Supplementary Information for "Cost and cost-effectiveness of a real-world HCV treatment program among HIV-infected individuals in Myanmar"

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1.1 Valuation of coordination costs

Yangon coordination: To determine the proportion of the Yangon country coordination budget attributable to the HCV treatment program in Dawei, we first separated out the budget which was attributable to the full Dawei program. First, we divided the total MSF Yangon budget into personnel and non-personnel. Staff interviews were performed to determine what proportion of personnel effort was attributable to the Dawei program, by staff type. The personnel budget was allocated accordingly by multiplying the personnel costs for each staff type by their stated proportion effort attributable to Dawei. Non-personnel costs were allocated to the Dawei program as a proportion of the total budget (e.g. roughly 45% of the total budget was comprised of Dawei costs).

Among the Yangon budget estimated to be attributable to Dawei coordination, we estimated what proportion of these costs were associated with HCV-related activities based on the proportion of all consultations in Dawei which were for HCV treatment in 2017 (14%). We then divided the Dawei HCV program coordination budget estimate by the number of HCV consultations in 2017 to obtain a per HCV consultation Yangon coordination cost ($5.23/consultation).

Dawei Coordination: The Dawei HCV-related coordination costs were estimated through obtaining the remainder of the personnel, recurrent and some capital costs (shared office supplies allocated to proportion of staff) associated with the HCV program, after extracting specific costs attributable to direct HCV visits by type (e.g. laboratory visit, pharmacy visit, etc). Some capital costs were fully allocated to coordination, such as general support items including cold chain and energy equipment, furniture, spare parts for vehicles, and construction/rehabilitation costs for building maintenance. The per HCV consultation coordination cost was obtained from dividing the total HCV-related Dawei coordination cost by the number of HCV consultations ($6.59/consultation).

1.2 Valuation of GeneXpert for HCV-related activities

GeneXpert costs were first costed separately by capital costs, personnel costs, consumables, and overheads. Since the GeneXpert was utilized to test for HIV and tuberculosis in addition to HCV, we multiplied shared costs by the proportion of HCV viral load tests performed in 2017 out of the total number of tests run on the GeneXpert for 2017. HCV viral load tests performed internally using the GeneXpert accounted for 29% of the total number of tests performed on the GeneXpert at the MSF-Dawei clinic in 2017.

1.3 Background (non-HCV related) mortality rate calculation

As all patients were on ART at HCV treatment initiation, we estimated a weighted background non-HCV related mortality rate based on the CD4 cell count distribution among the cohort at HCV treatment initiation (stratified by <200, 200-350, 350-500, >500 cells/μL, see **Table S4**), and expected survival on ART by stage, assuming a 3-4 fold increase in lifespan if on ART [1, 2]. With this calculation, the estimated average lifespan *excluding* HCV-related mortality among the HIV infected cohort was 30 years, only slightly less (3-4 years) than the expected lifespan among the general population in Myanmar [3]. The background death rate was then calculated as 1/weighted life expectancy.

1.4 HCV/HIV coinfection disability weights calculation

HCV/HIV coinfection disability weights were calculated as [1-((1-HIV disability weight)*(1-HCV disability weight))]. We obtained relevant disability weights from the WHO Global Burden of Disease Study 2013 [4]. For the HIV disability weight for this analysis, we use the disability weight for ART (0.078), as all were on ART in the treatment cohort. Disability weights for DC (0.178) and HCC (0.451) were obtained directly from the GBD. No disability weights were available for HCV METAVIR stages, so the weight for mild abdominopelvic problem (0.011) was

used for stages F0/F1, moderate abdominopelvic problem (0.114) was used for CC, and the midpoint between these two values was used for F2 (0.063) [4, 5].

