization

Table S3. Patient outcomes at the end of follow-up and tracing efforts in the dataset. Tracing codes refer to Table S1.

	n (%)
Outcomes at the end of follow-up (n=23,317)	
Alive and on ART at the original clinic (LH or MPC)	13302 (57.5%)
Alive and on ART at another official ART provider (transferred out)	4335 (18.7%)
Dead	1706 (7.4%)
Alive but not on ART	539 (2.3%)
Lost to follow-up (outcome unknown at end of follow-up)	3262 (14.1%)
Traced patients and their outcomes (tracing code; n=4851)	
No tracing attempt (5, 6, 12)	129 (2.7%)
Tracing attempted but patient not found (4)	1341 (27.6%)
Tracing attempted and patient found, outcome:	
Dead (7)	999 (20.6%)
Transfer out, silent (8)	117 (2.4%)
Transfer out, official(9)	624 (12.9%)
Stop antiretrovirals, self (10)	824 (17.0%)
Stop antiretrovirals, official (11)	135 (2.8%)
Never started antiretrovirals (13)	17 (0.4%)
On antiretrovirals, gaps (14)	219 (4.5%)
On antiretrovirals, no gaps (15)	428 (8.8%)

ART, antiretroviral therapy; LH, Lighthouse; MPC, Martin Preuss Centre

Table S4. Full description of the states and possible transitions in the mathematical model.

State	ART regimen	Virologic failure	Immunologic failure	Failure observed	Type of death	States to which the transition is possible			
						Within group	To other groups	Tracing	Death
Alive and on ART									
1	1st	No	No	No	n/a	2,8	14,27,40,53,66,67	-	108,109,112,113
2	1st	Yes	No	No	n/a	3,9	15,28,41,54,66,67	-	108,109,112,113
3	1st	Yes	VL-related	No	n/a	4,9	16,29,42,55,66,67	-	108,109,112,113
4	1st	Yes	VL-related	Yes	n/a	5,11	17,30,43,56,66,67	-	108,109,112,113
5	2nd	No	No	n/a	n/a	6,12	18,31,44,57,66,67	-	108,109,112,113
6	2nd	Yes	No	n/a	n/a	7,13	19,32,45,58,66,67	-	108,109,112,113
7	2nd	Yes	VL-related	n/a	n/a	13	20,33,46,59,66,67	-	108,109,112,113
8	1st	No	Non-VL-rel	No	n/a	9,10	21,34,47,60,66,67	-	108,109,112,113
9	1st	Yes	Non-VL-rel	No	n/a	11	22,35,48,61,66,67	-	108,109,112,113
10	1st	No	Non-VL-rel	Yes	n/a	11,12	23,36,49,62,66,67	-	108,109,112,113
11	1st	Yes	Non-VL-rel	Yes	n/a	12	24,37,50,63,66,67	-	108,109,112,113
12	2nd	No	Non-VL-rel	n/a	n/a	13	25,38,51,64,66,67	-	108,109,112,113
13	2nd	Yes	Non-VL-rel	n/a	n/a	-	26,39,52,65,66,67	-	108,109,112,113
Official transfer out, unregistered									
14	1st	No	No	No	n/a	15,21	53,66	69	108,109
15	1st	Yes	No	No	n/a	16,22	54,66	70	108,109
16	1st	Yes	VL-related	No	n/a	17,22	55,66	71	108,109
17	1st	Yes	VL-related	Yes	n/a	18,24	56,66	72	108,109
18	2nd	No	No	n/a	n/a	19,25	57,66	73	108,109
19	2nd	Yes	No	n/a	n/a	20,26	58,66	74	108,109
20	2nd	Yes	VL-related	n/a	n/a	26	59,66	75	108,109
21	1st	No	Non-VL-rel	No	n/a	22,23	60,66	76	108,109
22	1st	Yes	Non-VL-rel	No	n/a	24	61,66	77	108,109
23	1st	No	Non-VL-rel	Yes	n/a	24,25	62,66	78	108,109
24	1st	Yes	Non-VL-rel	Yes	n/a	25	63,66	79	108,109
25	2nd	No	Non-VL-rel	n/a	n/a	26	64,66	80	108,109
26	2nd	Yes	Non-VL-rel	n/a	n/a	-	65,66	81	108,109
Self-transfer out									
27	1st	No	No	No	n/a	28,34	53,66	69	108,109
28	1st	Yes	No	No	n/a	29,35	54,66	70	108,109
29	1st	Yes	VL-related	No	n/a	30,35	55,66	71	108,109
30	1st	Yes	VL-related	Yes	n/a	31,37	56,66	72	108,109
31	2nd	No	No	n/a	n/a	32,38	57,66	73	108,109
32	2nd	Yes	No	n/a	n/a	33,39	58,66	74	108,109
33	2nd	Yes	VL-related	n/a	n/a	39	59,66	75	108,109
34	1st	No	Non-VL-rel	No	n/a	35,36	60,66	76	108,109
35	1st	Yes	Non-VL-rel	No	n/a	37	61,66	77	108,109
36	1st	No	Non-VL-rel	Yes	n/a	37,38	62,66	78	108,109
37	1st	Yes	Non-VL-rel	Yes	n/a	38	63,66	79	108,109
38	2nd	No	Non-VL-rel	n/a	n/a	39	64,66	80	108,109

