

A Scalable, Integrated Intervention to Engage People Who Inject Drugs in HIV Care and Medication-Assisted Treatment: A Randomized, Controlled Vanguard Trial (HPTN 074)

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SUPPLEMENTAL MATERIALS

APPENDIX C: Additional Results and Figures

APPENDIX, PART 3, SUPPLEMENTAL RESULTS

Supplemental Table 1: Status transitions between 26 and 52 weeks, ART, viral suppression, and MAT			
	Status at 52 weeks*		
	Yes**	No	Deceased
	n (%)	n (%)	n (%)
<i>ART status at 26 weeks</i>			
Intervention			
On ART	73/79 (92%)	6/79 (8%)	0/79 (0%)
Not on ART	4/20 (20%)	16/20 (80%)	0/20 (0%)
SOC			
On ART	94/112 (84%)	8/112 (7%)	10/112 (9%)
Not on ART	40/175 (23%)	125/175 (71%)	10/175 (6%)
<i>MAT status at 26 weeks</i>			
Intervention			
On MAT	39/41 (95%)	2/41 (5%)	0/41 (0%)
Not on MAT	5/57 (9%)	52/57 (91%)	0/57 (0%)
SOC			
On MAT	61/77 (79%)	11/77 (14%)	5/77 (6%)
Not on MAT	14/210 (7%)	181/210 (86%)	15/210 (7%)

*Persons with missing visits are excluded for each time point (complete case analysis)

**Yes=On ART, Virally suppressed, or On MAT

Notes: Percentages reflect row percentages.

Abbreviations: ART=antiretroviral therapy; MAT=medication-assisted treatment; SOC=standard of care arm

Supplemental Table 2: Viral load categories, 26 and 52 weeks				
	Total	HIV RNA (copies/mL)		
		<40	40 to <1000	≥ 1000
		n (%)	n (%)	n (%)
<i>26 weeks</i>				
On ART	203	93 (46%)	36 (18%)	74 (36%)
Not on ART	216	2 (1%)	9 (4%)	205 (95%)
<i>52 weeks</i>				
On ART	220	120 (55%)	29 (13%)	71 (32%)
Not on ART	169	5 (3%)	10 (6%)	153 (91%)

Notes: Percentages reflect row percentages.

29 participants were deceased by week 26; 51 participants were deceased by week 52.

54 participants had missing data at week 26; 62 participants had missing data at week 52.

Abbreviations: ART=antiretroviral therapy

Supplemental Table 3: Viral load distributions for participants who were not virally suppressed, 26 and 52 weeks

	HIV RNA (copies/mL)					
	n	Median	10 th %ile	25 th %ile	75 th %ile	90 th %ile
<i>26 weeks</i>						
Intervention						
On ART	42	10846	61	204	82248	259184
Not on ART	24	24421	2735	6957	129590	232661
SOC						
On ART	68	10956	69	274	54522	324570
Not on ART	190	26586	2231	6692	99135	272691
<i>52 weeks</i>						
Intervention						
On ART	35	14765	64	526	49863	169553
Not on ART	24	23067	3159	12318	131650	218544
SOC						
On ART	65	16356	59	557	80168	251107
Not on ART	139	31673	1580	6041	85452	242103

Notes: complete case analyses are shown with missing data excluded.

Abbreviations: %ile=percentile; ART=antiretroviral therapy; SOC=standard of care arm

Supplemental Table 4: Status at 26 and 52 weeks and time to event for viral suppression (<1000 copies/mL)

	Status ¹ at 26 weeks			Status ¹ at 52 weeks			Time to Event ²
	Intervention	SOC	PR (95% CI)	Intervention	SOC	PR (95% CI)	HR (95% CI)
	Percentage	Percentage		Percentage	Percentage		
<i>Indexes</i>							
Viral suppression (<1000 copies/mL)	48%	26%	1.9 (1.4, 2.4)	51%	33%	1.5 (1.2, 1.9)	2.2 (1.6, 2.9)

Supplemental Table 5: Status transitions between 26 and 52 weeks, viral suppression

	Viral suppression status at 52 weeks (copies/mL)			
	<40	40 to <1000	VL≥1000	Deceased
	n (%)	n (%)		
<i>Viral suppression status at 26 weeks</i>				
<i>Intervention</i>				
VL <40 copies/mL	31 (79%)	5 (13%)	3 (8%)	0 (0%)
VL 40 to <1000 copies/mL	10 (83%)	2 (17%)	0 (0%)	0 (0%)
VL ≥1000 copies/mL	3 (6%)	4 (8%)	41 (85%)	0 (0%)
<i>SOC</i>				
VL <40 copies/mL	42 (82%)	4 (8%)	4 (8%)	1 (2%)
VL 40 to <1000 copies/mL	13 (46%)	7 (25%)	7 (25%)	1 (4%)
VL ≥1000 copies/mL	23 (11%)	15 (7%)	152 (73%)	18 (9%)

Notes: Missing values are excluded. Abbreviations: VL=viral load; SOC=standard of care

Supplemental Table 6: Mortality data, including causes of death

<i>Index Participants</i>		n/N (%)
Total deaths		66/502 (13%)
Intervention		9/126 (7%)
SOC		57/376 (15%)
<i>Causes of death</i>		n=66
		n (%)
HIV		17 (26%)
Unknown, CD4 cell count <200 cells/μl		16 (24%)
Unknown, CD4 cell count ≥200 cells/μl		12 (18%)
Medical, non-HIV		14 (21%)
Trauma		3 (5%)
Overdose		2 (3%)
Suicide		2 (3%)
<i>Partners</i>		n/N (%)
Total deaths		19/806 (2%)
Intervention		1/187 (1%)
SOC		18/619 (3%)
<i>Causes of death</i>		n=19
		n (%)
Unknown		4 (21%)
Medical, non-HIV		9 (47%)
Trauma		2 (11%)
Overdose		3 (16%)
Suicide		1 (5%)

Supplemental Table 7: Median viral loads, CD4 counts, and ART duration* at baseline, by site