1.5 HCV screening sensitivity analysis calculations

For a given HCV seroprevalence, we estimate chronic prevalence by assuming that 16% of individuals spontaneously clear their infection (as calculated from cohort data as 1- [Total # individuals HCV RNA-positive / Total # individuals HCV Ab tested]), and the remainder proceed to chronic infection. The number of antibody tests that would need to be performed to identify one chronic HCV case was calculated as the total number of individuals in the population divided by the number that were HCV RNA-positive, the number of RNA tests required to identify a single chronic case of HCV was calculated as the number of HCV Ab-positive individuals divided by the number of HCV RNA-positive individuals. For example, if there were 1000 total individuals in our population under a HCV seroprevalence of 8%, 80 individuals would be HCV Ab-positive, 67 would be HCV RNA-positive (assuming that 16% of HCV Ab-positive individuals spontaneously clear their HCV infection). Therefore, for each HCV RNA infection, we would need to test approximately 14.9 individuals for HCV antibody and 1.2 individuals for HCV RNA to identify a single chronic case of HCV.

1.6 HCV reinfection rate sensitivity analysis calculations

While not accounted for in our primary modeling analysis, we performed a sensitivity analysis to examine the impact of reinfection on the cost-effectiveness of the treatment scenarios. We implement a fixed annual rate of reinfection (5% per year) into the model which does not change over time. As such this fixed rate neglects change in risk over an individual's life, or changes in risk of acquiring HCV through treatment scale up (the latter of which requires a dynamic model).

SUPPLEMENTARY FIGURES

Figure S1. Distribution of patient-level HCV treatment costs (in 2017 US$) by liver disease stage among HIV-infected individuals in Dawei, Myanmar. Non-cirrhotic includes F0-F3, defined by METAVIR scores determined by transient elastography (<11.0 kPa); Cirrhotic includes CC: compensated cirrhosis (≥11.0 kPa); DC: decompensated cirrhosis (≥11.0 kPa and Child-Pugh score ≥6).

