

# THE LANCET

## Global Health

### Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Caniglia EC, Zash R, Swanson SA, et al. Iron, folic acid, and multiple micronutrient supplementation strategies during pregnancy and adverse birth outcomes in Botswana. *Lancet Glob Health* 2022; **10**: e850–61.

Appendix Table 1. Baseline characteristics measured at the first antenatal visit by supplementation strategy in the weighted pseudo-population, The Tsepamo Study

	Folic acid supplementation only (n=1,140)	Iron supplementation only (n=36,428)	Iron and Folic acid supplementation (n=23,085)	Multiple Micronutrient supplementation (n=32,005)
<b>Trimester of first ANC</b>				
First (<12 weeks)	25.34%	26.22%	26.46%	26.30%
Second (12-24 weeks)	74.66%	73.78%	73.54%	73.70%
<b>HIV</b>				
Women with HIV	20.06%	22.79%	22.43%	22.67%
Women without HIV	79.94%	77.21%	77.57%	77.33%
<b>Hemoglobin within 7 days of first ANC (g/dl)</b>				
<11	23.59%	23.00%	22.30%	22.64%
≥11	76.41%	77.00%	77.70%	77.36%
<b>Weight at first ANC</b>				
<50 kg	16.58%	14.85%	14.57%	14.73%
50-80kg	69.24%	69.34%	69.42%	69.13%
≥80kg	14.19%	15.81%	16.02%	16.14%
<b>Health district of first ANC</b>				
Rural – Northwest (Maun, Okavango, Chobe)	7.30%	8.84%	8.75%	9.98%
Rural – South (Ghanzi, Kgalagadi, Kweneng, Southern, Goodhope)	15.65%	15.53%	14.40%	14.78%
Urban – Gaborone	20.54%	23.82%	25.67%	25.74%
Urban - Francistown	13.35%	14.27%	13.80%	14.24%
Rural - East	43.17%	37.53%	37.38%	35.27%
<b>Age</b>				
<20 years	11.33%	11.36%	10.98%	10.94%
20-35 years	73.36%	72.71%	72.96%	73.28%
>=35 years	15.30%	15.93%	16.06%	15.78%
<b>Parity</b>				
1 or more children	58.25%	58.61%	58.41%	58.46%
0 children	41.75%	41.31%	41.53%	41.48%
Missing	0.00%	0.08%	0.07%	0.06%
<b>Occupation</b>				
Salaried	41.38%	37.73%	38.31%	38.75%
Other or missing	58.62%	62.27%	61.69%	61.25%
<b>Education</b>				
Secondary or higher	95.12%	93.50%	93.66%	93.53%
None or primary or missing	4.88%	6.50%	6.34%	6.47%
<b>Calendar year of first ANC</b>				
2013-2016	40.13%	39.83%	39.75%	41.22%
2017-2018	32.55%	31.71%	32.05%	31.05%
2019-2020	27.32%	28.46%	28.20%	27.73%
<b>Season</b>				
Rainy (November-March)	40.75%	41.89%	42.59%	42.43%
Dry (April-October)	59.25%	58.11%	57.41%	57.68%
<b>Smoking during pregnancy</b>				
No	94.45%	93.55%	93.49%	93.62%
Yes	1.01%	1.47%	1.50%	1.46%
Missing	4.54%	4.97%	5.01%	4.93%
<b>Alcohol during pregnancy</b>				
No	87.05%	85.36%	85.08%	85.28%
Yes	8.43%	9.70%	9.94%	9.81%
Missing	4.52%	4.94%	4.98%	4.91%

Appendix Table 2. Unadjusted risks for each adverse birth outcome by supplementation strategy, The Tsepamo Study

Outcome		No supplementation (n=4,185)	Folic acid supplementation only (n=1,133)	Iron supplementation only (n=36,334)	Iron and Folic acid supplementation (n=23,101)	Multiple Micronutrient supplementation (n=31,588)
<b>Stillbirth</b>	Risk	4.21%	2.74%	2.30%	1.80%	1.71%
	N/Total	176/4,184	31/1,133	835/36,332	416/23,101	541/31,584
<b>Preterm delivery</b>	Risk	22.32%	16.95%	14.75%	12.61%	11.60%
	N/Total	934/4,185	192/1,133	5,359/36,334	2,913/23,101	3,663/31,588
<b>Very preterm delivery</b>	Risk	8.24%	4.06%	3.20%	2.39%	1.98%
	N/Total	345/4,185	46/1,133	1,163/36,334	551/23,101	626/31,588
<b>SGA</b>	Risk	15.52%	13.49%	15.22%	15.42%	16.22%
	N/Total	643/4,142	152/1,127	5,487/36,063	3,536/22,933	5,082/31,330
<b>Very SGA</b>	Risk	6.33%	4.53%	5.70%	5.53%	6.03%
	N/Total	262/4,142	51/1,127	2,054/36,063	1,269/22,933	1,888/31,330
<b>Neonatal death</b>	Risk	2.41%	1.00%	1.18%	0.94%	0.86%
	N/Total	96/3,988	11/1,096	418/35,405	213/22,624	268/30,988
<b>Stillbirth/ neonatal death</b>	Risk	6.53%	3.73%	3.46%	2.73%	2.57%
	N/Total	272/4,164	42/1,127	1,253/36,240	629/23,040	809/31,529
<b>Low birthweight</b>	Risk	18.11%	14.30%	12.46%	11.34%	10.70%
	N/Total	757/4,181	162/1,133	4,522/36,305	2,617/23,076	3,379/31,573
<b>Very low birthweight</b>	Risk	10.26%	6.35%	5.11%	4.26%	3.81%
	N/Total	429/4,181	72/1,133	1,856/36,305	983/23,076	1,203/31,573
<b>3rd trimester anemia</b>	Risk	37.03%	49.08%	27.66%	37.71%	29.47%
	N/Total	761/2,055	321/654	5,437/19,656	4,835/12,823	5,054/17,150
<b>C-section</b>	Risk	22.69%	23.59%	23.27%	23.96%	20.82%
	N/Total	948/4,178	267/1,132	8,446/36,296	5,530/23,083	6,571/31,560
<b>Short length-for-age</b>	Risk	10.35%	8.20%	10.10%	9.46%	10.31%
	N/Total	420/4,058	91/1,110	3,588/35,508	2,136/22,578	3,187/30,919