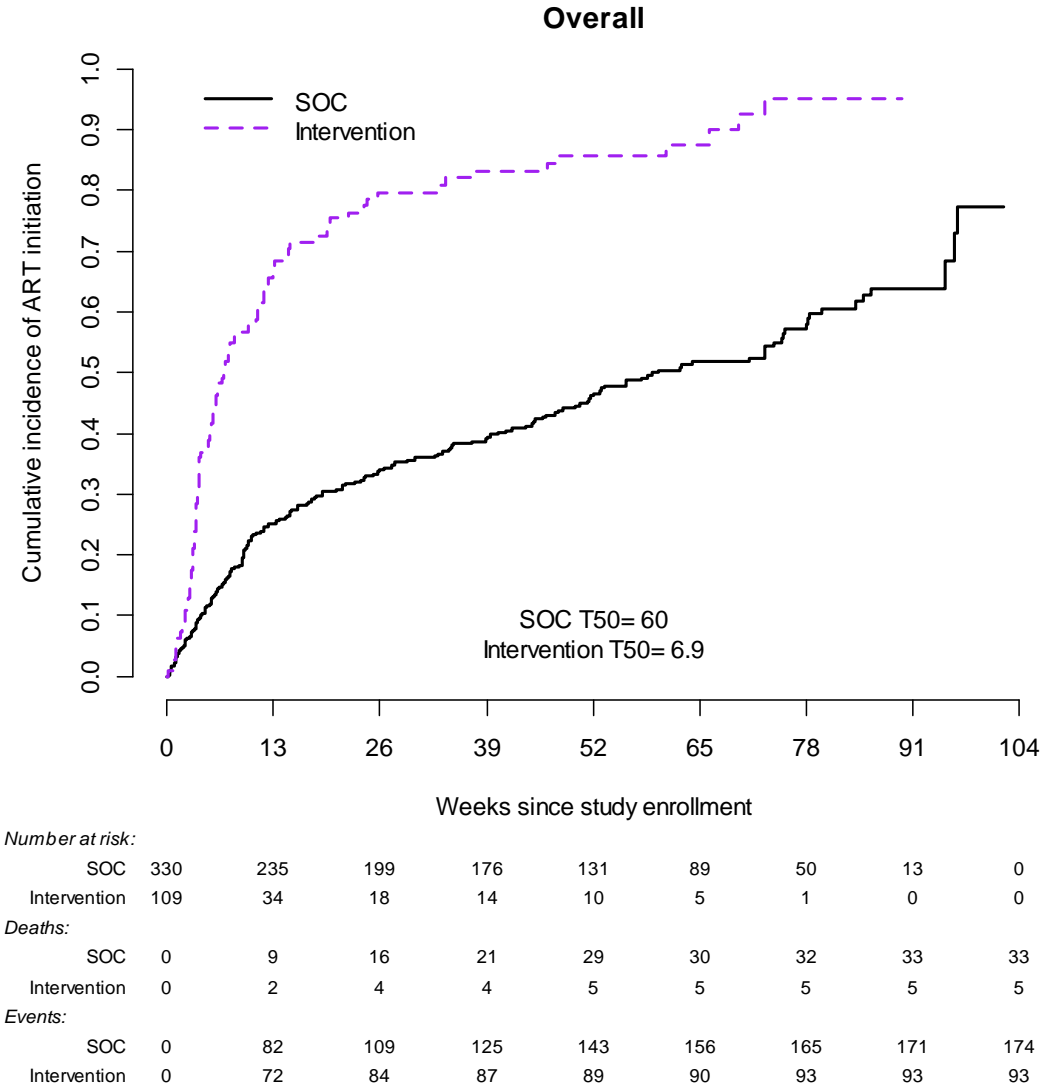
	Ukraine		Vietnam		Indonesia	
	Median	(IQR)	Median	(IQR)	Median	(IQR)
Viral load (copies/mL)	4.5	(3.8, 5.1)	4.6	(4.1, 5.0)	4.5	(4.2, 4.9)
CD4 count (cells/μl)	310	(178, 465)	314	(187, 492)	271	(147, 418)
Median ART duration (years)*	0.05	(0.01, 0.12)	0.15	(0.04, 2.0)	5.0	(1.2, 6.9)

*Only among those currently on ART (Ukraine, n=3; Vietnam, n=28; Indonesia, n=23)

Supplemental Table 8: Primary endpoints as listed in the HPTN 074 protocol, results and status