39	2nd	Yes	Non-VL-rel	n/a	n/a	-	65,66	81	108,109
Official transfer out, registered									
40	1st	No	No	No	n/a	41,47	53,66,67	-	108,109,112,113
41	1st	Yes	No	No	n/a	42,48	54,66,67	-	108,109,112,113
42	1st	Yes	VL-related	No	n/a	43,48	55,66,67	-	108,109,112,113
43	1st	Yes	VL-related	Yes	n/a	44,50	56,66,67	-	108,109,112,113
44	2nd	No	No	n/a	n/a	45,51	57,66,67	-	108,109,112,113
45	2nd	Yes	No	n/a	n/a	46,52	58,66,67	-	108,109,112,113
46	2nd	Yes	VL-related	n/a	n/a	52	59,66,67	-	108,109,112,113
47	1st	No	Non-VL-rel	No	n/a	48,49	60,66,67	-	108,109,112,113
48	1st	Yes	Non-VL-rel	No	n/a	50	61,66,67	-	108,109,112,113
49	1st	No	Non-VL-rel	Yes	n/a	50,51	62,66,67	-	108,109,112,113
50	1st	Yes	Non-VL-rel	Yes	n/a	51	63,66,67	-	108,109,112,113
51	2nd	No	Non-VL-rel	n/a	n/a	52	64,66,67	-	108,109,112,113
52	2nd	Yes	Non-VL-rel	n/a	n/a	-	65,66,67	-	108,109,112,113
On ART outside official providers									
53	1st	No	No	No	n/a	54,60	66,95	69	108,109
54	1st	Yes	No	No	n/a	55,61	66,96	70	108,109
55	1st	Yes	VL-related	No	n/a	61	66,97	71	108,109
56	1st	Yes	VL-related	Yes	n/a	63	66,98	72	108,109
57	2nd	No	No	n/a	n/a	58,64	66,99	73	108,109
58	2nd	Yes	No	n/a	n/a	59,65	66,100	74	108,109
59	2nd	Yes	VL-related	n/a	n/a	65	66,101	75	108,109
60	1st	No	Non-VL-rel	No	n/a	61	66,102	76	108,109
61	1st	Yes	Non-VL-rel	No	n/a	-	66,103	77	108,109
62	1st	No	Non-VL-rel	Yes	n/a	63	66,104	78	108,109
63	1st	Yes	Non-VL-rel	Yes	n/a	-	66,105	79	108,109
64	2nd	No	Non-VL-rel	n/a	n/a	65	66,106	80	108,109
65	2nd	Yes	Non-VL-rel	n/a	n/a	-	66,107	81	108,109
ART discontinuation, unregistered									
66	None	n/a	n/a	n/a	n/a	-	95-107	68	108,109
ART discontinuation, registered									
67	None	n/a	n/a	n/a	n/a	-	95-107	-	108,109,112,113
In tracing process, not on ART									
68	None	n/a	n/a	n/a	n/a	-	68-106	-	108,109,112,113
In tracing process, on ART									
69	1st	No	No	No	n/a	70,76	82,95	-	108,109,112,113
70	1st	Yes	No	No	n/a	71,77	83,96	-	108,109,112,113
71	1st	Yes	VL-related	No	n/a	72,77	84,97	-	108,109,112,113
72	1st	Yes	VL-related	Yes	n/a	73,79	85,98	-	108,109,112,113
73	2nd	No	No	n/a	n/a	74,80	86,99	-	108,109,112,113
74	2nd	Yes	No	n/a	n/a	75,81	87,100	-	108,109,112,113
75	2nd	Yes	VL-related	n/a	n/a	81	88,101	-	108,109,112,113
76	1st	No	Non-VL-rel	No	n/a	77,78	89,102	-	108,109,112,113
77	1st	Yes	Non-VL-rel	No	n/a	79	90,103	-	108,109,112,113
78	1st	No	Non-VL-rel	Yes	n/a	79,80	91,104	-	108,109,112,113