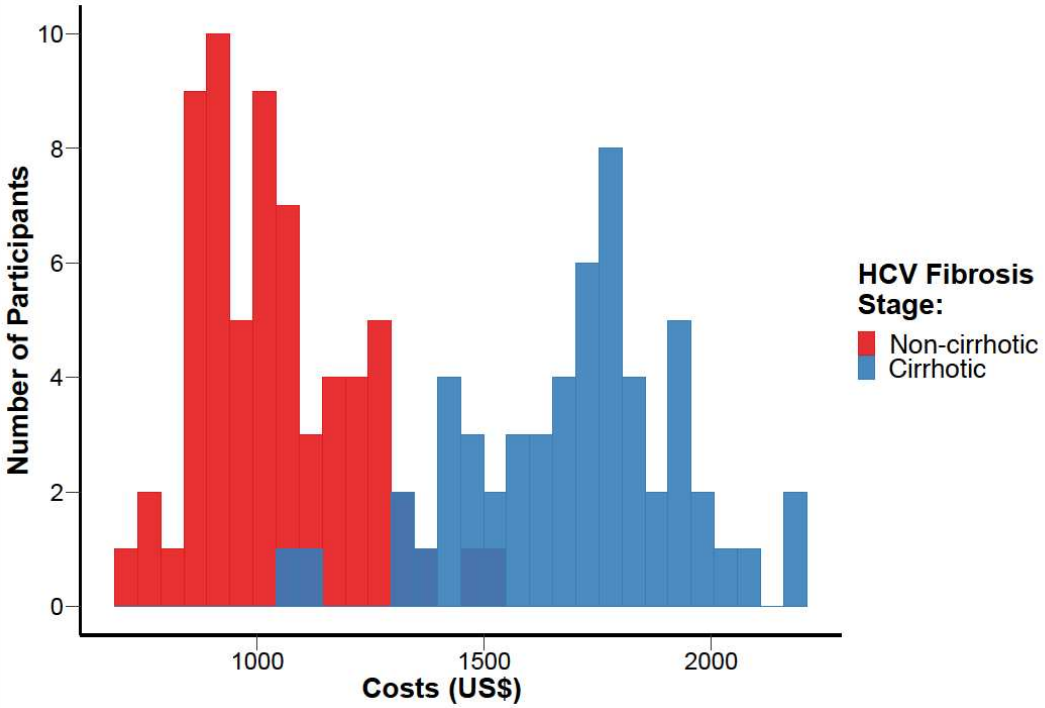


Figure S2. Sensitivity analysis of the cost-effectiveness of the "MSF updated DAA cost" model of care with 2018 DAA Access drug costs. 12-week Sofosbuvir/Daclatasvir treatment cost: US$120; 24-week Sofosbuvir/Daclatasvir treatment cost: US$240. DAA: direct-acting antiviral therapy; SVR: sustained virologic response at 12 weeks. Baseline parameter values are shown in Table 1. Fibroscan cost (US$3.89) reflects fibroscan cost estimated in similar setting (Cambodia, US$2017; $4.31; GDP-adjusted (Myanmar, US$1250/Cambodia, US$1385). Dark and light orange bars displayed when two values of a parameter were examined and resulted in ICER values lower and above the baseline ICER value (US$488).

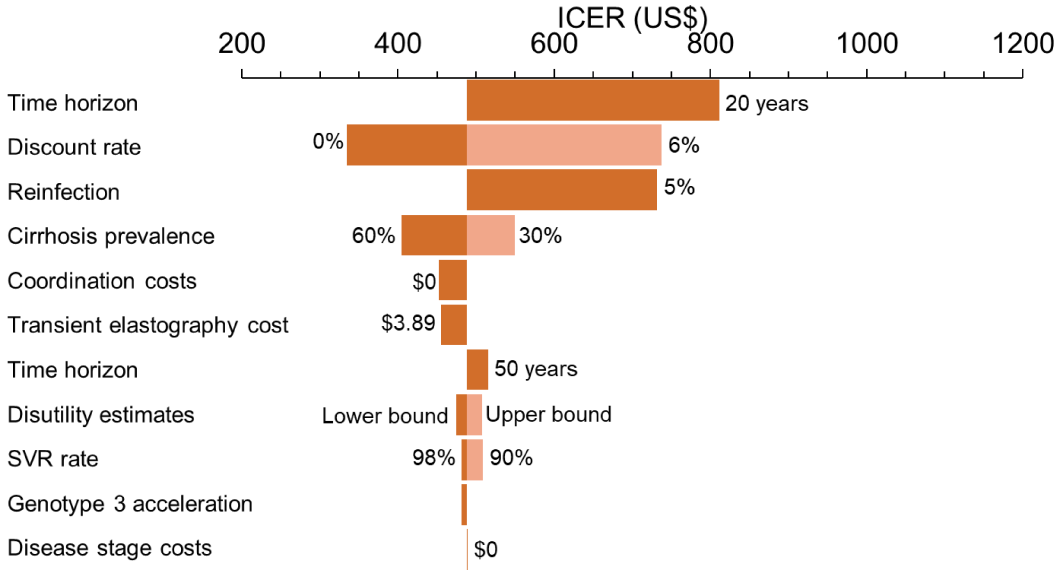


Figure S3. Sensitivity analysis of the cost-effectiveness of the "Simplified MoH" model of care with 2018 DAA costs. DAA: direct-acting antiviral therapy; SVR: sustained virologic response at 12 weeks. Task shifting to nurse-led care increased nurse-led consultations by 3 times. Dark and light green bars displayed when two values of a parameter were examined and resulted in ICER values lower and above the baseline ICER value (US$316).