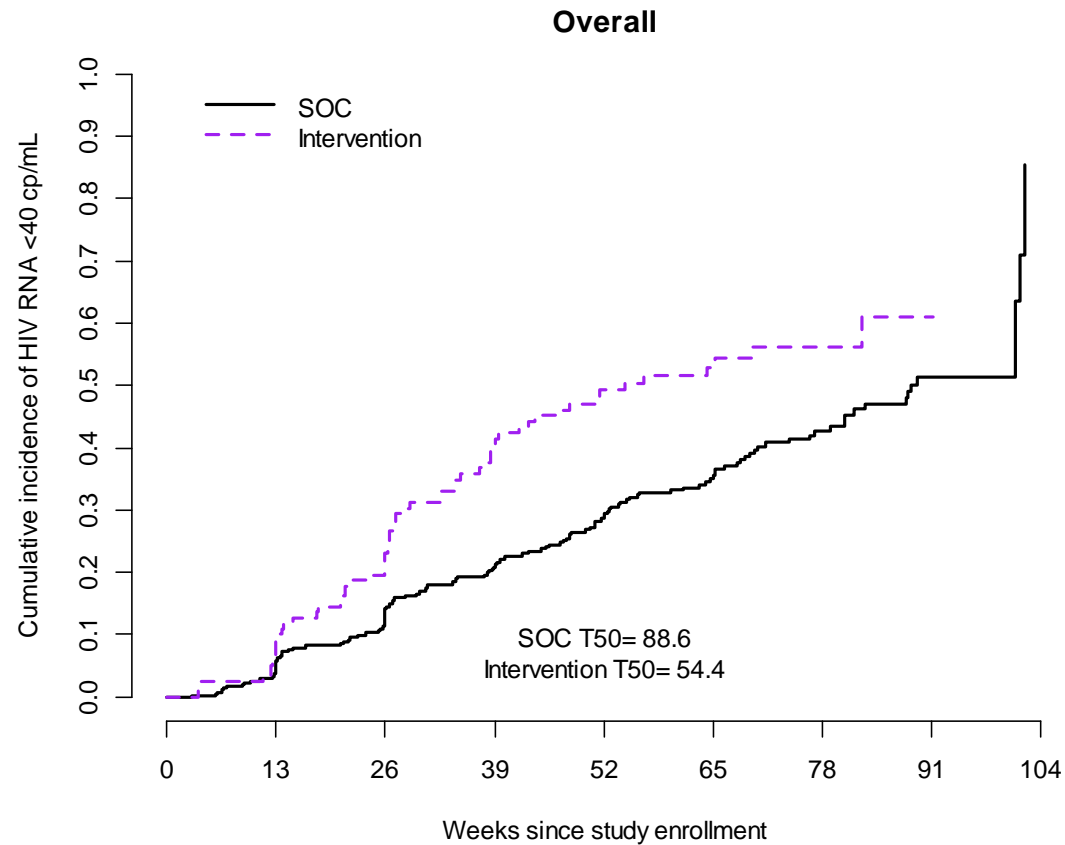
Primary Endpoints as listed in the HPTN 074 protocol	Results, Status, Comments
HIV incidence - Overall and by site HIV seroconversion rates of network injection partners in the standard of care arm	Overall incidence in the standard of care arm is presented in the text. Incidence rates were too low to compute meaningful site-specific incidence rates.
Enrolment and retention	These are operational endpoints intended to inform site-selection and accrual/follow-up timing when planning a larger trial.
1) Calendar time to enroll and allocate to study arm 500 eligible HIV-infected PWID overall and 167 eligible HIV-infected PWID by study site	Presented in text
2) Number of eligible HIV-uninfected network injection partners overall and at each site	Presented in text
3) Proportion of index participants retained at each visit overall and at each site	Retention at 52 weeks presented in text; retention by site available on request Week 4: 451/496 (91%) Week 13: 436/485 (90%) Week 26: 419/473 (89%) Week 39: 401/458 (88%)
4) Proportion of network injection partners, enrolled at index participant's allocation to study arm, retained at each visit overall and at each site	Retention at 52 weeks presented in text; retention by site available on request Week 4: 714/805 (89%) Week 13: 561/674 (83%) Week 26: 583/704 (83%) Week 39: 586/721 (81%)
5) Mean (SE) person years at risk accumulated per index participant overall and at each site	Median (IQR) person-years of follow-up among index participants: Overall: 1.3 (1.0, 1.7) Indonesia-SOC 1.2 (1.0, 1.5); Intervention 1.2 (1.0, 1.5) Ukraine – SOC 1.4 (1.2, 1.7); Intervention 1.4 (1.2, 1.7) Vietnam – SOC 1.4 (1.0, 1.7); Intervention 1.5 (1.2, 1.7)
Uptake measures, Intervention component: Systems navigators	These measures are intended to inform and refine the intervention for future trials and/or in clinical practice; Additional results will be presented in future manuscripts
1) Overall: Proportion of index participants using systems navigators at least once.	Presented in main text
2) Overall: Mean (standard error) number of contacts (text, email, telephone call, home visit, other) with index participants made with systems navigators (mean contacts per index participant)	Indonesia mean: 19; Ukraine mean: 4; Vietnam mean: 17
3) Use of navigators for ART: Mean (SE) number of contacts with HIV care sites made by systems navigators per index initiating ART.	Variation (proportion) presented in main text
4) Use of navigators for uptake of substance use treatment: Mean (SE) number of contacts with medication-assisted substance use treatment centers made by systems navigators per index initiating substance use treatment.	Variation (proportion): 124/1605 sessions (8%)
Uptake measures, Intervention component: Psychosocial counseling	These measures are intended to inform and refine the intervention for future trials and/or in clinical practice; Additional results will be presented in future manuscripts
1) Proportion of index participants completing two counseling sessions within four weeks of enrollment	Presented in main text
Uptake measures, Intervention component: Social network support	These measures are intended to inform and refine the intervention for future trials and/or in clinical practice; Additional results will be presented in future manuscripts
1) Proportion of index participants with an identified social support person within 13 and 52 weeks of enrollment	Results to be presented in future manuscript
2) Proportion of index participants completing a joint counseling session with an identified HIV medical care social support person within 13 and 52 weeks of enrollment	Results to be presented in future manuscript
Uptake measures, Intervention component: Substance use treatment	
1) Proportion of index participants self-reporting substance use treatment by 4 and 13 weeks	These results are presented graphically in the Appendix. Complementary results are presented in the main text.
2) Proportion of index participants with detectable methadone or buprenorphine at selected study visits	Laboratory testing for methadone and buprenorphine are not yet complete. These data will be analyzed and published separately.
Uptake measures, Intervention component: Supported ART	
1) Proportion of index participants self-reporting initiating ART by 4 and 13 weeks	These results are presented graphically in the Appendix. Complementary results are presented in the main text
2) Proportion of index participants on ART with detectable antiretroviral drugs at selected study visits	Laboratory-based ART assays are ongoing, and will be addressed in a separate manuscript.
3) Proportion of index participants who achieve virologic suppression by 26 and 52 weeks	Presented in text
Feasibility and Barriers	
Analyses for feasibility of and barriers to the intervention will be exploratory. Feasibility of the intervention will be assessed through individual semi-structured interviews with the systems navigators, counselors, additional stakeholders, and a subset of index participants randomized to the intervention arm. Barriers will be assessed through the barrier questionnaire with the participants, systems navigators' and counselors' data forms/log books, and interviews with additional stakeholders.	These qualitative results will be presented in a separate manuscript.

Supplemental Figure 1



Supplemental Figure 1: Cumulative incidence of ART initiation among indexes who reported that they were not on ART at baseline. T50 is the time in weeks when 50% of the participants had initiated ART. At each time point below the x-axis, the number remaining at risk is provided, as well as the number of accumulated deaths that occurred before ART initiation (i.e., death as a competing risk), and the number of accumulated events (people who initiated ART). Purple dashed line: intervention; black solid line: standard of care.

