Low functional antibodies to *P. falciparum* antigens in Beninese neonates further reduced the time to first malaria infection in infancy following placental malaria.

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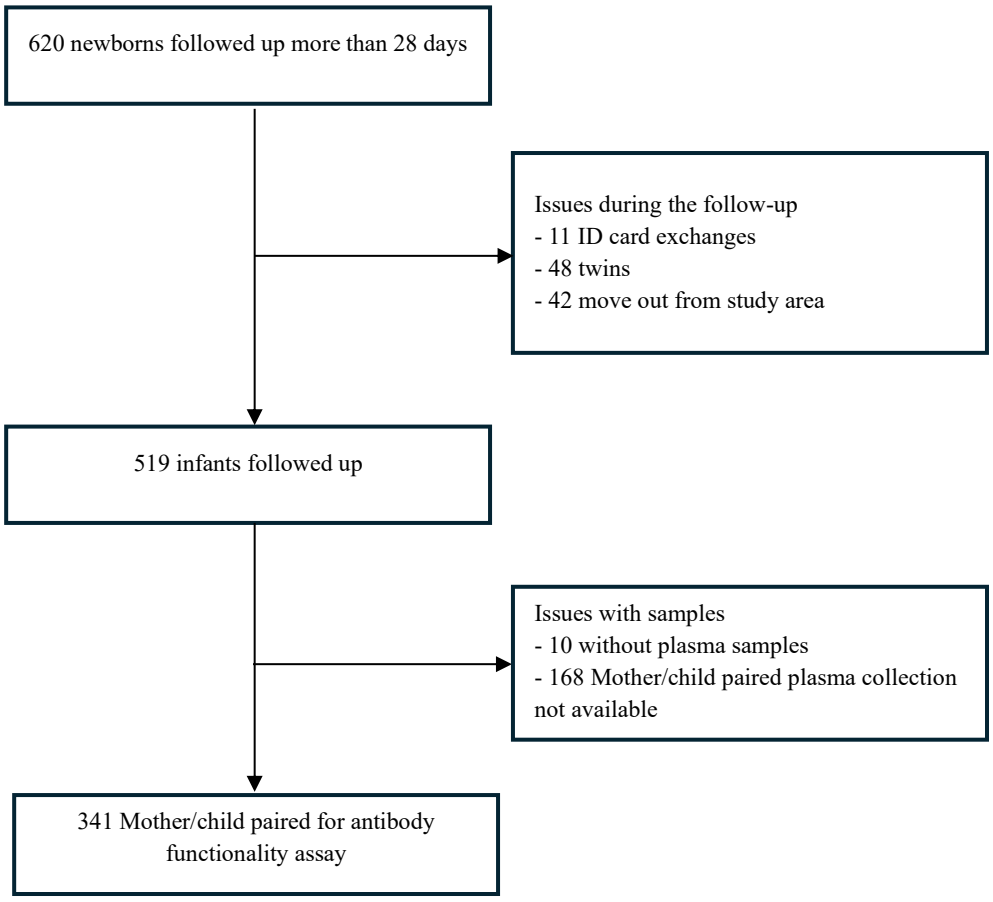