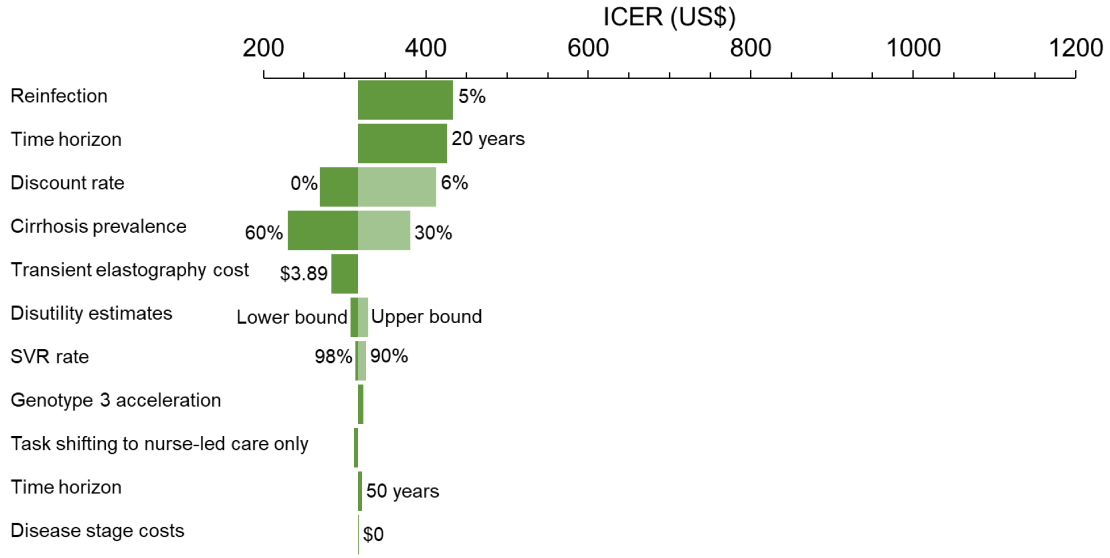
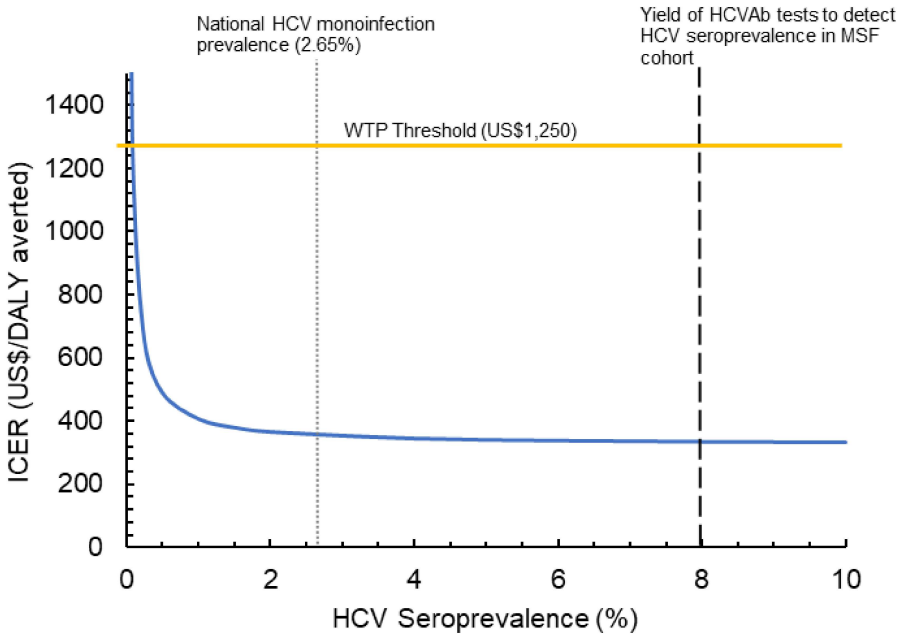


Figure S4. Incremental cost-effectiveness ratio (ICER) for HCV screening and treatment among HIV-infected individuals compared to no screening for various HCV seroprevalences. HCV treatment protocol examined is the proposed Myanmar Ministry of Health HCV treatment strategy. MSF cohort HCV seroprevalence (HCV Ab-positive) was 8%. ICER: incremental cost-effectiveness ratio; DALY: disability-adjusted life years; HCV: hepatitis C virus; Ab: antibody; MSF: Médecins sans Frontières.