79	1st	Yes	Non-VL-rel	Yes	n/a	80	92,105	-	108,109,112,113
80	2nd	No	Non-VL-rel	n/a	n/a	81	93,106	-	108,109,112,113
81	2nd	Yes	Non-VL-rel	n/a	n/a	-	94,107	-	108,109,112,113
Back in care through tracing									
82	1st	No	No	No	n/a	83,89	-	-	108,109,112,113
83	1st	Yes	No	No	n/a	84,90	-	-	108,109,112,113
84	1st	Yes	VL-related	No	n/a	85,90	-	-	108,109,112,113
85	1st	Yes	VL-related	Yes	n/a	86,92	-	-	108,109,112,113
86	2nd	No	No	n/a	n/a	87,93	-	-	108,109,112,113
87	2nd	Yes	No	n/a	n/a	88,94	-	-	108,109,112,113
88	2nd	Yes	VL-related	n/a	n/a	94	-	-	108,109,112,113
89	1st	No	Non-VL-rel	No	n/a	90,91	-	-	108,109,112,113
90	1st	Yes	Non-VL-rel	No	n/a	92	-	-	108,109,112,113
91	1st	No	Non-VL-rel	Yes	n/a	92,93	-	-	108,109,112,113
92	1st	Yes	Non-VL-rel	Yes	n/a	93	-	-	108,109,112,113
93	2nd	No	Non-VL-rel	n/a	n/a	94	-	-	108,109,112,113
94	2nd	Yes	Non-VL-rel	n/a	n/a	-	-	-	108,109,112,113
Back in care spontaneously									
95	1st	No	No	No	n/a	96,102	-	-	108,109,112,113
96	1st	Yes	No	No	n/a	97,103	-	-	108,109,112,113
97	1st	Yes	VL-related	No	n/a	98,103	-	-	108,109,112,113
98	1st	Yes	VL-related	Yes	n/a	99,105	-	-	108,109,112,113
99	2nd	No	No	n/a	n/a	100,106	-	-	108,109,112,113
100	2nd	Yes	No	n/a	n/a	101,107	-	-	108,109,112,113
101	2nd	Yes	VL-related	n/a	n/a	107	-	-	108,109,112,113
102	1st	No	Non-VL-rel	No	n/a	103,104	-	-	108,109,112,113
103	1st	Yes	Non-VL-rel	No	n/a	105	-	-	108,109,112,113
104	1st	No	Non-VL-rel	Yes	n/a	105,106	-	-	108,109,112,113
105	1st	Yes	Non-VL-rel	Yes	n/a	106	-	-	108,109,112,113
106	2nd	No	Non-VL-rel	n/a	n/a	107	-	-	108,109,112,113
107	2nd	Yes	Non-VL-rel	n/a	n/a	-	-	-	108,109,112,113
Dead, unregistered									
108	n/a	n/a	n/a	n/a	HIV	-	-	110	-
109	n/a	n/a	n/a	n/a	Natural	-	-	111	-
Dead, in tracing process									
110	n/a	n/a	n/a	n/a	HIV	-	112	-	-
111	n/a	n/a	n/a	n/a	Natural	-	113	-	-
Dead, registered									
112	n/a	n/a	n/a	n/a	HIV	-	-	-	-
113	n/a	n/a	n/a	n/a	Natural	-	-	-	-

ART, antiretroviral therapy; n/a, not applicable; VL, viral load. Immunologic failure is separated into VL-related (consequence of virologic failure) and non-VL-related (can happen before or after virologic failure and will not be affected by switching). Death is separated into HIV (caused by HIV) and natural (from other causes, estimated by HIV-free mortality rates).

Table S5. Additional model parameters. The key parameters of the model are presented in Table 1 of the main text.