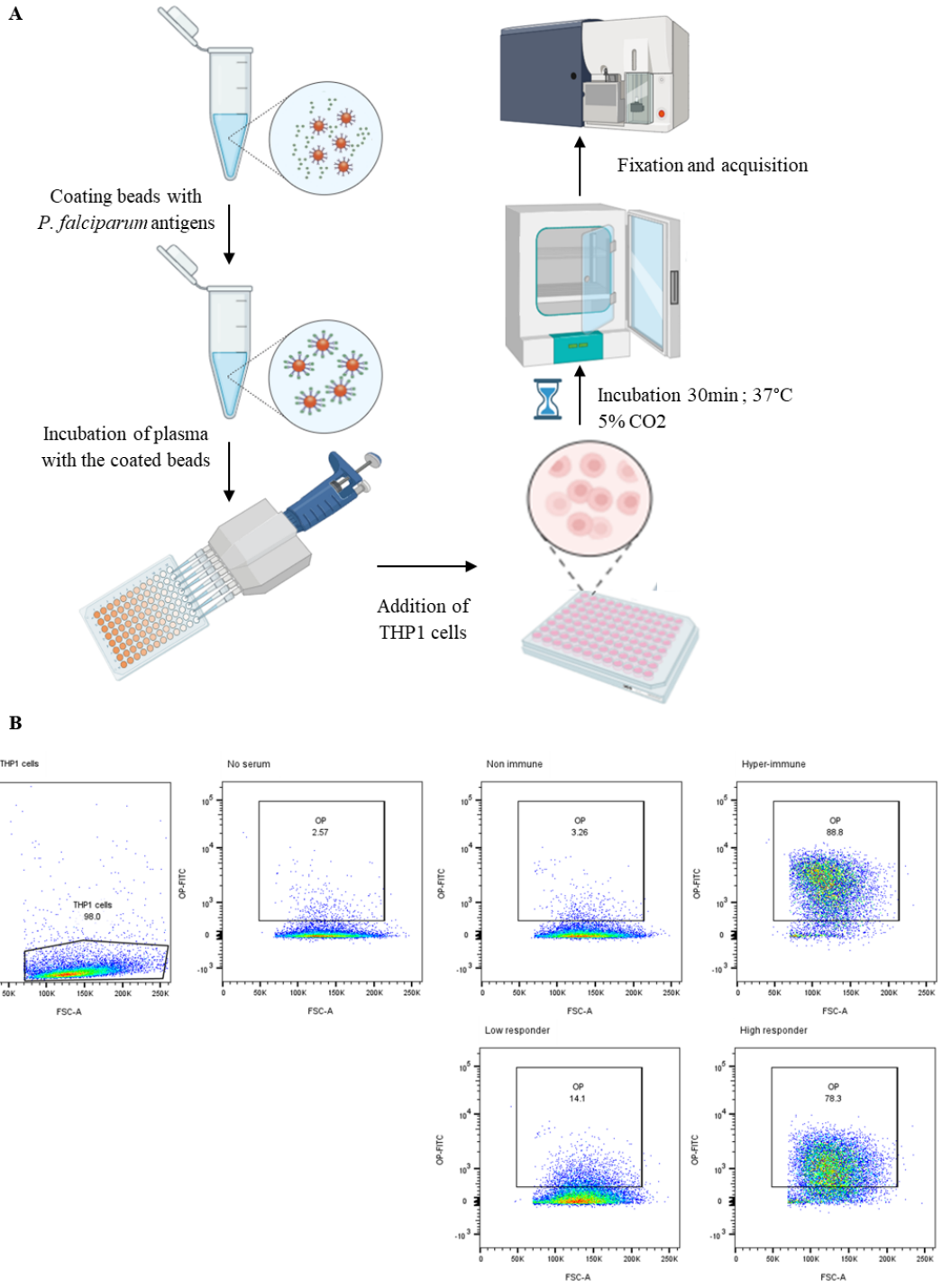
Figure Supplementary 1: Study flow chart

The Tori Bossito cohort is a birth cohort designed to evaluate malaria incidence and its determinants during early life. The follow-up includes 519 newborns until 18 months. The opsonic phagocytosis (BPA) was evaluated at birth for 341 mother/child paired plasma from available samples.