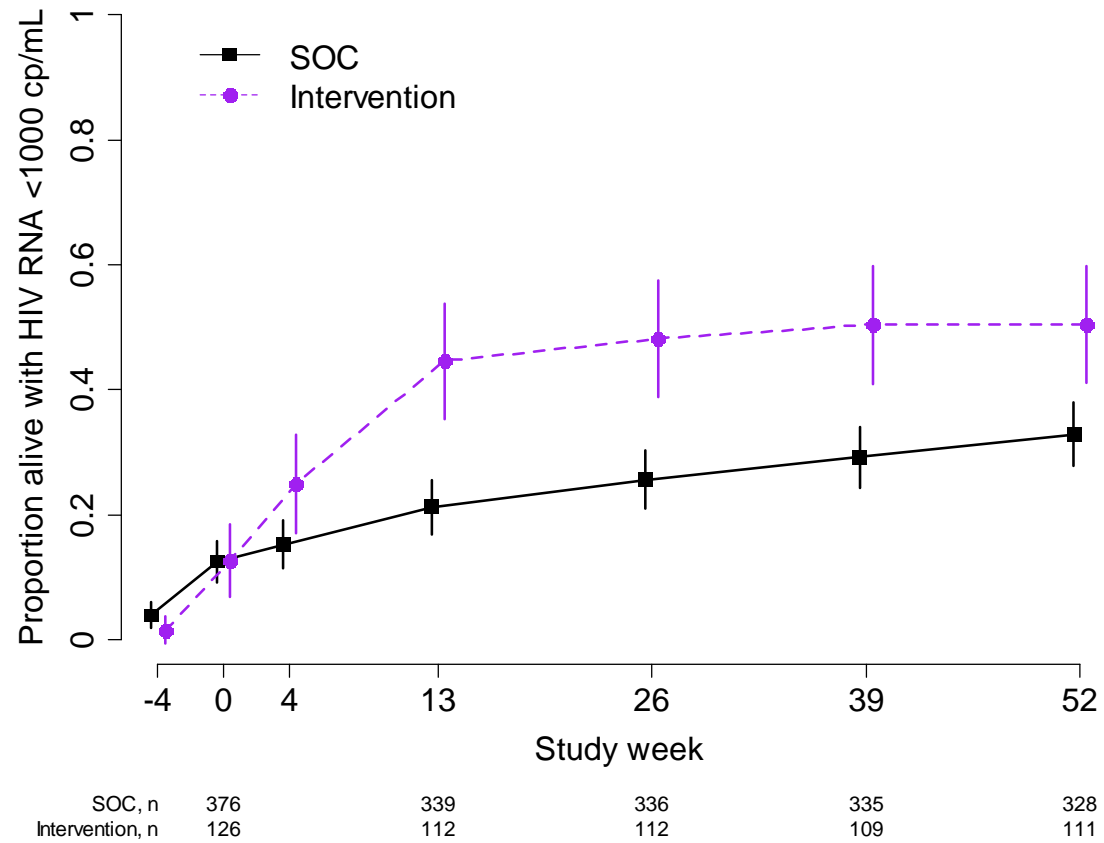
Supplemental Figure 2



<i>Number at risk:</i>		0	13	26	39	52	65	78	91	104
SOC	365	335	294	251	191	132	78	22	0	
Intervention	124	109	90	64	47	31	15	2	0	
<i>Deaths:</i>		0	13	26	39	52	65	78	91	104
SOC	0	10	19	29	42	44	47	49	51	
Intervention	0	3	6	6	7	7	8	9	9	
<i>Events:</i>		0	13	26	39	52	65	78	91	104
SOC	0	21	49	72	95	111	124	133	137	
Intervention	0	12	27	47	55	58	60	61	61	

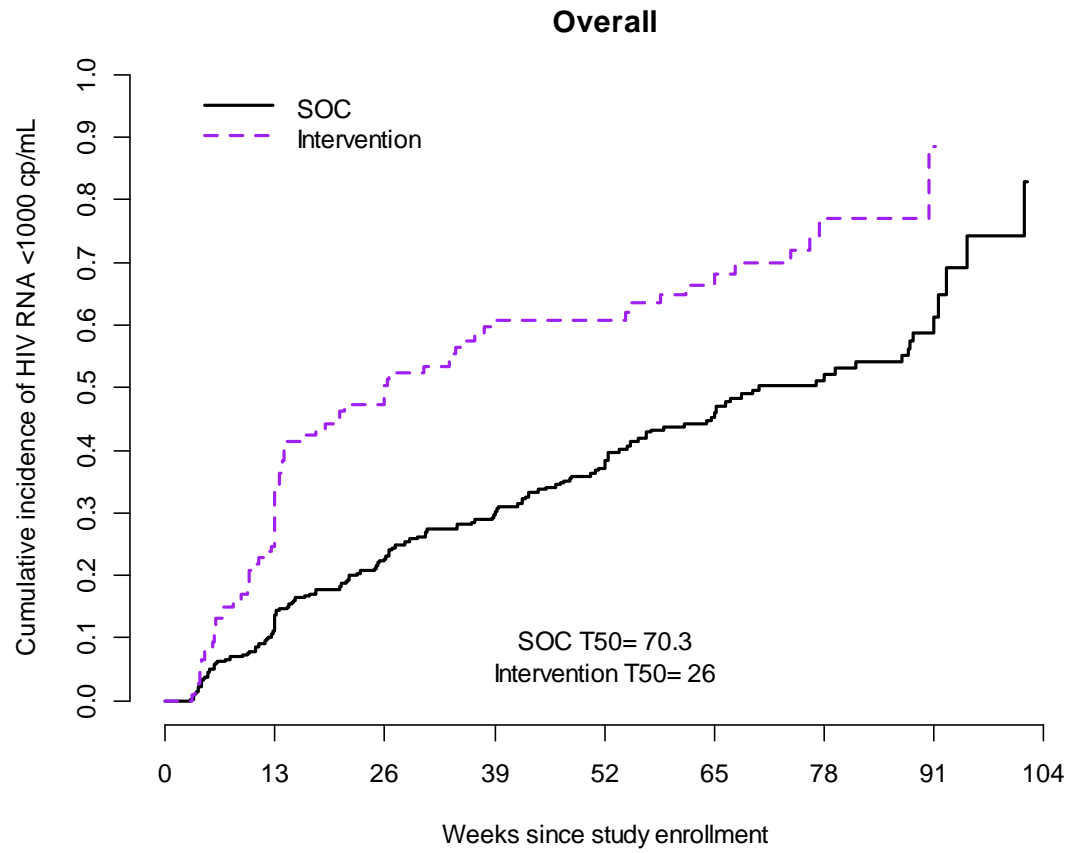
Supplemental Figure 2: Cumulative incidence of viral suppression (HIV RNA <40 copies/mL) among indexes who were not virally suppressed at baseline. T50 is the time in weeks for 50% of the population to become virally suppressed. At each time point below the x-axis, the number remaining at risk is provided, as well as the number of accumulated deaths that occurred before viral suppression (i.e., death as a competing risk), and the number of accumulated events (people who achieved HIV RNA <40 cp/mL). Purple dashed line: intervention; black solid line: standard of care. cp/ml = copies/mL

Supplemental Figure 3



Supplemental Figure 3 Proportion of indexes alive and virally suppressed with HIV RNA <1000 copies/mL. 95% confidence intervals are calculated with the Wald method. Purple dashed line: intervention; black solid line: standard of care. cp/ml = copies/mL