Appendix Table 3. Adjusted risk ratios for each adverse birth outcome by supplementation strategy, The Tsepamo Study

Outcome	Folic acid supplementation only (n=1,133)	Iron supplementation only (n=36,334)	Iron and Folic acid supplementation (n=23,101)	Multiple Micronutrient supplementation (n=31,588)
Stillbirth	1.95 (0.94, 4.04)	1.31 (1.16, 1.49)	1.00 (reference)	0.97 (0.84, 1.11)
Preterm delivery	1.50 (1.18, 1.90)	1.20 (1.14, 1.25)	1.00 (reference)	0.92 (0.88, 0.97)
Very preterm delivery	1.47 (0.96, 2.26)	1.40 (1.26, 1.55)	1.00 (reference)	0.79 (0.70, 0.90)
SGA	0.96 (0.73, 1.26)	1.00 (0.96, 1.04)	1.00 (reference)	1.03 (0.99, 1.08)
Very SGA	1.04 (0.59, 1.83)	1.04 (0.96, 1.11)	1.00 (reference)	1.07 (0.99, 1.16)
Neonatal death	1.79 (0.71, 4.47)	1.23 (1.03, 1.47)	1.00 (reference)	0.90 (0.74, 1.11)
Stillbirth/neonatal death	1.89 (1.07, 3.33)	1.28 (1.16, 1.42)	1.00 (reference)	0.94 (0.84, 1.06)
Low birth weight	1.49 (1.15, 1.93)	1.11 (1.06, 1.16)	1.00 (reference)	0.91 (0.97, 0.97)
Very low birth weight	1.74 (1.14, 2.66)	1.24 (1.14, 1.34)	1.00 (reference)	0.87 (0.79, 0.95)
3rd trimester anemia	1.29 (1.11, 1.50)	0.84 (0.81, 0.86)	1.00 (reference)	0.94 (0.91, 0.98)
C-section	1.14 (0.94, 1.38)	0.97 (0.94, 1.00)	1.00 (reference)	0.89 (0.86, 0.92)
Short length-for-age	0.97 (0.70, 1.35)	1.06 (1.01, 1.12)	1.00 (reference)	1.05 (0.99, 1.11)

Risk ratios are adjusted for HIV status (positive, negative), first hemoglobin in pregnancy (restricted cubic splines with 5 knots at 9.5 g/dL, 10.2 g/dL, 11.9 g/dL, 13.4 g/dL, and 13.8 g/dL), first weight in pregnancy (restricted cubic splines with 5 knots at 47.9 kg, 53.5 kg, 62.0 kg, 73.5 kg, and 86.0 kg), region of first ANC, age (restricted cubic splines with 3 knots at 19, 27, and 36 years), year of booking (2014-2016, 2017-2018, 2019-2020), trimester of booking (1 [ $<12$  weeks gestation], 2 [12-24 weeks gestation]), employment (salaried, other or unknown), education (secondary or higher, primary or lower, missing), parity (first or missing, second or more), season (dry [April-October], rainy [November-March]), smoking (yes, no, missing), and alcohol (yes, no, missing) via inverse probability weighting. The models for each outcome are additionally adjusted for first hemoglobin in pregnancy (modeled linearly).

