Zika Virus Infection during Pregnancy and Early Childhood Development, French Polynesia, 2013–2016

Technical Appendix

		Zika seropositive,	Zika seronegative,	
	All, n = 107 (n,% or	n = 81 (n,% or median,	n = 26 (n,% or median,	
Data	median, range)	range)	range)	p value†
Child corrected age‡ (months)	22.5 (13.4–28.3)	23.2 (13.6–28.3)	19.1 (13.4–25.4)	0.0046
12–14.9	17 (16)	13 (16)	4 (15)	0.009
15–17.9	13 (12)	5 (6)	8 (31)	
18–20.9	12 (11)	10 (12)	2 (8)	
21–23.9	35 (33)	26 (32)	9 (35)	
24–30.9	30 (28)	27 (33)	3 (12)	
Anthropometry at birth	n, % or median, IQR	n, % or median, IQR	n, % or median, IQR	
Weight (kg)	3.254 (2.950-3.682)	NA	NA	
Weight Z score§	1.26 (0.68–2.01)	1.43 (0.81–2.03)	0.99 (0.39–2.01)	0.14
Underweight (Z <u><</u> 2 SD)	0 (0)			
Length (cm)	49 (47–50)	NA	NA	
Length Z score	1.01 (0.43–1.64)	1.09 (0.43–1.72)	0.84 (0.00-1.48)	0.19
Stunted (Z <u><2</u> SD)	1 (1)	1 (1)	0 (0)	NA
Head circumference Z score	1.14 (0.44–2.16)	1.16 (0.45–2.28)	0.99 (0.37-1.80)	0.36
Microcephaly (Z <u><</u> 2 SD)	0 (0)			
Anthropometry at enrollment	n, % or median, IQR	n, % or median, IQR	n, % or median, IQR	
Weight (kg)	12.0 (10.8–13)	NA	NA	
Weight for age (Z score)	0.46 (-0.17 to 1.07)	0.52 (-0.21 to 1.18)	0.32 (0.01–0.81)	0.61
Underweight (Z<2 SD)	0 (0)	NA	NA	
Height/length (cm)	84 (80-87.5)	NA	NA	
Height/length for age (Z score)	-0.05 (-0.89 to 0.69)	-0.06 (-0.89 to 0.62)	0.17 (-0.19 to 0.87)	0.66
Stunted (Z<2 SD)	0 (0)	,	, , , , , , , , , , , , , , , , , , ,	
Weight for height/length (Z score)	0.63 (-0.12 to 1.28)	0.62 (-0.12 to 1.33)	0.66 (-0.12 to 1.14)	0.54
Wasted (Z<-2 SD)	0 (0)	````	· · · · · · · · · · · · · · · · · · ·	
Head circumference (cm)	48 (47–49)	NA	NA	
Head circumference for age (Z score) Microcephaly (Z <u><</u> 2SD)	0.57 (0.04–1.33) 0 (0)	0.63 (0.11–1.33)	0.41 (0.04–0.89)	0.38

*IQR, interquartile range; NA, not applicable; SD, standard deviation

 $\dagger\,^a\text{Pearson}\,\chi^2$ test for proportions and Mann-Whitney test for means

‡ Theoretical age if children were born at term.

§ Z-scores were generated using Intergrowth-21st for anthropometry at birth (1) and using the WHO 2005 growth charts (2) for anthropometry during the visit. A Z-score is defined as the deviation from the mean value of the gender-specific and age-specific reference populations, divided by the standard deviation for the reference population.

Technical Appendix Table 2. Early childhood development scores for French Polynesian children and reference children aged 12–30
months*

	Reference	(n = 269)	Study particip		
ECD domain	Mean score	SD	Mean score	SD	p value†
Socioemotional	90	10	92	10	0.69‡
Cognitive	64	19	57	26	0.001
Motor	64	20	60	20	0.08

*ECD, early childhood development; SD, standard deviation

†t-test unless specified.

 $\pm\chi^2$ -test using information on children with suspected "abnormal" development (7/107 among study participants and 21/248 among the reference population). The *t*-test was not done because socioemotional scores were not normally distributed.

	1. Socioemotional domain			2. Cognitive domain			3. Motor domain					
	А,	Q,	Ρ,	р	Α,	Q,	Ρ,	р	А,	Q,	Ρ,	р
Mothers	n (%)	n (%)	n (%)	value†	n (%)	n (%)	n (%)	value	n (%)	n (%)	n (%)	value
All (N = 107)	100 (93)	3 (3)	4 (4)	NA	68 (64)	23 (22)	16 (15)	NA	81 (76)	20 (18)	6 (6)	NA
Zika virus seropositivity												
No	25 (96)	1 (4)	0 (0)	0.63	18 (69)	6 (23)	2 (8)	0.54	19 (73)	6 (23)	1 (4)	0.84
Yes	75 (93)	2 (2)	4 (5)	NA	50 (62)	17 (21)	14 (17)	NA	62 (76)	14 (17)	5 (6)	NA
History of Zika infection												
No infection during pregnancy‡	33 (97)	1 (3)	0 (0)	0.67	24 (71)	8 (24)	2 (6)	0.48	25 (74)	8 (24)	1 (3)	0.26
Asymptomatic (timing unknown)§	51 (91)	2 (4)	3 (5)	NA	33 (59)	12 (21)	11 (20)	NA	44 (79)	10 (18)	2 (4)	NA
Symptomatic during pregnancy¶	16 (94)	0 (0)	1 (6)	NA	11 (65)	3 (18)	3 (18)	NA	12 (71)	2 (12)	3 (18)	NA