Variables	n (%)	**No Placenta malaria n=465 (%) [Conf. Int]**	**Placenta malaria n=54 (%) [Conf. Int]**	*p-value*
Hypergammaglobulinemia				0,99[a]
<16 g.L-1	358 (69,0)	321 (61,8)	37 (7,1)	
≥16 g.L-1	161 (31,0)	144 (27,7)	17 (3,3)	
Gestation				**0,01**[a]
Primigravid	441 (85,0)	402 (77,5)	39 (7,5)	
Multigravid	78 (15,0)	63 (12,1)	15 (2,9)	
Maternal parasite density (/µL)	518	0,1 [0 ; 1,4]	781,2 [0 ; 3799,7]	**<0,0001**[b]
Mother's weight (kg)	521	61,8 [60,5 ; 63,1]	57,9 [56,2 ; 59,8]	**0,0008**[b]
Mother's age (years)	525	27,8 [27,3 ; 28,3]	25,6 [23,9 ; 27,2]	**0,01**[b]
Mousquito net				0,28[a]
No user	182 (35,0)	159 (87,4)	23 (12,6)	
User	337 (65,0)	306 (90,8)	31 (09,2)	
Sickle cell trait (SCT)				0,26[a]
No SCT	384 (78,2)	347 (90,4)	37 (09,6)	
SCT	107 (21,8)	92 (86,0)	15 (14,0)	
Maternity				0,04[a]
Avame	174 (33,5)	164 (94,2)	10 (05,8)	
Cada	252 (48,5)	219 (86,9)	33 (13,1)	
Gare	93 (18,0)	82 (88,2)	11 (11,8)	
Birth weight (g)				0,21[a]
< 2500	48 (9,2)	40 (7,7)	8 (1,5)	
≥2500	471 (90,8)	425 (81,9)	46 (8,9)	
Prematurity				0,75[a]
No Prema	469 (90,4)	416 (80,2)	47 (9,1)	
Prema	56 (10,8)	49 (9,4)	7 (1,3)	
IPTp				0,99[a]
Not treated	64 (12,3)	77 (14,8)	9 (1,7)	
At least one dose	277 (53,4)	388 (74,8)	45 (8,7)	

Supplementary table 1: Population characteristics of the Tori Bossito cohort

Conf. Int: 95% confidence intervale, n: number of participants, %, a: x2 test, b: Student's t-test, SCT: Sickle cell trait, IPTp: Intermittent preventive antimalarial treatments, g.L-1: gram per liter (IgG quantity), p/µL: parasites per microliter; kg: kilogram (mother weight), g: gram (weight of newborn at birth), Prematurity was defined as birth less or equal to 37 SA (using Balard score).



Supplementary Figure 2: Beads-based opsonic phagocytosis assay ang gating strategy

Bead-based opsonic phagocytosis (BPA) assay: **(A)** The BPA procedure includes the following steps: i) coupling beads with antigens, ii) incubating the antigen-coated beads with plasma, iii) incubating with THP-1 cells, and iv) analysis by flow cytometry. **(B)** Gating strategy showing the BPA percentage of the controls included in the assay, after gating on single cells.

	no PM				PM			
Maternal BPA	Coefficient	[95% conf.	interval]	p.value	Coefficient	[95% conf.	interval]	p.value
Maternal IgG (log)	4,806	3,892	5,72	**<0,0001**	3,331	0,939	5,722	**0,0072**
Antigens (ref AMA1)								
MSP3	21,973	16,819	27,126	**<0,0001**	22,365	8,263	36,468	**0,0023**
GLURP-R0	20,022	14,591	25,454	**<0,0001**	10,434	-4,138	25,007	0,1627
GLURP-R2	43,004	38,819	47,19	**<0,0001**	36,801	25,543	48,059	**<0,0001**
Primigest	-5,007	-9,735	-0,28	**0,0388**	-0,799	-10,056	8,459	0,8667
Sickle cell trait	0,502	-3,619	4,622	0,8116	5,541	-3,489	14,571	0,2366
Maternal weight	-0,087	-0,193	0,02	0,1113	-0,498	-1,161	0,166	0,1502
Maternal IgG1 (log)	2,394	1,695	3,093	**<0,0001**	1,3	-0,656	3,257	0,1953
Antigens (ref AMA1)								
MSP3	13,681	8,807	18,555	**<0,0001**	14,107	0,203	28,012	**0,0488**
GLURP-R0	8,997	4,177	13,818	**0,0003**	0,945	-12,657	14,548	0,8918
GLURP-R2	39,146	34,754	43,537	**<0,0001**	32,8	20,371	45,228	**<0,0001**
Primigest	-4,354	-9,535	0,826	0,1006	-0,808	-10,983	9,367	0,877
Sickle cell trait	0,035	-4,402	4,473	0,9876	6,509	-3,01	16,027	0,1886
Maternal weight	-0,084	-0,197	0,029	0,1459	-0,534	-1,238	0,169	0,1454
Maternal IgG3 (log)	3,09	2,502	3,677	**<0,0001**	1,979	0,207	3,752	**0,0303**
Antigens (ref AMA1)								
MSP3	3,103	-0,236	6,443	0,0689	11,871	2,098	21,645	**0,019**
GLURP-R0	1,759	-1,727	5,245	0,3231	-1,755	-11,888	8,379	0,735
GLURP-R2	26,444	23,073	29,815	**<0,0001**	27,394	18,112	36,676	**<0,0001**
Primigest	-3,522	-8,341	1,298	0,1533	-1,23	-10,481	8,02	0,7959
Sickle cell trait	0,43	-3,776	4,637	0,8412	7,702	-1,453	16,857	0,1077
Maternal weight	-0,045	-0,152	0,062	0,4102	-0,444	-1,13	0,243	0,2131