Appendix Table 4. Adjusted risk differences for adverse birth outcomes by supplementation strategy and key subgroups, The Tsepamo Study

Subgroup	Strategy (vs. IFAS)	Stillbirth			Stillbirth/neonatal death			Preterm delivery					
		Baseline Risk* (%)	Risk Diff (%)	95% CI (%)	Baseline Risk* (%)	Risk Diff (%)	95% CI (%)	Baseline Risk* (%)	Risk Diff (%)	95% CI (%)			
Overall	Folic acid	1.80	1.71	-0.83	4.26	2.73	2.43	-0.48	5.34	12.61	5.75	1.38	10.13
	Iron		0.56	0.31	0.81		0.77	0.47	1.08		2.39	1.78	3
	MMS		-0.06	-0.32	0.19		-0.15	-0.46	0.16		-1.06	-1.69	-0.42
Trimester 1	Folic acid	2.04	5.88	-3.2	14.96	3.07	5.09	-4.05	14.24	12.72	5.69	-4.37	15.76
	Iron		0.7	0.18	1.23		0.81	0.18	1.44		2.46	1.24	3.68
	MMS		-0.06	-0.54	0.43		-0.07	-0.68	0.54		-1.19	-2.37	0
Trimester 2	Folic acid	1.71	0.3	-0.85	1.45	2.61	1.59	-0.76	3.94	12.57	5.77	1.05	10.5
	Iron		0.51	0.23	0.79		0.76	0.41	1.11		2.36	1.66	3.06
	MMS		-0.07	-0.36	0.23		-0.19	-0.55	0.17		-1	-1.75	-0.25
HIV-negative	Folic acid	1.72	-0.04	-1.14	1.05	2.61	0.86	-1.28	3	11.53	2.83	-1.47	7.13
	Iron		0.37	0.1	0.65		0.57	0.23	0.91		2.1	1.43	2.78
	MMS		-0.04	-0.33	0.25		-0.13	-0.48	0.22		-0.84	-1.54	-0.13
Women with HIV	Folic acid	2.05	8.73	-2.33	19.8	3.12	8.71	-2.28	19.71	16.04	18.01	6.28	29.74
	Iron		1.19	0.61	1.78		1.45	0.75	2.15		3.4	2.01	4.78
	MMS		-0.15	-0.69	0.4		-0.22	-0.88	0.44		-1.8	-3.23	-0.37
<50kg	Folic acid	1.62	-1	-1.95	-0.05	2.53	2.42	-3.6	8.45	14.28	6.38	-5.78	18.54
	Iron		0.3	-0.33	0.92		0.35	-0.42	1.13		4.37	2.54	6.2
	MMS		0.11	-0.51	0.73		0.17	-0.59	0.93		0.02	-1.75	1.8
50-80kg	Folic acid	1.65	2.55	-1.02	6.13	2.58	2.65	-1.12	6.42	12.67	6.53	1.06	12
	Iron		0.79	0.5	1.09		0.98	0.62	1.34		2.3	1.58	3.02
	MMS		0.03	-0.26	0.33		-0.12	-0.48	0.24		-1.12	-1.88	-0.37
>80kg	Folic acid	2.62	0.92	-2.7	4.54	3.58	0.88	-2.98	4.74	10.90	1	-4.81	6.82
	Iron		-0.13	-0.81	0.56		0.31	-0.49	1.12		0.95	-0.41	2.3
	MMS		-0.58	-1.34	0.18		-0.52	-1.42	0.38		-1.72	-3.24	-0.19
Hb <11 g/dl	Folic acid	1.95	0.03	-2.41	2.48	2.87	3.49	-2.32	9.3	14.68	10.75	0.74	20.76
	Iron		0.59	0.07	1.12		0.62	0	1.24		3.53	2.19	4.86
	MMS		-0.08	-0.59	0.43		-0.09	-0.71	0.54		-0.31	-1.7	1.08
Hb ≥11 g/dl	Folic acid	1.74	2.26	-0.98	5.5	2.67	2.03	-1.25	5.32	11.77	4.47	-0.37	9.31
	Iron		0.55	0.27	0.83		0.82	0.47	1.17		2.11	1.43	2.79
	MMS		-0.05	-0.35	0.24		-0.16	-0.52	0.2		-1.23	-1.94	-0.51
Age<20	Folic acid	1.01	0.02	-1.77	1.8	1.89	4.83	-4.41	14.08	14.42	0.5	-9.02	10.03
	Iron		0.37	-0.14	0.89		0.23	-0.46	0.92		4.17	2.13	6.2
	MMS		0.07	-0.41	0.55		-0.07	-0.74	0.61		0.62	-1.48	2.71
Age 20-35	Folic acid	1.68	0.7	-0.57	1.97	2.58	0.34	-1.04	1.71	11.80	4.08	-0.5	8.66
	Iron		0.5	0.22	0.79		0.71	0.36	1.06		2.3	1.61	2.99
	MMS		0.06	-0.24	0.36		-0.04	-0.4	0.32		-0.9	-1.62	-0.17
Age ≥35	Folic acid	2.85	7.91	-6.42	22.23	3.95	10.4	-4.33	25.14	15.11	17.31	2.55	32.07
	Iron		1.06	0.25	1.88		1.53	0.58	2.48		1.5	-0.11	3.11
	MMS		-0.67	-1.42	0.08		-0.66	-1.58	0.26		-2.79	-4.44	-1.15
Urban	Folic acid	2.40	2.91	-2.77	8.6	3.61	5.07	-1.42	11.57	14.81	11.45	3.73	19.17
	Iron		0.67	0.25	1.09		1.08	0.57	1.6		2.72	1.77	3.67
	MMS		-0.19	-0.64	0.27		-0.1	-0.66	0.45		-0.78	-1.84	0.29
Rural	Folic acid	1.30	0.93	-0.45	2.31	2.00	0.69	-0.81	2.18	10.77	2.11	-2.64	6.85
	Iron		0.52	0.22	0.82		0.59	0.23	0.95		2.27	1.49	3.06
	MMS		0.12	-0.16	0.41		-0.05	-0.39	0.3		-0.94	-1.71	-0.17
First birth	Folic acid	1.55	0.05	-1.04	1.14	2.51	0.89	-1.93	3.71	11.68	0.96	-4.28	6.21
	Iron		0.46	0.1	0.81		0.56	0.12	1.01		2.86	1.93	3.79
	MMS		0.1	-0.27	0.46		-0.01	-0.48	0.45		-0.61	-1.56	0.34
Second or more birth	Folic acid	1.97	2.91	-1.33	7.15	2.88	3.46	-1	7.92	13.26	9.17	2.84	15.51
	Iron		0.65	0.3	0.99		0.94	0.52	1.35		2.07	1.27	2.87
	MMS		-0.16	-0.51	0.19		-0.24	-0.65	0.18		-1.35	-2.20	-0.50
2ndary education	Folic acid	1.82	1.69	-0.96	4.34	2.76	2.37	-0.66	5.41	12.45	5.70	1.14	10.25
	Iron		0.50	0.24	0.76		0.67	0.36	0.98		2.32	1.70	2.94
	MMS		-0.07	-0.33	0.20		-0.17	-0.49	0.16		-0.96	-1.61	-0.30
Primary education	Folic acid	1.42	2.10	-4.72	8.93	2.21	3.34	-4.38	11.05	15.45	7.86	-5.43	21.16
	Iron		1.42	0.40	2.45		2.28	0.95	3.60		3.31	0.49	6.12
	MMS		0.05	-0.86	0.96		0.05	-1.04	1.14		-2.53	-5.27	0.20
Salaried	Folic acid	1.97	3.42	-2.48	9.32	3.01	3.67	-2.50	9.83	11.89	8.87	0.64	17.10
	Iron		0.62	0.20	1.04		0.86	0.35	1.37		1.52	0.59	2.45