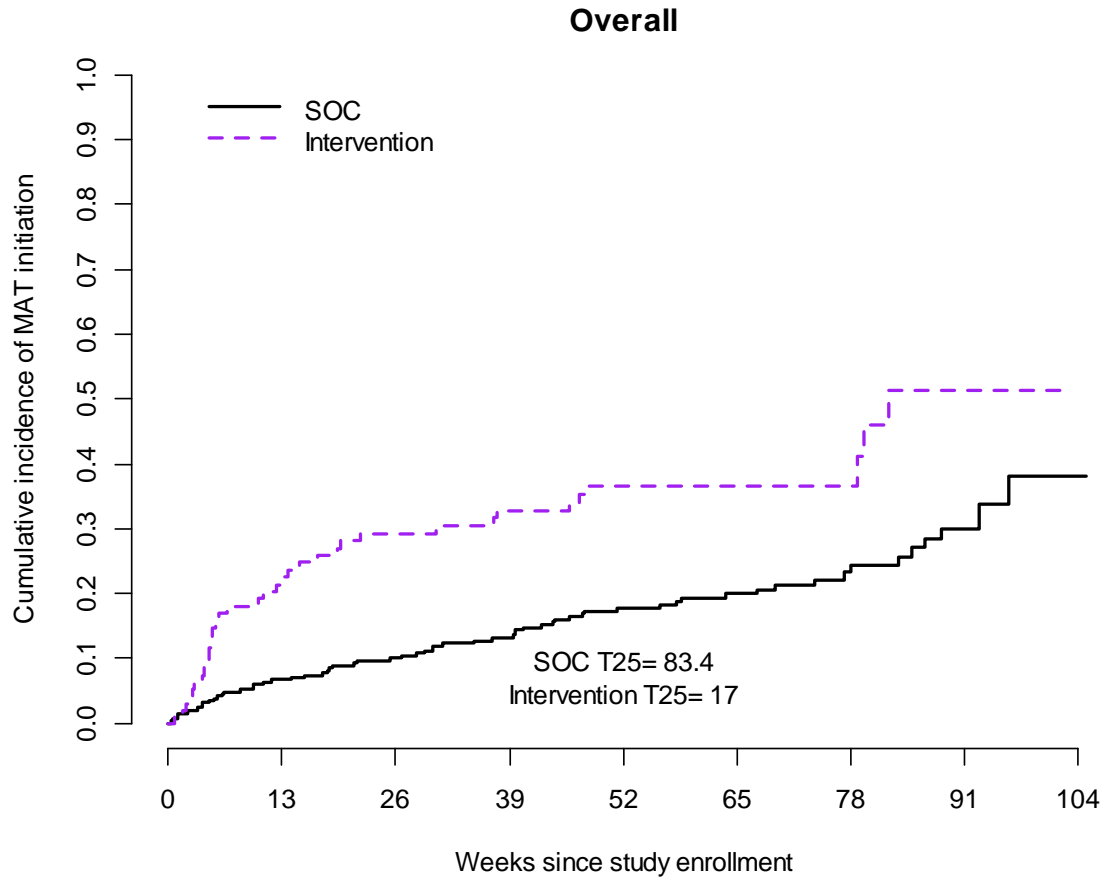
Supplemental Figure 4



		0	13	26	39	52	65	78	91	104
<i>Number at risk:</i>										
SOC		321	273	228	196	148	93	55	17	0
Intervention		108	77	51	37	31	19	6	1	0
<i>Deaths:</i>										
SOC		0	9	17	25	35	37	40	42	43
Intervention		0	3	5	5	6	6	7	8	8
<i>Events:</i>										
SOC		0	43	70	92	110	129	138	145	149
Intervention		0	35	52	62	62	67	71	72	72

Supplemental Figure 4: Cumulative incidence of viral suppression (HIV RNA <1,000 copies/mL) among indexes who were not virally suppressed at baseline. T50 is the time in weeks for 50% of the population to become virally suppressed. At each time point below the x-axis, the number remaining at risk is provided, as well as the number of accumulated deaths that occurred before viral suppression (i.e., death as a competing risk), and the number of accumulated events (people who achieved HIV RNA <1,000 cp/mL). Purple dashed line: intervention; black solid line: standard of care. cp/ml = copies/mL

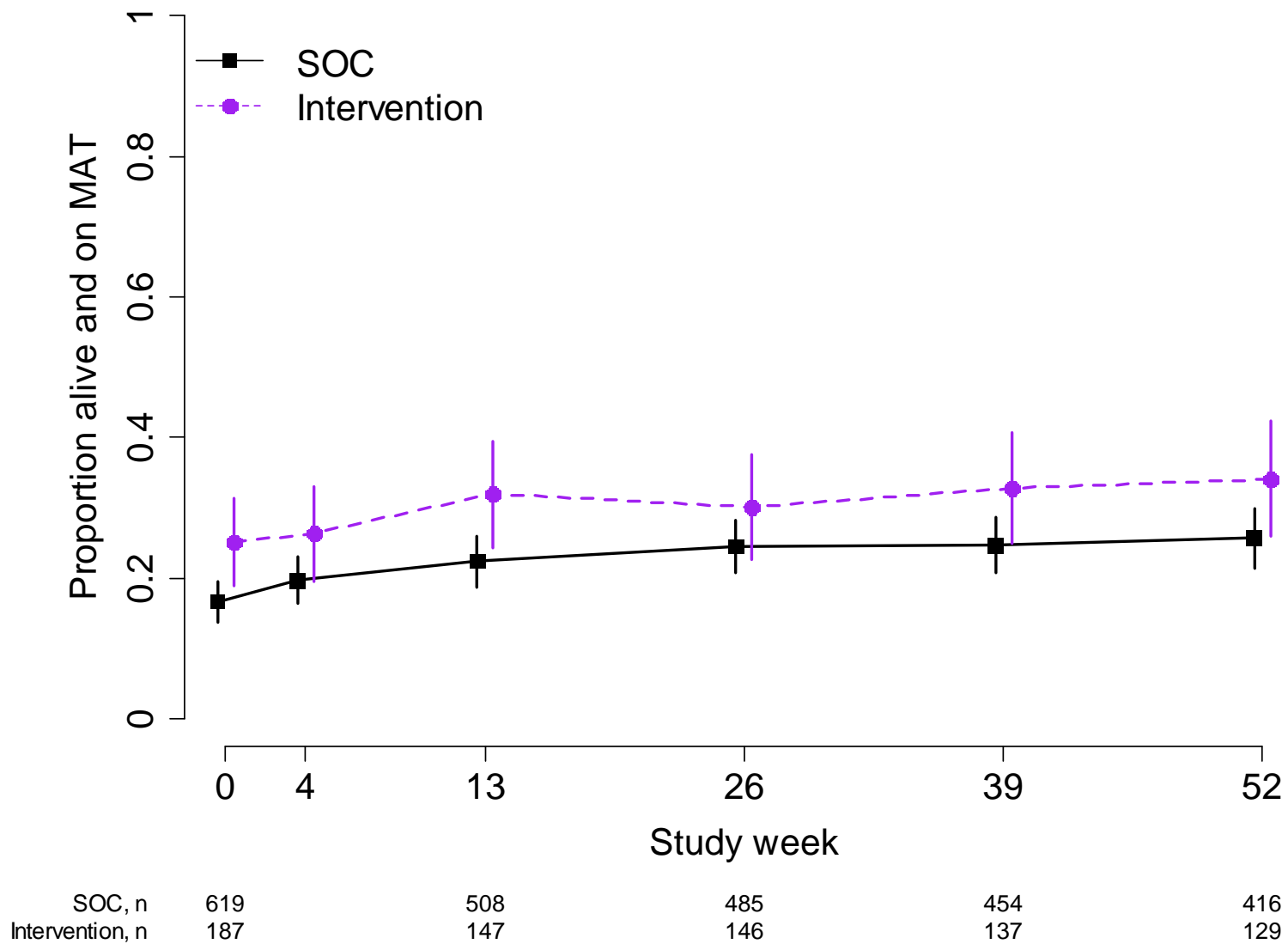
Supplemental Figure 5



		0	13	26	39	52	65	78	91	104
<i>Number at risk:</i>										
SOC	288	257	236	217	171	121	69	25	2	
Intervention	96	70	61	55	46	30	16	6	0	
<i>Deaths:</i>										
SOC	0	8	15	22	32	34	37	38	39	
Intervention	0	2	3	3	3	3	3	3	3	
<i>Events:</i>										
SOC	0	19	28	36	47	51	56	60	62	
Intervention	0	20	27	30	33	33	33	36	36	