Technical Appendix Table 3. Early childhood development and maternal Zika virus infection status, French Polynesia, 2013–2016*

*A, Adequate; NA, not applicable; Q, Question; P, Problem †P values obtained using Fisher's exact test.

¹Seronegative mothers and seropositive mothers who reported Zika-like illness outside pregnancy.

§ Seropositive mothers who did not report Zika-like illness during or outside pregnancy.

Seropositive mothers who reported Zika-like illness during pregnancy.

Technical Appendix Table 4. Crude OR for the association of ECD	by domain with Zika virus infection, French Polynesia, 2013–2016*

 Socioemotional domain† (logistic regression, Adequate vs. Question/Problem) 		(ordered logistic re Adequate vs. Que	egression, estion vs.	3. Motor domain (ordered logistic regression, Adequate vs. Question vs. Problem)		
Crude OR	LRT	Crude OR	LRT	Crude OR	LRT	
(95% CI)	p-value	(95% CI)	p-value	(95% CI)	p value	
2.00 (0.23-17.4)	0.50	1.51 (0.60–3.81)	0.37	0.87 (0.32-2.36)	0.74	
3.24 (0.36-28.9)	0.50	1.55 (0.60-4.00)	0.66	0.77 (0.27-2.17)	0.63	
2.06 (0.12-35.1)	NA	1.37 (0.38-4.89)	NA	1.37 (0.35–5.31)	NA	
	(logistic regression, vs. Question/Pr Crude OR (95% CI) 2.00 (0.23–17.4) 3.24 (0.36–28.9)	(logistic regression, Adequate vs. Question/Problem) Crude OR LRT (95% Cl) p-value 2.00 (0.23–17.4) 0.50 3.24 (0.36–28.9) 0.50	1. Socioemotional domain† (logistic regression, Adequate vs. Question/Problem)(ordered logistic reg Adequate vs. Question/Problem)Crude ORLRTCrude OR (95% Cl)Problem)2.00 (0.23–17.4)0.501.51 (0.60–3.81)3.24 (0.36–28.9)0.501.55 (0.60–4.00)	(logistic regression, Adequate vs. Question/Problem) Adequate vs. Question vs. Problem) Crude OR LRT Crude OR LRT (95% Cl) p-value (95% Cl) p-value 2.00 (0.23–17.4) 0.50 1.51 (0.60–3.81) 0.37 3.24 (0.36–28.9) 0.50 1.55 (0.60–4.00) 0.66	1. Socioemotional domain† (logistic regression, Adequate vs. Question/Problem)(ordered logistic regression, Adequate vs. Question vs. Problem)(ordered logistic re Adequate vs. Question vs. Problem)(ordered logistic re Adequate vs. Question vs. Problem)(ordered logistic re Adequate vs. Question vs. Problem)Crude OR (95% Cl)LRT P-valueCrude OR (95% Cl)LRT P-valueCrude OR (95% Cl)Crude OR (95% Cl)2.00 (0.23–17.4)0.501.51 (0.60–3.81)0.370.87 (0.32–2.36)3.24 (0.36–28.9)0.501.55 (0.60–4.00)0.660.77 (0.27–2.17)	

*CI, confidence interval; LRT, likelihood ratio test; OR, odds ratio

+Because of the limited number of observations in the socioemotional domain, Question and Problem categories were grouped together and logistic regression was performed.

\$\$ Seropositive mothers who did not report Zika-like illness during or outside pregnancy.

§Seropositive mothers who reported Zika-like illness during pregnancy.

References

- 1. Cheikh Ismail L, Knight HE, Bhutta Z, Chumlea WC; International Fetal and Newborn Growth Consortium for the 21st Century. Anthropometric protocols for the construction of new international fetal and newborn growth standards: the INTERGROWTH-21st Project. BJOG. 2013;120(Suppl 2):42-7. PubMed http://dx.doi.org/10.1111/1471-0528.12125
- 2. de Onis M, Garza C, Victora CG, Onyango AW, Frongillo EA, Martines J. The WHO Multicentre Growth Reference Study: planning, study design, and methodology. Food Nutr Bull. 2004;25(Suppl):S15-26. PubMed http://dx.doi.org/10.1177/15648265040251S103