employment	MMS		-0.15	-0.59	0.29		-0.15	-0.69	0.40		-2.19	-3.18	-1.21
Non-salaried	Folic acid	1.69	0.50	-0.60	1.59	2.55	1.61	-0.89	4.10	13.09	3.63	-0.94	8.20
employment	Iron		0.51	0.20	0.82		0.71	0.33	1.09		2.92	2.12	3.72
	MMS		-0.01	-0.32	0.30		-0.16	-0.53	0.20		-0.31	-1.13	0.52
HIV-, present	Folic acid	1.82	-0.38	-1.5	0.73	2.77	-0.04	-2.06	1.98	11.50	1.85	-2.94	6.65
to care <20	Iron		0.32	0.01	0.63		0.45	0.07	0.84		1.83	1.09	2.57
weeks	MMS		-0.07	-0.39	0.25		-0.16	-0.56	0.24		-1.12	-1.88	-0.35

Appendix Table 4 continued. Adjusted risk differences for adverse birth outcomes by supplementation strategy and key subgroups, The Tsepamo Study

Subgroup	Strategy (vs. IFAS)	SGA			Neonatal death			Low birthweight					
		Baseline Risk* (%)	Risk Diff (%)	95% CI (%)	Baseline Risk* (%)	Risk Diff (%)	95% CI (%)	Baseline Risk* (%)	Risk Diff (%)	95% CI (%)			
Overall	Folic acid	15.42	-0.66	-4.69	3.36	0.94	0.77	-0.8	2.34	11.34	5.46	1.09	9.83
	Iron		-0.05	-0.69	0.59		0.22	0.04	0.4		1.24	0.66	1.82
	MMS		0.53	-0.17	1.24		-0.09	-0.27	0.09		-0.99	-1.59	-0.38
Trimester 1	Folic acid	14.31	1.42	-8.67	11.51	1.05				11.81	8.54	-2.38	19.47
	Iron		0.38	-0.86	1.62						1.3	0.14	2.47
	MMS		0.26	-0.99	1.52						-1.08	-2.22	0.07
Trimester 2	Folic acid	15.82	-1.35	-5.5	2.81	0.90	1.26	-0.77	3.29	11.17	4.4	-0.04	8.84
	Iron		-0.19	-0.94	0.56		0.26	0.05	0.46		1.22	0.56	1.89
	MMS		0.63	-0.22	1.47		-0.13	-0.34	0.08		-0.96	-1.67	-0.25
HIV-negative	Folic acid	13.94	-3.45	-6.89	-0.01	0.89	0.92	-0.98	2.81	9.83	3.35	-0.94	7.65
	Iron		0.08	-0.63	0.78		0.2	0	0.4		1.15	0.52	1.78
	MMS		0.82	0.04	1.6		-0.09	-0.3	0.11		-0.76	-1.41	-0.11
Women with HIV	Folic acid	20.11	11.16	-0.84	23.17	1.09	0.13	-1.34	1.59	16.15	14.93	3.05	26.82
	Iron		-0.55	-2.02	0.92		0.28	-0.13	0.69		1.53	0.16	2.91
	MMS		-0.51	-2.12	1.1		-0.08	-0.46	0.3		-1.81	-3.26	-0.37
<50kg	Folic acid	23.81	-10.41	-16.5	-4.33	0.92	3.77	-2.97	10.5	16.35	0.82	-7.81	9.45
	Iron		-1.22	-3.28	0.84		0.06	-0.4	0.53		2.34	0.45	4.22
	MMS		0.92	-1.2	3.04		0.06	-0.39	0.51		-1.16	-2.99	0.68
50-80kg	Folic acid	14.90	2.07	-3.35	7.5	0.94	0.12	-1.23	1.48	10.92	7.5	1.68	13.32
	Iron		0	-0.75	0.75		0.2	-0.01	0.42		1.04	0.37	1.71
	MMS		0.56	-0.27	1.4		-0.15	-0.37	0.06		-0.8	-1.52	-0.09
>80kg	Folic acid	10.42	-4.87	-8.56	-1.19	0.97	-0.04	-1.42	1.34	8.81	0.07	-5.03	5.17
	Iron		0.65	-0.66	1.95		0.44	0	0.88		1.03	-0.18	2.25