Supplementary table 2: Association between PM and the functional maternal IgG, IgG1 and IgG3 specific for malaria antigens

All six stratified linear mixed-effects models converged successfully. Robust standard errors were used to account for mild heteroscedasticity, confirmed by the Breusch-Pagan test for the IgG model ($F = 5.28$, $p = 0.022$, $R^2 = 0.004$). Residual distributions were approximately symmetric and centered on zero across all models. All six models were considered valid for inference, with residual heteroscedasticity and non-Gaussian random effects acknowledged as consistent limitations.

	no PM				PM			
Fetal BPA	Coefficient	[95% conf.	interval]	p.value	Coefficient	[95% conf.	interval]	p.value
Fetal IgG (log)	3,041	2,42	3,663	**<0,0001**	5,428	3,78	7,076	**<0,0001**
Antigens (ref AMA1)								
MSP3	9,707	6,124	13,29	**<0,0001**	18,931	9,214	28,648	**<0,0001**
GLURP-R0	0,127	-3,674	3,927	0,948	8,464	-1,606	18,534	0,102
GLURP-R2	7,381	4,047	10,714	**<0,0001**	12,614	4,011	21,217	**0,005**
Maternal BPA	0,861	0,823	0,898	**<0,0001**	0,828	0,727	0,928	**<0,0001**
Hypergammaglobulinen	1,826	-0,229	3,881	0,083	-5,925	-11,209	-0,641	**0,0349**
Primigravidae	0,722	-2,069	3,513	0,613	3,241	-2,355	8,837	0,265
Sickle cell trait	-1,29	-3,714	1,133	0,298	2,649	-3,078	8,376	0,371
Maternal weight	0,05	-0,013	0,113	0,118	-0,252	-0,658	0,155	0,234
Fetal IgG1 (log)	1,361	0,906	1,816	**<0,0001**	3,4	1,942	4,858	**<0,0001**
Antigens (ref AMA1)								
MSP3	2,447	-0,706	5,599	0,129	11,334	1,667	21,001	**0,023**
GLURP-R0	-8,178	-11,39	-4,966	**<0,0001**	-0,664	-10,343	9,016	0,893
GLURP-R2	2,435	-0,84	5,71	0,145	8,705	-0,499	17,909	0,066
Maternal BPA	0,892	0,855	0,93	**<0,0001**	0,877	0,772	0,981	**<0,0001**
Hypergammaglobulinen	2,134	-0,061	4,329	0,058	-4,764	-11,014	1,485	0,144
Primigravidae	0,768	-2,243	3,779	0,617	3,681	-3,087	10,449	0,293
Sickle cell trait	-1,791	-4,373	0,791	0,175	4,285	-2,49	11,06	0,223
Maternal weight	0,055	-0,012	0,121	0,108	-0,283	-0,768	0,201	0,260
Fetal IgG3 (log)	1,368	0,979	1,756	**<0,0001**	1,847	0,562	3,132	0,006
Antigens (ref AMA1)								
MSP3	-2,812	-4,955	-0,668	**0,010**	-3,391	-9,996	3,215	0,317
GLURP-R0	-12,264	-14,534	-9,995	**<0,0001**	-14,265	-21,158	-7,373	**<0,0001**
GLURP-R2	-3,532	-5,903	-1,16	**0,004**	-5,643	-12,471	1,185	0,108
Maternal BPA	0,876	0,838	0,914	**<0,0001**	0,855	0,744	0,966	**<0,0001**
Hypergammaglobulinen	2,671	0,447	4,895	**0,019**	-3,417	-9,717	2,883	0,295
Primigravidae	1,388	-1,638	4,413	0,370	2,061	-4,764	8,886	0,558
Sickle cell trait	-1,52	-4,145	1,106	0,258	4,216	-2,676	11,108	0,239
Maternal weight	0,062	-0,005	0,129	0,073	-0,172	-0,665	0,321	0,498

