

Supplemental Digital Content 4: Results of additional analyses

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Posterior β estimates of all co-variates and representation of the prior and posterior distributions

Results of the Bayesian linear regression model are reported for all co-variates in terms of β estimates [80% credible interval] and probability of strictly negative/positive prior. For simplicity, and given that Bayesian analysis using neutral, skeptical and enthusiastic priors provided consistent results, only the results of the neutral prior, for desaturation and mean SctO₂ of the first 12 hours of monitoring time are reported, see Table 2 and Table 3 respectively. Visual representation of the prior and posterior distributions of all covariates is provided uniquely for the Bayesian model on mean SctO₂, Figure 2 to Figure 8.

Table 1 Posterior β estimates for all co-variates. Bayesian linear regression model for SctO₂ desaturation.

Covariates	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)
Desaturation	-0.009 [-0.02 to -0.001]	90% (-)
Age	-0.04 [-0.11 to 0.02]	75% (-)
Syndrome	-8.73 [-15.24 to -3.15]	95% (-)
Nutrition strategy [§]	-5.56 [-9.07 to -2.06]	95% (-)
Cyanotic cardiopathy	-3.26 [-7.52 to 1.43]	80% (-)
PIM3	-1.42 [-3.61 to 0.73]	70% (-)
Intercept	93.00 [1.00 to 85.00]	97.5% (+)

[§] Late PN vs early PN

Table 2 Posterior β estimates for all co-variates. Bayesian linear regression model for mean SctO₂.

Covariates	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)
Mean SctO ₂	0.23 [0.047 to 0.41]	90% (+)
Age	-0.04 [-0.10 to 0.02]	75% (-)
Syndrome	-9.08 [-15.32 to -3.23]	95% (-)
Nutrition strategy [§]	-5.32 [-8.98 to -1.72]	90% (+)
Cyanotic cardiopathy	-3.56 [-7.93 to 0.58]	85% (-)
PIM3	-1.39 [-3.58 to 0.86]	80% (-)
Intercept	77.35 [62.37 to 91.92]	97.5% (+)

[§] Late PN vs early PN

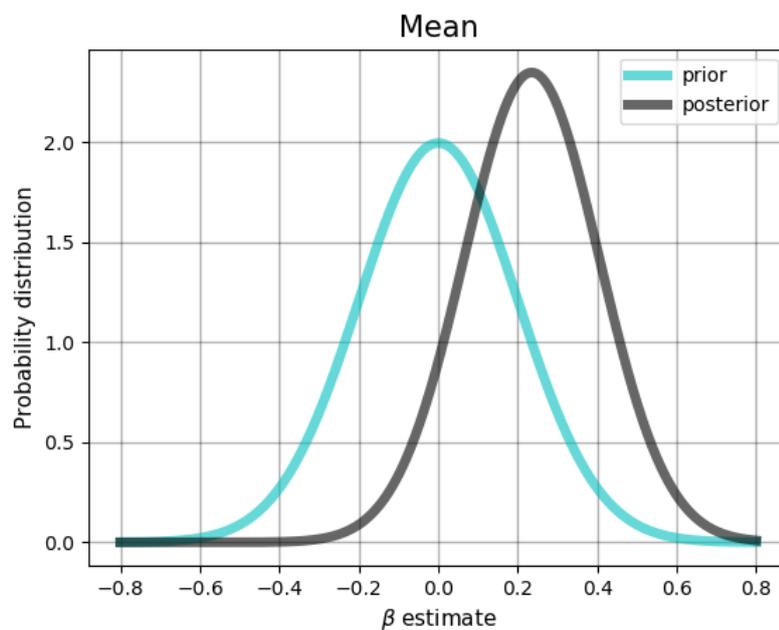


Figure 1 Comparison between the β priors and β posteriors probability distribution for the covariate mean SctO₂ of the multivariable Bayesian model on the relation between mean SctO₂ and total IQ (neutral prior, first 12 hours of monitoring time).

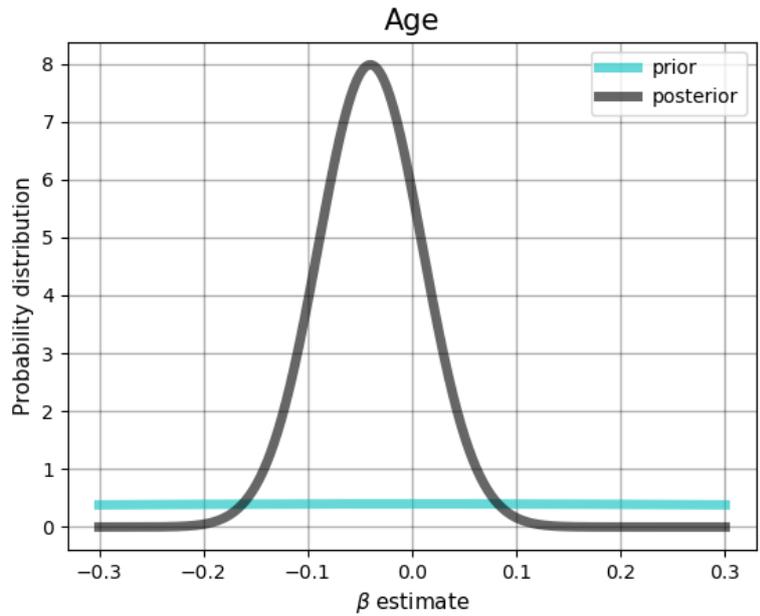


Figure 2 Comparison between the β priors and β posteriors probability distribution for the covariate age of the multivariable Bayesian model on the relation between mean SctO₂ and total IQ (neutral prior, first 12 hours of monitoring time). The β prior is non informative, as it is shown by the flat probability distribution.