	MMS		-0.05	-1.54	1.44		0.05	-0.46	0.56		-1.63	-2.91	-0.35
Hb <11 g/dl	Folic acid	15.75	1.15	-6.12	8.42	0.94	3.6	-2.01	9.22	12.60	12.54	2.52	22.56
	Iron		-0.25	-1.56	1.06		0.03	-0.31	0.38		1.76	0.53	2.99
	MMS		-0.5	-1.89	0.89		-0.02	-0.38	0.35		-1.22	-2.45	0.02
Hb ≥11 g/dl	Folic acid	15.28	-1.26	-6.03	3.52	0.94	-0.23	-0.79	0.33	10.83	3.37	-1.34	8.08
	Iron		-0.02	-0.75	0.71		0.28	0.08	0.49		1.08	0.43	1.74
	MMS		0.83	0.01	1.65		-0.11	-0.32	0.1		-0.93	-1.62	-0.24
Age<20	Folic acid	17.23	-5.89	-	12.61	0.89	5.05	-4.55	14.65	11.41	3.54	-7.55	14.63
	Iron		-2.23	-4.3	-0.16		-0.13	-0.59	0.33		1.3	-0.55	3.14
	MMS		-1.15	-3.37	1.06		-0.13	-0.61	0.35		-1.01	-2.84	0.83
Age 20-35	Folic acid	15.01	-1.86	-5.95	2.23	0.91	-0.38	-0.87	0.1	10.53	4.12	-0.47	8.72
	Iron		-0.08	-0.82	0.65		0.22	0.01	0.43		1.28	0.63	1.94
	MMS		0.69	-0.13	1.51		-0.09	-0.3	0.11		-0.72	-1.4	-0.03
Age ≥35	Folic acid	16.12	10.03	-5.63	25.69	1.13	2.88	-3.19	8.95	14.97	13.7	-1.27	28.67
	Iron		1.61	-0.02	3.24		0.5	-0.02	1.03		1.01	-0.57	2.59
	MMS		0.97	-0.81	2.76		0.01	-0.55	0.56		-2.17	-3.82	-0.52
Urban	Folic acid	15.00	1.82	-5.33	8.98	1.23	2.28	-1.4	5.96	13.97	9.78	1.89	17.66
	Iron		0.9	-0.03	1.82		0.43	0.12	0.74		1.78	0.86	2.71
	MMS		0.84	-0.26	1.94		0.08	-0.26	0.42		-0.91	-1.94	0.12
Rural	Folic acid	15.77	-2.54	-7.07	1.99	0.70	-0.23	-0.79	0.32	9.15	2.71	-1.82	7.23
	Iron		-0.81	-1.69	0.07		0.09	-0.13	0.3		0.99	0.27	1.72
	MMS		0.25	-0.68	1.18		-0.17	-0.36	0.03		-0.7	-1.42	0.02
First birth	Folic acid	17.86	-3.84	-8.44	0.75	0.97	0.84	-1.83	3.51	11.41	-0.21	-4.9	4.48
	Iron		-0.5	-1.55	0.56		0.11	-0.17	0.39		1.5	0.58	2.41
	MMS		0.41	-0.74	1.57		-0.12	-0.41	0.18		-0.95	-1.88	-0.02
Second or more birth	Folic acid	13.69	1.61	-4.45	7.68	0.92	0.63	-1.07	2.33	11.29	9.53	3.03	16.04
	Iron		0.26	-0.53	1.06		0.3	0.07	0.54		1.07	0.33	1.82
	MMS		0.60	-0.28	1.49		-0.08	-0.30	0.15		-0.99	-1.79	-0.20
2ndary education	Folic acid	15.17	-0.45	-4.64	3.75	0.95	0.74	-0.90	2.37	11.08	5.74	1.19	10.30
	Iron		0.05	-0.60	0.71		0.18	-0.01	0.36		1.39	0.81	1.98
	MMS		0.63	-0.09	1.36		-0.10	-0.29	0.10		-0.85	-1.47	-0.24
Primary education	Folic acid	19.68	-3.57	-	14.34	0.80	1.38	-2.76	5.53	15.77	1.55	-10.28	13.39
	Iron		-1.70	-4.63	1.24		0.97	0.02	1.91		-1.16	-3.91	1.59
	MMS		-1.07	-4.13	1.99		0.01	-0.56	0.58		-3.08	-5.86	-0.31
Salaried	Folic acid		1.66	-5.80	9.12		0.26	-1.79	2.32		9.30	1.17	17.42