SUPPLEMENTARY TABLES

Table S1. Unit cost in US$ of HCV therapy by drug type. 2017 drug costs are based on costs obtained from MSF invoices, which include MSF overhead charges. Updated unit drug costs from the Access campaign shown for sofosbuvir (400mg) and daclatasvir (60mg), excluding MSF overhead costs. †Ribavirin was not included in the Access campaign, but was prescribed in the "Observed MSF" intervention. Costs for Ribavirin were only included in the "Observed MSF" and "MSF with updated DAA costs" scenarios.

HCV treatment drug	2017 Cost	2018 Cost
Sofosbuvir (400mg)	3.52	1.04
Daclatasvir (60mg)	1.38	0.39
Ribavirin (200mg)	0.35	0.35†

Table S2. HCV treatment outcomes by liver fibrosis stage among cohort of HIV-infected patients in Dawei, Myanmar initiated on DAA treatment from 11/2016-10/2017. F0-F3 are METAVIR scores determined by transient elastography (<11.0 kPa); CC: compensated cirrhosis (≥11.0 kPa); HCV: hepatitis C virus; SVR: sustained viral response at 12 weeks; CC: compensated cirrhosis; DC: decompensated cirrhosis; HCC: hepatocellular carcinoma

HCV disease stage	N (% of total)	Number achieved SVR	SVR rate by HCV stage	Number failed treatment, lost-to-follow-up, or died
F0	39 (32%)	37	94.5%	2
F1	9 (7%)	8	88.9%	1
F2	6 (5%)	5	83.3%	1
F3	12 (10%)	11	91.7%	1
CC	54 (44%)	54	100%	0
DC	2 (2%)	2	100%	0
HCC	0 (0%)	0	-	0
Total	122 (100%)	117	95.9%	5

Table S3. Economic model parameters and their distributions. HCV: hepatitis C virus; SVR: sustained virologic response; ART: antiretroviral therapy; CC: compensated cirrhosis; DC: decompensated cirrhosis; HCC: hepatocellular carcinoma; GDP: gross domestic product. †2017 USD$

Variable	Sampled Value mean (95%CI)	Distribution and input parameters	Source
HCV disease stage costs† (annual)			
No hepatic fibrosis – F0	0	-	[6, 7] No Myanmar data; 2017 costs from Cambodia (Walker JG, unpublished) for F0-CC adjusted by GDP (Myanmar GDP $1250)/(Cambodia GDP $1385); Minimum/maximum values ±50% point estimate. Multiplier of 5.3 used from Cambodia cohort data for DC calculation; 6.5 for HCC.
Mild hepatic fibrosis– F1	34.87 (18.88, 51.85)	Uniform (min=17.64, max=52.92)	
Moderate hepatic fibrosis – F2	80.45 (41.89, 117.55)	Uniform (min=39.85, max=119.55)	
Severe hepatic fibrosis – F3	137.03 (71.72, 199.60)	Uniform (min=67.62, max=202.86)	
Compensated cirrhosis (F4, CC)	206.93 (109.23, 301.92)	Uniform (min=102.25, max=306.75)	
Decompensated cirrhosis (DC)	313.51 (161.53, 460.81)	Uniform (min=156.70, max=470.10)	
Hepatocellular carcinoma (HCC)	378.09 (202.34, 561.70)	Uniform (min=191.47, max=574.42)	
HIV care costs (annual)			
HIV care visit cost	191.70 (154.69, 227.36)	Uniform (min=152.74, max=229.12)	Dawei Cohort, including visit and ARV drug costs. See Table S4 for specific ARV costs. Bounds ±20% point estimate
Transition rates			
F0 to F1 (per year)	0.122 (0.094, 0.155)	Gamma (shape=61.95, scale=.00197)	[8]
F1 to F2 (per year)	0.115 (0.091, 0.142)	Gamma (shape=84.64, scale=0.00136)	[8]
F2 to F3 (per year)	0.124 (0.091, 0.16)	Gamma (shape=50.21, scale=0.0025)	[8]
F3 to CC (per year)	0.115 (0.096, 0.134)	Gamma (shape= 132.25, scale=0.0009)	[8]
CC to DC (per year)	0.039 (0.022, 0.062)	Beta (alpha=14.6168, beta=360.1732)	[5, 9-12] Transition probability sampled, converted to rate