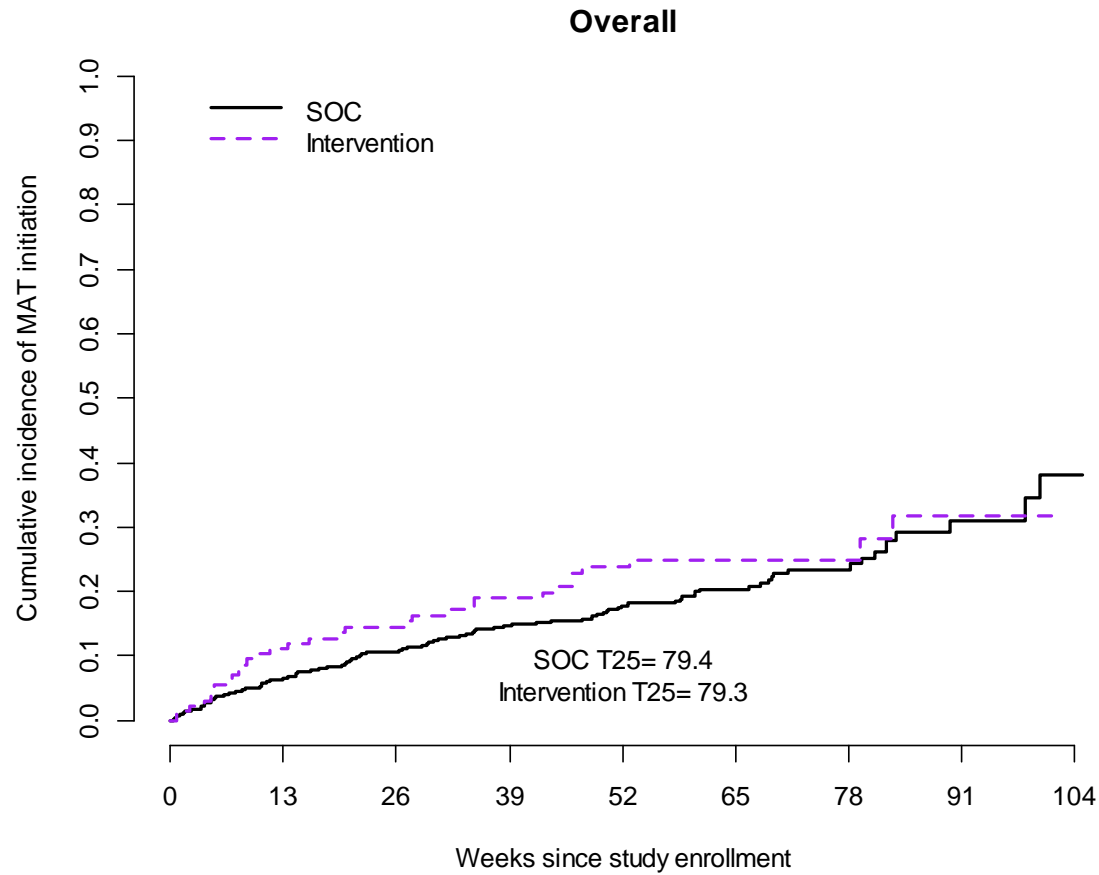
Supplemental Figure 5: Cumulative incidence of medication assisted treatment (MAT) initiation among indexes not on MAT at baseline. T25 is the time in weeks for 25% of the population to initiate MAT. At each time point below the x-axis, the number remaining at risk is provided, as well as the number of accumulated deaths that occurred before MAT initiation (i.e., death as a competing risk), and the number of accumulated events (people who initiated MAT). Purple dashed line: intervention; black solid line: standard of care.

Supplemental Figure 6



Supplemental Figure 6: Proportion of partners alive and on medication assisted treatment (MAT) at specific time points. Purple dashed line: intervention; black solid line: standard of care.