	Distribution and value	Source
Virologic failure (time from 3 months after ART start or switch)	Weibull with penalty	[6]
Shape	0.467	
Scale	330.47	
Resistance penalty for failing ART	0.05	
Resistance penalty for ART discontinuation	0.1	
Immunologic failure related to virologic failure (time from virologic failure)	Exponential	[6]
Rate	0.079	
Immunologic failure unrelated to virologic failure (time from 3 months after ART start)	Weibull	[6]
Shape	0.221	
Scale	$5.46*10^6$	
Effect of unsuccessful treatment on mortality	Hazard ratios	[6]
Present virologic failure	1.21	
Present immunologic failure	1.75	
Off ART	2.12	
Prevalence of HIV among partners	Percentage	Assumption
First partnership	30%	
Subsequent partnerships	15%	
CD4 cell measurement schedule	Interval between tests	Assumption
Regular measurements	6 months	
Measurement after suspected failure	3 months	

ART, antiretroviral therapy. Weibull distribution is parameterised using the following formula for cumulative incidence (*CI*): $CI(t) = 1 - e^{-\left(\frac{t}{\lambda}\right)^k}$, where k is the shape parameter and λ the scale parameter. Weibull distribution with penalty includes a resistance penalty factor, which increases the hazard depending on the time the patient spent previously with failing ART or without ART. If the resistance penalty factor is r, the time the patient spent with unsuccessful ART $\Delta\tau$ and the time to event sampled from the Weibull distribution is t', the true time to event will be $t = e^{-r\Delta\tau}t'$.

Table S6. Sensitivity analysis 1: Outcomes and potential transmission from simulated cohorts of 1000 patients with either no tracing, tracing after 6 months (Delayed tracing) or tracing immediately (Immediate tracing).

Outcome	Immediate tracing	Delayed tracing	No tracing
Loss to follow-up			
Unrecorded deaths	163 (138-186)	179 (155-200)	193 (169-213)
Unrecorded official transfers out	34 (21-48)	37 (28-49)	36 (24-47)
Self-transfers out	20 (12-30)	19 (10-28)	21 (13-31)
Irregular ART	63 (44-77)	63 (43-80)	67 (52-84)
Discontinuation of ART	224 (197-255)	229 (198-261)	237 (205-264)
Total*	459 (433-493)	462 (428-498)	461 (426-488)
No. of tracings attempted	440 (415-468)	383 (351-416)	0
Returned to care	196 (173-224)	177 (153-200)	157 (132-183)
HIV transmission			
Cohort viral load (10^6 copies/ml)**	9.6 (8.4-11.0)	10.1 (8.8-11.5)	10.9 (9.5-12.2)
No. of new infections	57.8 (52.8-64.7)	59.6 (54.0-66.6)	62.9 (56.9-68.8)

ART, antiretroviral therapy

Results are given as mean values over 100 model runs with 95% prediction intervals.

* Number of patients lost to follow-up at least once; patients were allowed to have at maximum one of the following events: unrecorded official transfer-out, self-transfer out, irregular ART, discontinuation of ART; and in addition to this, unrecorded death.

** Cohort viral load is defined as the sum of mean viral loads of all patients across the 5 years of follow-up.

Table S7. Sensitivity analysis 2: Outcomes and potential transmission from simulated cohorts of 1000 patients with either no tracing, tracing after 6 months (Delayed tracing) or tracing immediately (Immediate tracing).

Outcome	Immediate tracing	Delayed tracing	No tracing
Loss to follow-up			
Unrecorded deaths	159 (134-179)	172 (149-193)	192 (171-215)
Unrecorded official transfers out	37 (27-46)	36 (27-46)	37 (27-49)
Self-transfers out	20 (12-31)	21 (13-31)	21 (13-30)
Irregular ART	106 (88-126)	107 (84-127)	113 (92-133)
Discontinuation of ART	153 (130-173)	152 (135-170)	162 (140-184)
Total*	438 (414-469)	435 (402-461)	439 (411-462)
No. of tracings attempted	427 (403-460)	386 (356-409)	0
Returned to care	129 (106-150)	95 (78-111)	58 (45-71)
HIV transmission			
Cohort viral load (10^6 copies/ml)**	9.4 (8.1-10.7)	9.7 (8.4-11.3)	10.6 (8.5-12.6)
No. of new infections	56.8 (51.1-62.3)	58.3 (52.7-65.6)	61.7 (53.1-70.7)

ART, antiretroviral therapy

Results are given as mean values over 100 model runs with 95% prediction intervals.

* Number of patients lost to follow-up at least once; patients were allowed to have at maximum one of the following events: unrecorded official transfer-out, self-transfer out, irregular ART, discontinuation of ART; and in addition to this, unrecorded death.

** Cohort viral load is defined as the sum of mean viral loads of all patients across the 5 years of follow-up.