Supplementary table 3: Association between PM and the functional transmitted (fetal) IgG, IgG1 and IgG3 specific for malaria antigens

All six linear mixed-effects models showed good fit (IgG, IgG1, and IgG3, stratified by group). ICC values were low to moderate (0.091–0.195), justifying the use of random intercepts. Residuals were randomly scattered around zero with no systematic trend, supporting homoscedasticity and linearity. Residual distributions were approximately normal and zero-centered. VIF values were low for all predictors (VIF $\leq$ 5.19), indicating no problematic multicollinearity.

CMTR functional IgG	Variables	Coefficient	[95% conf.	interval]	p.value
IgG	Maternal_IgG	0,037	0,017	0,057	**<0,0001**
	PM	-0,215	-0,371	-0,059	**0,007**
	Maternal_IgGxPM	0,045	0,018	0,071	**0,001**
	Antigens (ref AMA1)				
	MSP3	0,042	-0,052	0,135	0,383
	GLURP-R0	-0,204	-0,301	-0,108	**<0,0001**
	GLURP-R2	-0,106	-0,173	-0,039	**0,002**
	Primigest	0,028	-0,039	0,095	0,419
	Maternal weight	0,002	0,000	0,004	0,128
	Sickle cell trait	-0,002	-0,063	0,059	0,954
IgG1	Maternal_IgG	0,024	0,011	0,036	**<0,0001**
	PM	-0,133	-0,240	-0,026	**0,015**
	Maternal_IgGxPM	0,033	0,014	0,053	**0,001**
	Antigens (ref AMA1)				
	MSP3	0,000	-0,073	0,072	0,996
	GLURP-R0	-0,268	-0,367	-0,170	**<0,0001**
	GLURP-R2	-0,112	-0,174	-0,050	**<0,0001**
	Primigest	0,020	-0,051	0,091	0,577
	Maternal weight	0,002	0,000	0,004	0,083
	Sickle cell trait	0,000	-0,062	0,063	0,992
IgG3	Maternal_IgG	0,012	0,001	0,023	**0,030**
	PM	-0,044	-0,140	0,051	0,361
	Maternal_IgGxPM	0,032	0,008	0,057	**0,010**
	Antigens (ref AMA1)				
	MSP3	-0,130	-0,178	-0,082	**<0,0001**
	GLURP-R0	-0,376	-0,451	-0,301	**<0,0001**
	GLURP-R2	-0,236	-0,282	-0,190	**<0,0001**
	Primigest	0,023	-0,048	0,095	0,522
	Maternal weight	0,002	0,000	0,004	0,068
	Sickle cell trait	-0,001	-0,065	0,064	0,984

Supplementary table 4: Association between the cord-to-mother transfer ratio (CMTR) of functional IgG, IgG1 and IgG3 with PM

Graphical diagnostics showed Pearson residuals approximately symmetrically distributed around zero, with Q-Q plots confirming near-normality. Residuals across quartiles of fitted values showed stable medians and homogeneous spread, with modest heteroscedasticity in the highest quartile, typical of gamma models. Random effects followed a normal distribution centered at zero. The Breusch-Pagan test confirmed residual heteroscedasticity ($p < 0.001$ for IgG and IgG1), addressed by the robust variance estimator. Overall, these diagnostics support the adequacy of the modelling approach.