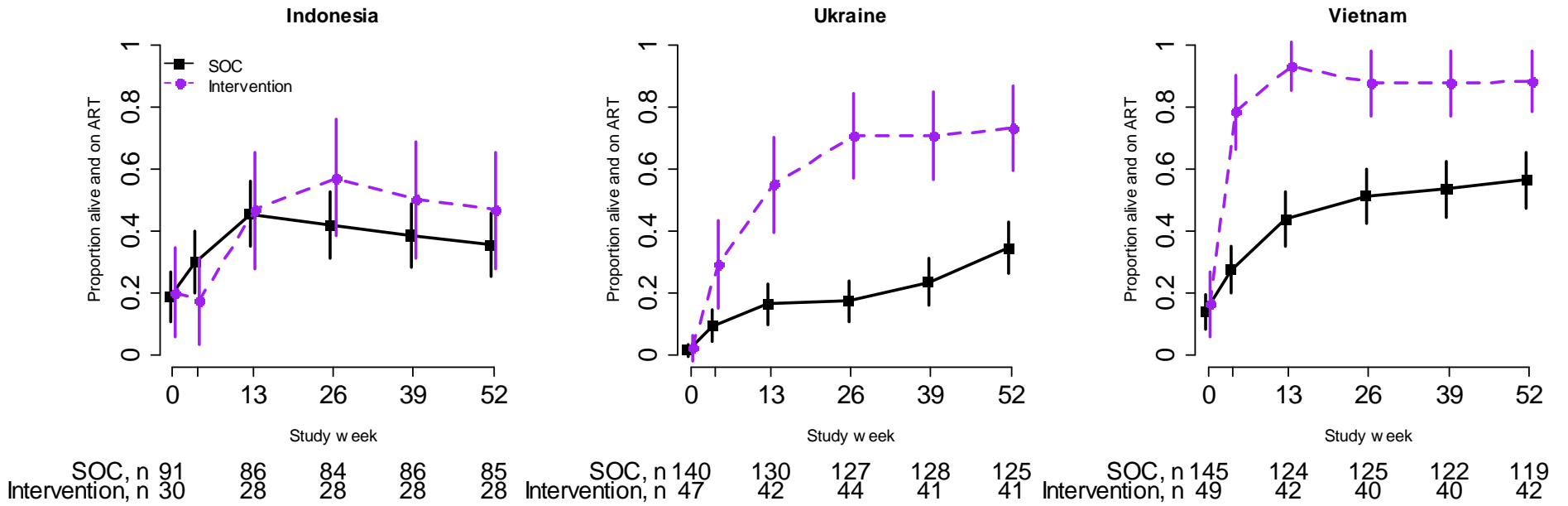
Supplemental Figure 7



	0	13	26	39	52	65	78	91	104
<i>Number at risk:</i>									
SOC	497	436	386	331	266	169	89	28	1
Intervention	130	109	98	87	70	51	25	7	0
<i>Deaths:</i>									
SOC	0	1	7	9	12	15	15	15	15
Intervention	0	0	0	0	0	1	1	1	1
<i>Events:</i>									
SOC	0	32	50	67	78	85	91	98	100
Intervention	0	14	18	23	28	29	29	31	31

Supplemental Figure 7: Cumulative incidence of medication assisted treatment (MAT) initiation among partners not on MAT at baseline. T25 is the time in weeks for 25% of the population to initiate MAT. At each time point below the x-axis, the number remaining at risk is provided, as well as the number of accumulated deaths that occurred before MAT initiation (i.e., death as a competing risk), and the number of accumulated events (people who initiated MAT). Purple dashed line: intervention; black solid line: standard of care.

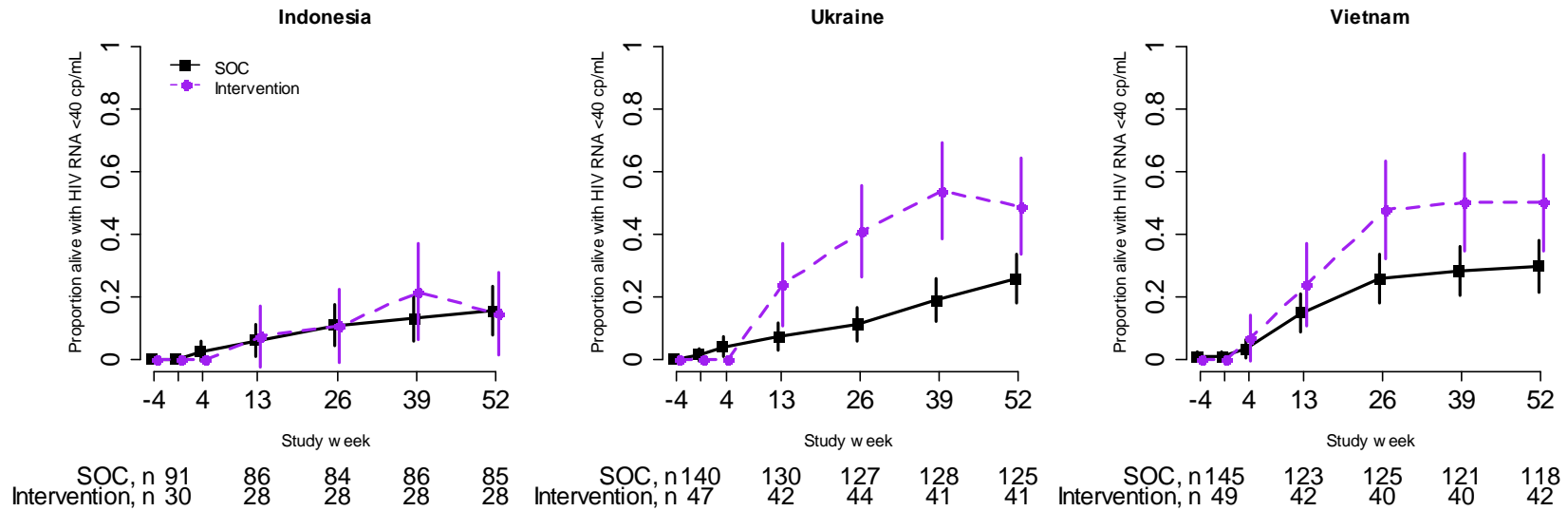
Supplemental Figure 8



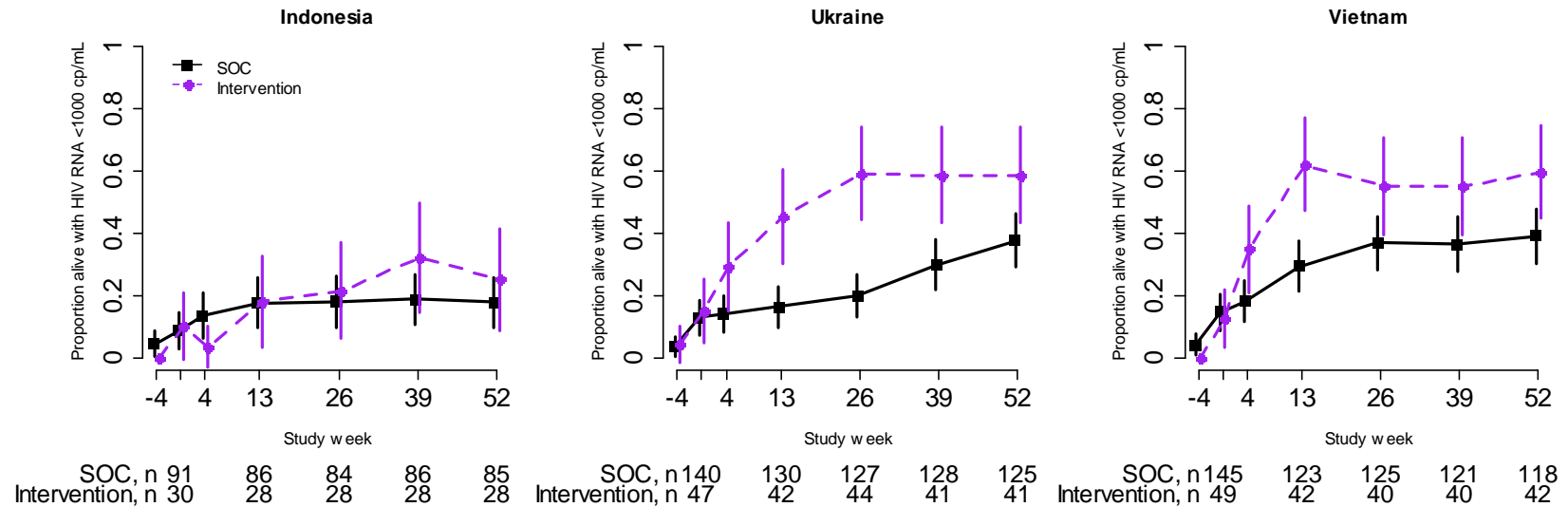
Supplemental Figure 8: Proportion of index participants alive and reporting that they are on ART by site. Purple dashed line: intervention; black solid line: standard of care.