CC or DC to HCC (per year)	0.015 (0.002, 0.04)	Beta (alpha=1.19326, beta=136.1074)	[5, 9-13] Transition probability sampled, converted to rate
Relative risk of CC to DC with SVR	0.078 (0.023, 0.190)	Lognormal (mean 0.07, 95%CI 0.03-0.2)	[14, 15]
Relative risk of CC/DC to HCC with SVR	0.236 (0.151, 0.352)	Lognormal (mean 0.23, 95%CI 0.16-0.35)	[16]
Background (non-HCV related) mortality	0.0336 (0.0292, 0.0378)	Uniform (min=0.029, max=0.038)	[1, 2] Weighted by CD4 status at HCV treatment initiation (Table S3), with all patients on ART as per cohort. See supplement for details.
Relative risk of DC to liver-related death in HIV/HCV coinfection compared to HCV monoinfection	2.3 (1.57, 3.38)	Lognormal (mean 2.26, 95%CI 1.51-3.38)	[5, 17-19]
DC to liver-related death for HCV monoinfection	0.130 (0.111, 0.150)	Beta (alpha=147.03, beta=983.97)	[9, 10] Transition probability sampled, converted to rate
HCC to liver-related death	0.429 (0.370, 0.482)	Beta (alpha=117.1, beta=155.23)	[5, 20-22] Transition probability sampled, converted to rate
SVR	96%	-	Dawei cohort
Discount rate	3%	-	[23]
Disability weights			
HCV/HIV coinfection (no SVR)			
F0/F1	0.088	-	Calculated as [1-((1-HIV disability weight)*(1-HCV disability weight))] using ART disability weight as all on ART in cohort. See supplement for details. [4, 5]
F2/F3	0.136	-	[5, 24]
Compensated cirrhosis (CC)	0.183	-	[4, 5]
Decompensated cirrhosis (DC)	0.242	-	[4, 5]
Hepatocellular carcinoma (HCC)	0.494	-	[4, 5]
HCV/HIV coinfection (achieved SVR)			
Disutility improvement on achieving SVR	0.045 (0.04, 0.05)	Uniform (min=0.05, max=0.05)	[25-27]

Table S4. Average unit cost in 2017 US$ of an HCV visit to Dawei clinic by cost category and visit component. Distribution of visit component by cost category expressed as row percentage. HCV: hepatitis C virus.

	Cost category		
Visit component	**Recurrent cost (%)**	**Personnel cost (%)**	**Capital cost (%)**
General coordination	20.31 (59.0)	13.46 (39.1)	0.66 (1.9)
HCV consultation	0.75 (65.2)	0.20 (17.7)	0.19 (17.1)
Laboratory	2.83 (90.5)	0.26 (8.4)	0.04 (1.2)
Pharmacy	0.22 (59.6)	0.13 (34.6)	0.02 (5.8)
HCV counselling	0.48 (74.2)	0.13 (20.2)	0.04 (5.6)