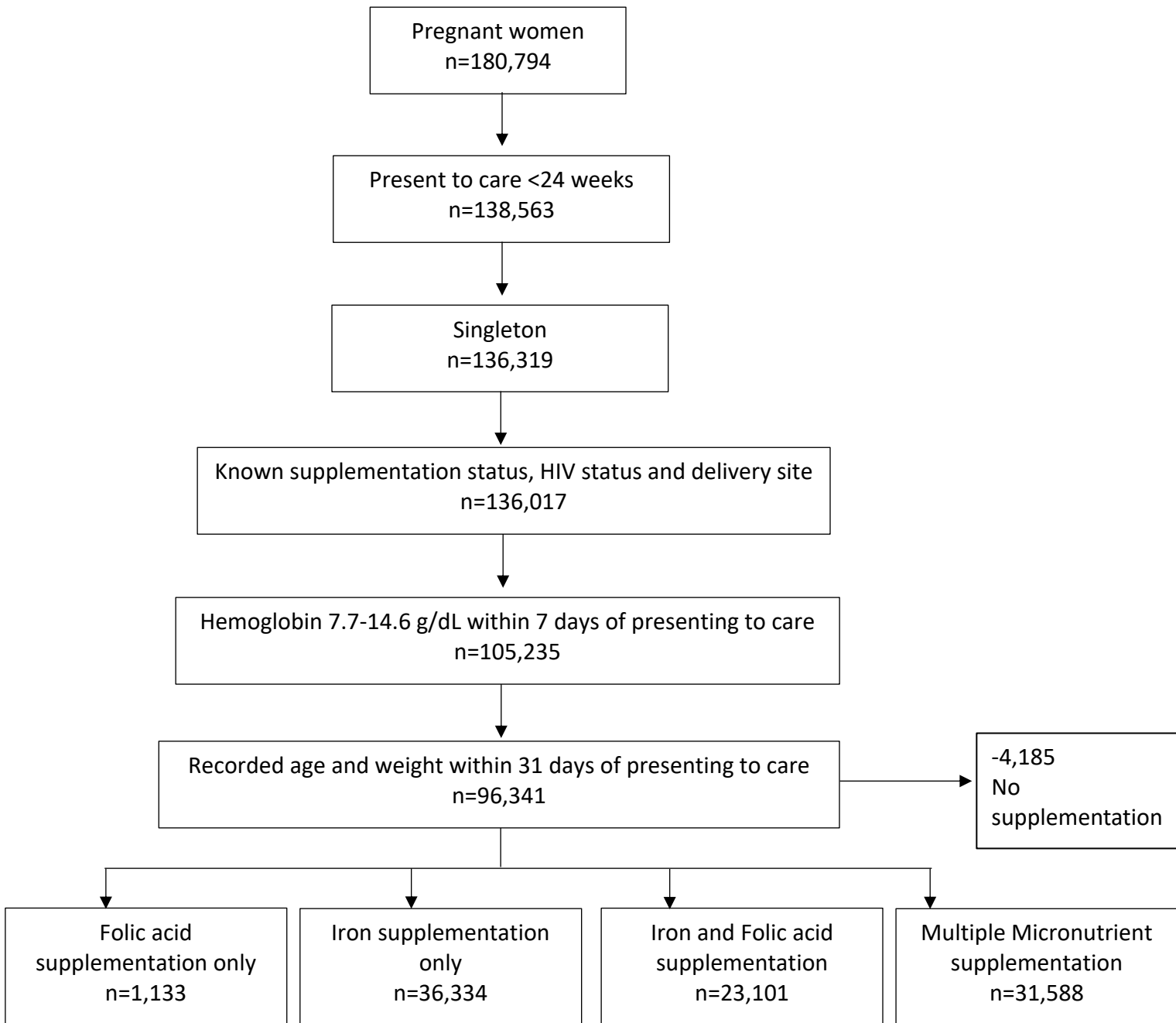
employment	Iron	13.95	1.09	0.11	2.07	1.05	0.26	-0.05	0.56	10.97	1.55	0.65	2.45
	MMS		0.68	-0.42	1.79		0.01	-0.33	0.34		-1.13	-2.10	-0.16
Non-salaried employment	Folic acid	16.38	-2.13	-6.51	2.25	0.87	1.14	-1.19	3.46	11.58	2.77	-1.84	7.39
	Iron		-0.76	-1.60	0.08		0.21	-0.01	0.43		1.05	0.30	1.80
	MMS		0.45	-0.46	1.37		-0.15	-0.36	0.06		-0.91	-1.68	-0.14
HIV-, present to care <20 weeks	Folic acid	13.73	-3.84	-7.71	0.03	0.96	0.36	-1.4	2.11	9.90	2.44	-2.33	7.21
	Iron		0.12	-0.66	0.89		0.14	-0.09	0.37		1.05	0.35	1.74
	MMS		1.07	0.22	1.92		-0.09	-0.33	0.15		-0.74	-1.46	-0.02

\*Baseline risks are the unadjusted risks of each outcome among those who receive IFAS.