Supplemental Figure 9

A. HIV RNA <40 copies/mL

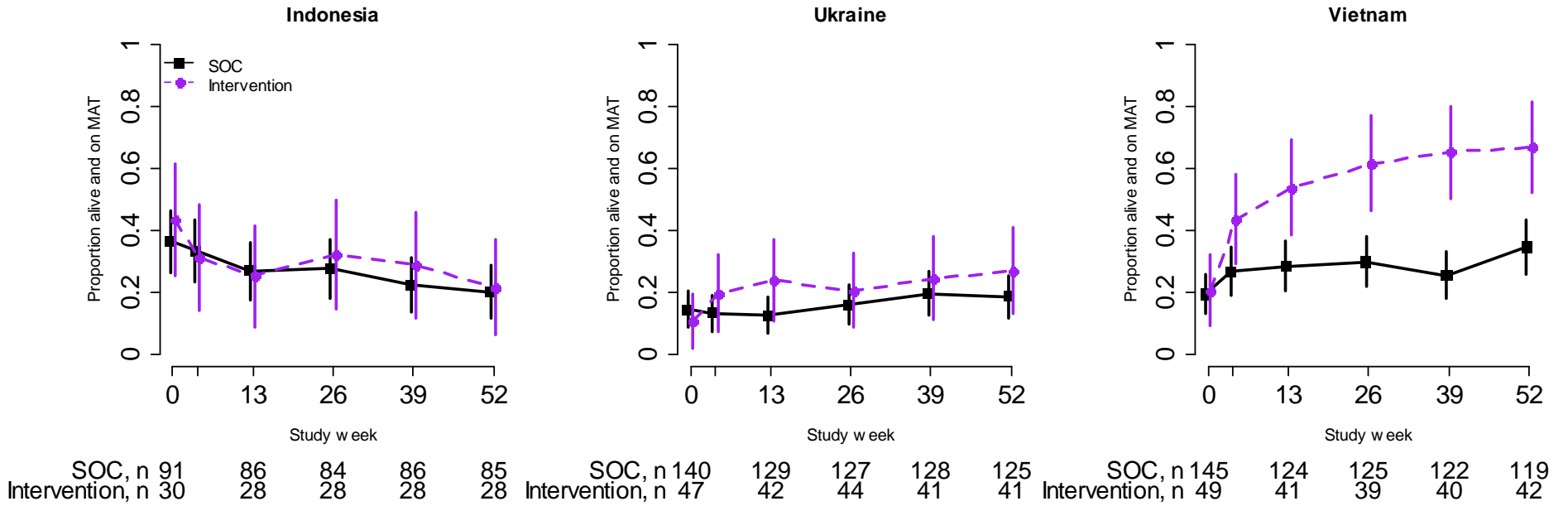


B. HIV RNA <1000 copies/mL



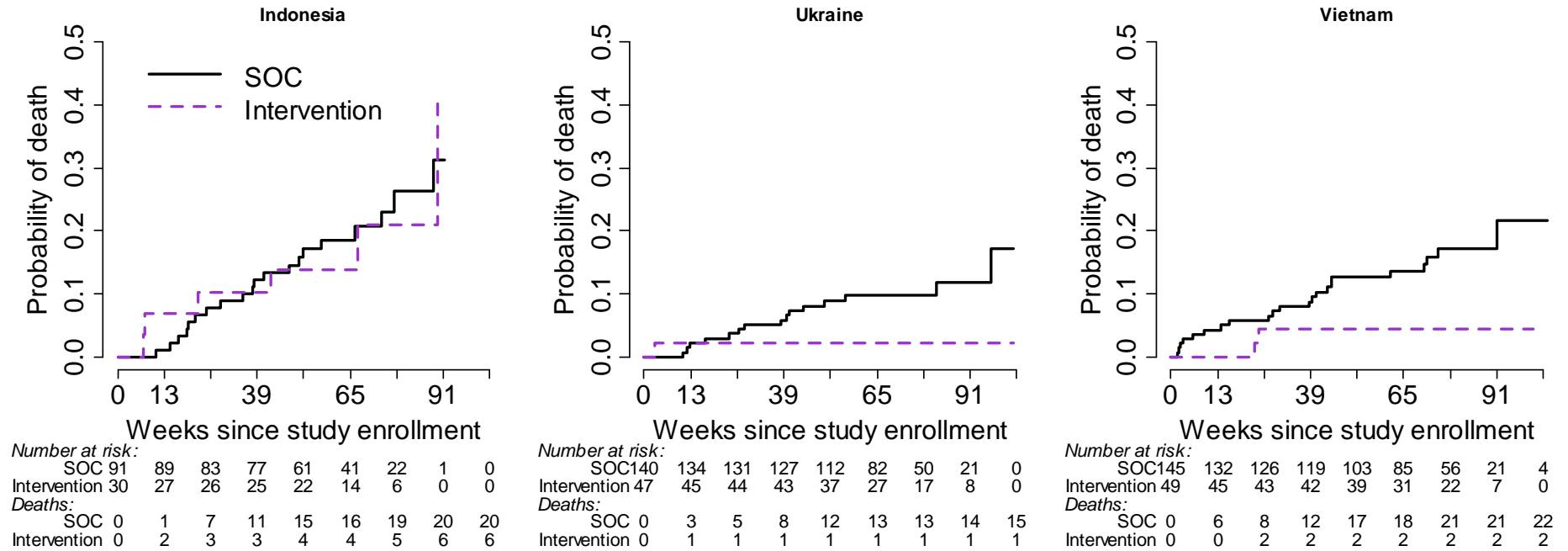
Supplemental Figure 9: Proportion of index participants alive and virally suppressed by site. **A.** Viral suppression < 40 copies/mL; **B.** Viral suppression < 1000 copies/mL. Purple dashed line: intervention; black solid line: standard of care. cp/ml = copies/mL

Supplemental Figure 10



Supplemental Figure 10: Proportion of index participants alive and on MAT by site. Purple dashed line: intervention; black solid line: standard of care.

Supplemental Figure 11



Supplemental Figure 11: Cumulative probability of death for index participants by site. At each time point below the x-axis, the number remaining at risk is provided, as well as the number of accumulated deaths. Note that the number of participants with follow-up beyond 91 weeks is limited. Purple dashed line: intervention; black solid line: standard of care.