Table S5. Cost components by intervention scenario. †"Observed MSF intervention" presents summary data from observational study, including 2017 DAA prices. ‡"MSF with updated DAA costs" estimates costs with updated DAA prices for quality-assured generic DAAs negotiated in 2018. §"Simplified MoH" strategy estimates costs with generic DAAs and a proposed simplified protocol (Figure 1), with local staff costs and no overheads. HCV treatment costs are assumed to be standard for all patients ($120/12-week treatment course of sofosbuvir/daclatasvir for non-cirrhotic patients; $240/24-week treatment course of sofosbuvir/daclatasvir for cirrhotic patients). 95% confidence intervals are presented for the observed cost data reflecting patient variations in observed costs. For estimations of costs using updated cost data or simplified strategies, patients were assumed to adhere to the exact clinical schedule (see Fig 1) and so no uncertainty is provided. MSF: Médecins sans Frontières; DAA: direct-acting antiviral treatment; MoH: Ministry of Health; CI: confidence interval.

	Per patient cost (95% CI)		
Strategy	**HCV treatment**	**HIV treatment**	**HCV disease stage**
Baseline	0	2,306.63 (1,785.13, 2,868.67)	1,685.08 (1,106.88, 2,367.23)
Observed MSF treatment program†	1,563.92 (1,309.88, 1,855.96)	2,866.59 (2,252.05, 3,520.34)	1,682.21 (1,030.56, 2,346.50)
MSF program with updated DAA costs‡	1,076.13 (870.05, 1,314.11)	2,866.59 (2,252.05, 3,520.34)	1,682.21 (1,030.56, 2,346.50)
Simplified MoH§	501.50	2,866.59 (2,252.05, 3,520.34)	1,682.21 (1,030.56, 2,346.50)

Table S6. HIV characteristics of study participants at baseline enrollment (n=121). WHO HIV staging categories defined as: Stage 1: Asymptomatic; Stage 2: mildly symptomatic; Stage 3: moderately symptomatic; Stage 4: severely symptomatic/AIDS [28].TDF: Tenofovir (300mg daily); 3TC: Lamivudine (300mg daily); EFV: Efavirenz (600mg daily); AZT: Zidovudine (300mg twice daily); NVP: Nevirapine (200mg twice daily); ABC: Abacavir (600mg daily); LPV/r: Kaletra/ Lopinavir/Rionavir (400mg/100mg twice daily);

Characteristic	n	%
CD4 Count (cells/μL) upon HCV treatment initiation		
<200	13	10.7
200-350	23	18.9
350-500	24	19.7
>500	62	50.8
WHO HIV staging at HIV care enrollment		
Stage 1	10	8.3
Stage 2	20	16.5
Stage 3	73	60.3
Stage 4	17	14.1
Unknown	1	0.8
HIV treatment regimen		
AZT + 3TC + NVP	19	15.7
AZT + 3TC + EFV	5	4.1
TDF + 3TC + EFV	84	69.4
ABC + 3TC + EFV	3	2.5
LPV/r + 3TC + AZT	5	4.1
TDF + 3TC + LPV/r	4	3.3
AZT + TDF + 3TC + LPV/r	1	0.8

Table S7. Unit cost in US$ of HIV therapy by drug type. 2017 drug costs are based on costs obtained from MSF invoices, which include MSF overhead charges. TDF: Tenofovir (300mg daily); 3TC: Lamivudine (300mg daily); EFV: Efavirenz (600mg daily); AZT: Zidovudine (300mg twice daily); NVP: Nevirapine (200mg twice daily); ABC: Abacavir (600mg daily); LPV/r: Kaletra/ Lopinavir/Rionavir (400mg/100mg twice daily)

ARV regimen	2017 Cost (Annual)
AZT+3TC+NVP	34.23
AZT+3TC+EFV	54.32
TDF+3TC+EFV	79.40
ABC+3TC+EFV	152.45
LPV/r+3TC+AZT	239.63
TDF+3TC+LPV/r	219.00
AZT+TDF+3TC+LPV/r	301.08

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