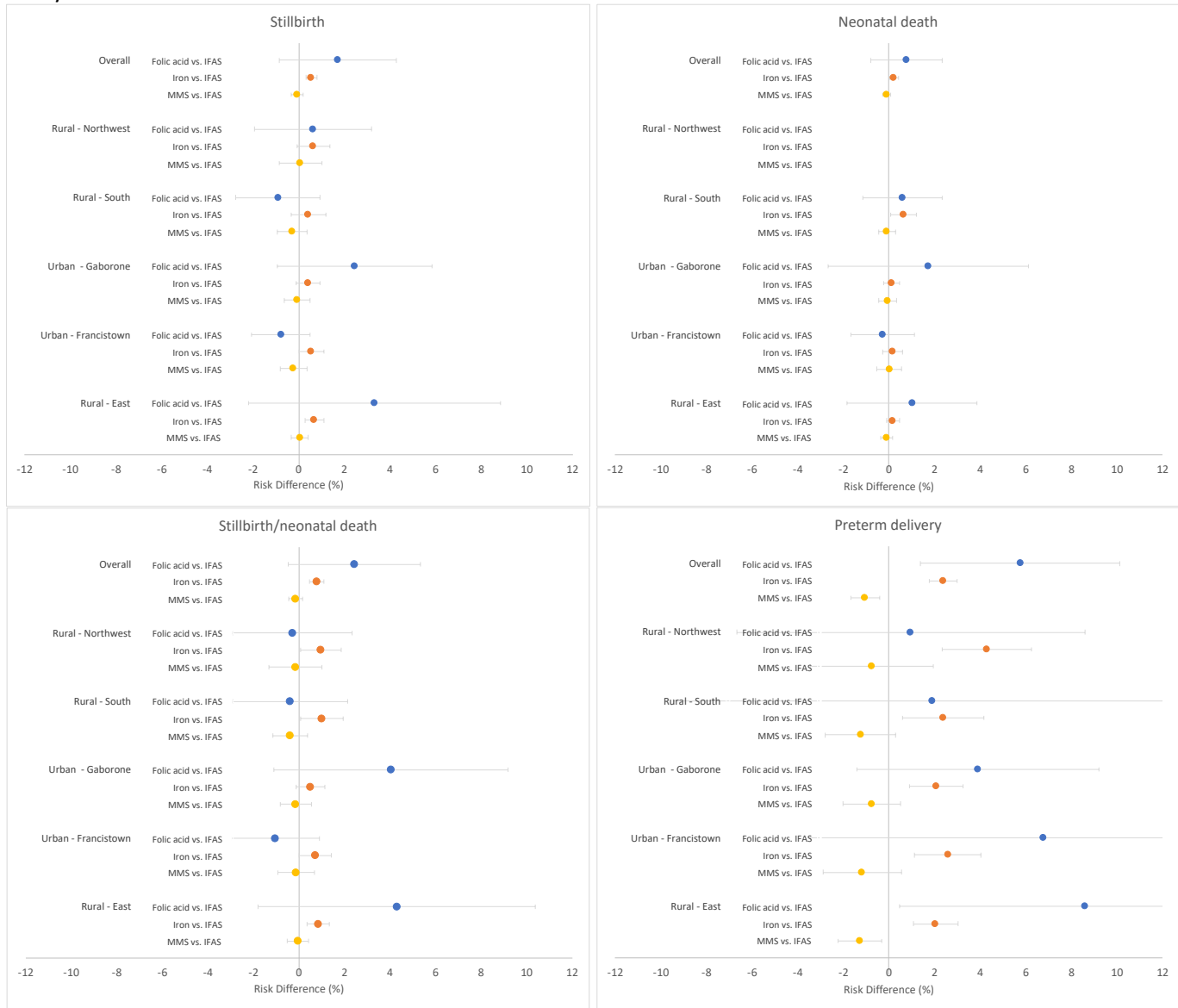
Risk differences are adjusted for HIV status (positive, negative), first hemoglobin in pregnancy (restricted cubic splines with 5 knots at 9.5 g/dL, 10.2 g/dL, 11.9 g/dL, 13.4 g/dL, and 13.8 g/dL), first weight in pregnancy (restricted cubic splines with 5 knots at 47.9 kg, 53.5 kg, 62.0 kg, 73.5 kg, and 86.0 kg), region of first ANC, age (restricted cubic splines with 3 knots at 19, 27, and 36 years), year of booking (2014-2016, 2017-2018, 2019-2020), trimester of booking (1 [<12 weeks gestation], 2 [12-24 weeks gestation]), employment (salaried, other or unknown), education (secondary or higher, primary or lower, missing), parity (first or missing, second or more), season (dry [April-October], rainy [November-March]), smoking (yes, no, missing), and alcohol (yes, no, missing) via inverse probability weighting. The models for each outcome are additionally adjusted for first hemoglobin in pregnancy (modeled linearly).