Cox proportional hazards model with time-varying coefficients

	Variables	HR	Std. Err.	z	P>z	[95% conf.	interval]
Fetal IgG levels							
	PM	1,660	0,368	2,290	**0,022**	1,075	2,563
	Hypergamma (≥16g/dL)	1,703	0,275	3,290	**0,001**	1,240	2,338
	Environm. expo.	1,101	0,014	7,330	**<0,0001**	1,073	1,129
	High IgG levels (fixed)	0,000	0,000	-3,300	**0,001**	0,000	0,012
	High IgG levels (Time-varying)	5,513	3,271	2,880	**0,004**	1,723	17,640
Fetal IgG BPA							
	PM	1,624	0,360	2,190	**0,029**	1,051	2,508
	Hypergamma (≥16g/dL)	1,486	0,239	2,460	**0,014**	1,084	2,037
	Environm. expo.	1,101	0,015	7,270	**<0,0001**	1,073	1,129
	High IgG BPA (fixed)	0,003	0,006	-2,940	**0,003**	0,000	0,147
	High IgG BPA (Time-varying)	2,685	0,980	2,710	**0,007**	1,313	5,491

Time-varying hazard ratios BPA breadthscore or IgG breadthscore

Time	**BPA**			**IgG levels**		
(days)	HR	IC 95%	p	HR	IC 95%	p
30	0.092	[0.022 – 0.378]	**0.001**	0.002	[0.000 – 0.034]	**<0.001**
100	0.301	[0.164 – 0.554]	**<0.001**	0.032	[0.009 – 0.112]	**<0.001**
200	0.597	[0.435 – 0.821]	**0.002**	0.147	[0.087 – 0.247]	**<0.001**
300	0.892	[0.589 – 1.350]	0.588	0.360	[0.231 – 0.561]	**<0.001**
365	1.082	[0.646 – 1.813]	0.764	0.556	[0.308 – 1.003]	0.051

Supplementary table 5: Levels or functional fetal IgG in protection from malaria in infancy

A Cox proportional hazards model was fitted with four covariates and IgG breadth score dichotomized at the median. Multicollinearity was ruled out (mean VIF = 1.00). Following an initial Schoenfeld test, a time-varying coefficient was introduced by splitting follow-up time and adding an interaction term IgG breadth score × ln(t). The logarithmic transformation ln(t) was chosen to model the time-varying effect of IgG breadth score, as it captures a progressive attenuation of protection over time, consistent with both the biological expectation of maternal antibody waning and the observed pattern of hazard ratios across follow-up. This fully resolved the non-proportionality issue (global Schoenfeld test $p = 0.394$). The hazard ratio for IgG breadth score reached statistical significance from day 200 (HR = 0.15, $p < 0.001$) to day 300 (HR = 0.36, $p < 0.001$), with a borderline estimate at day 365 (HR = 0.56, $p = 0.051$). Residual diagnostics supported adequate model fit

	Hazard Ratio	Std. Err.	z	P>|z|	[95% conf.	interval]
Fixed effect						
IgG levels	0,022	0,014	-5,880	**<0,0001**	0,006	0,079
BPA	0,271	0,091	-3,870	**<0,0001**	0,140	0,525
PM	2,138	0,581	2,790	**0,005**	1,255	3,643
BPA x PM	0,433	0,212	-1,710	0,088	0,166	1,132
Hypergamma (≥16g/dL)	1,815	0,297	3,640	**<0,0001**	1,316	2,503
Environm. expo.	1,519	0,095	6,710	**<0,0001**	1,344	1,716
Time-Varying Covariate						
IgG levels	0,988	0,003	-4,120	**<0,0001**	0,982	0,994
IgG BPA	1,008	0,002	4,290	**<0,0001**	1,004	1,012

Supplementary table 6: Levels or functional fetal IgG in protection from malaria in infancy

The proportional hazards assumption was assessed using Schoenfeld residuals; IgG levels and IgG function violated this assumption and were modeled as time-varying covariates. A significant interaction between IgG function and disease status was retained in the final model ($\chi^2(1) = 4.65$, $p = 0.031$). Multicollinearity was negligible (mean VIF = 1.57). No major outliers were detected (all deviance residuals within ±3), and removal of one potentially influential observation did not substantially alter model estimates. Cox-Snell residuals confirmed adequate overall goodness-of-fit.