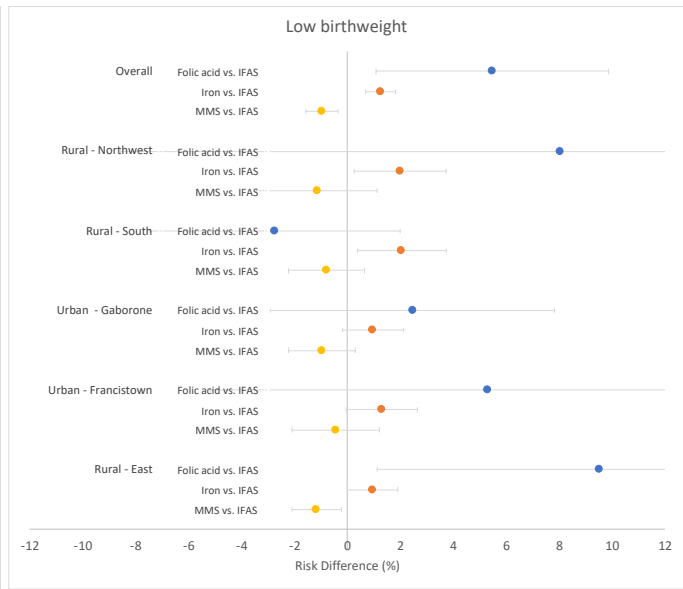
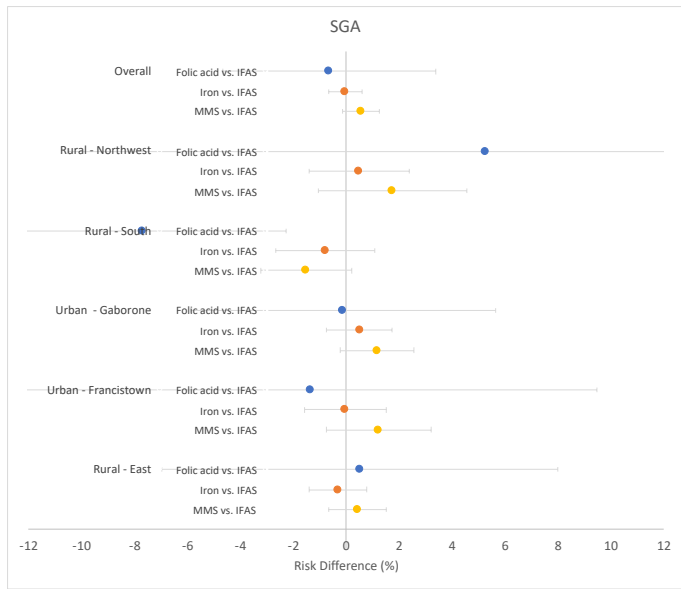


Appendix Figure 1. CONSORT diagram



Appendix Figure 2. Adjusted risk differences for adverse birth outcomes by supplementation strategy and by health district region, The Tsepamo Study





Additional Table 2. Adjusted mean differences and adjusted absolute means for **continuous gestational age at delivery and birthweight** by supplementation strategy, The Tsepamo Study

Outcome	Estimate	Folic acid supplementation only (n=1,133)	Iron supplementation only (n=36,334)	Iron and Folic acid supplementation (n=23,101)	Multiple Micronutrient supplementation (n=31,588)
<b>Gestational age at delivery (weeks)</b>	Mean Diff (95% CI)	-0.45 (-0.74, -0.16)	-0.22 (-0.26, -0.17)	0.0 (reference)	0.11 (0.07, 0.16)
	Mean	38.17	38.40	38.62	38.73
<b>Birthweight (grams)</b>	Mean Diff (95% CI)	-82.38 (-159.26, -5.49)	-35.88 (-46.23, -25.53)	0.0 (reference)	1.22 (-9.66, 12.10)
	Mean	2997.99	3044.48	3080.36	3081.58

Mean differences are adjusted for HIV status (positive, negative), first hemoglobin in pregnancy (restricted cubic splines with 5 knots at 9.5 g/dL, 10.2 g/dL, 11.9 g/dL, 13.4 g/dL, and 13.8 g/dL), first weight in pregnancy (restricted cubic splines with 5 knots at 47.9 kg, 53.5 kg, 62.0 kg, 73.5 kg, and 86.0 kg), region of first ANC, age (restricted cubic splines with 3 knots at 19, 27, and 36 years), year of booking (2014-2016, 2017-2018, 2019-2020), trimester of booking (1 [<12 weeks gestation], 2 [12-24 weeks gestation]), employment (salaried, other or unknown), education (secondary or higher, primary or lower, missing), parity (first or missing, second or more), season (dry [April-October], rainy [November-March]), smoking (yes, no, missing), and alcohol (yes, no, missing) via inverse probability weighting. The models for each outcome are additionally adjusted for first hemoglobin in pregnancy (modeled linearly).

We used linear regression models to estimate mean differences.