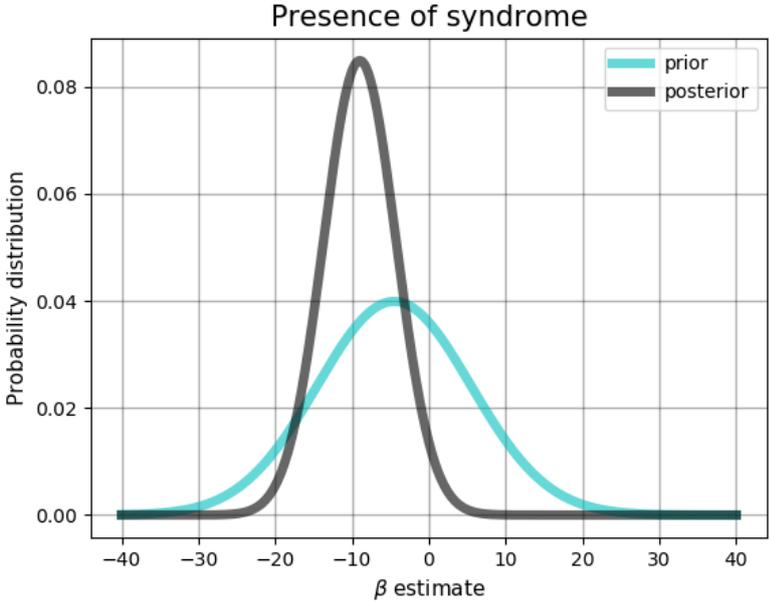


Figure 3 Comparison between the β priors and β posteriors probability distribution for the covariate presence of syndrome of the multivariable Bayesian model on the relation between mean SctO₂ and total IQ (neutral prior, first 12 hours of monitoring time).

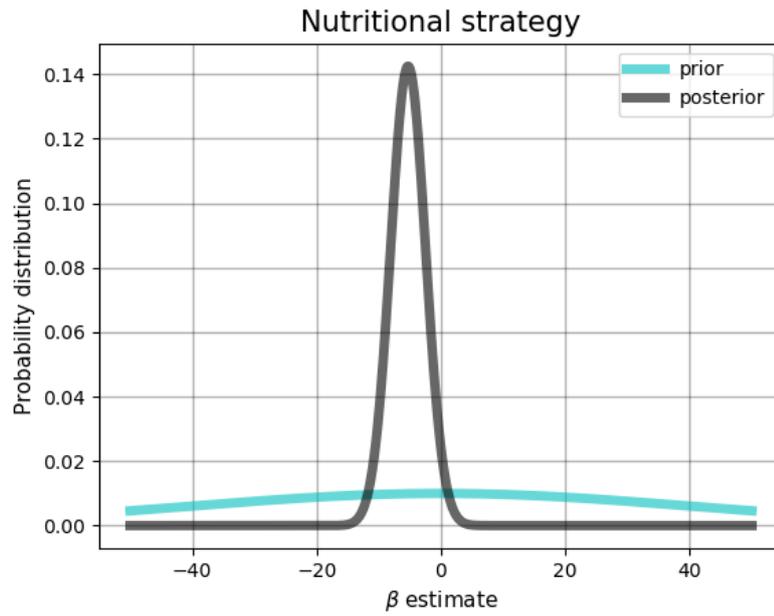


Figure 4 Comparison between the β priors and β posteriors probability distribution for the covariate nutritional strategy of the multivariable Bayesian model on the relation between mean SctO₂ and total IQ (neutral prior, first 12 hours of monitoring time).

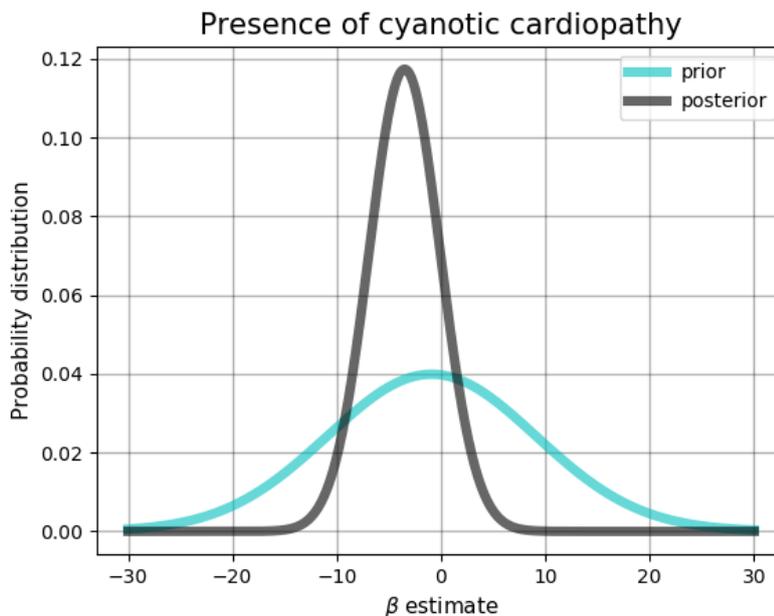


Figure 5 Comparison between the β priors and β posteriors probability distribution for the covariate presence of cyanotic cardiopathy of the multivariable Bayesian model on the relation between mean SctO₂ and total IQ (neutral prior, first 12 hours of monitoring time).

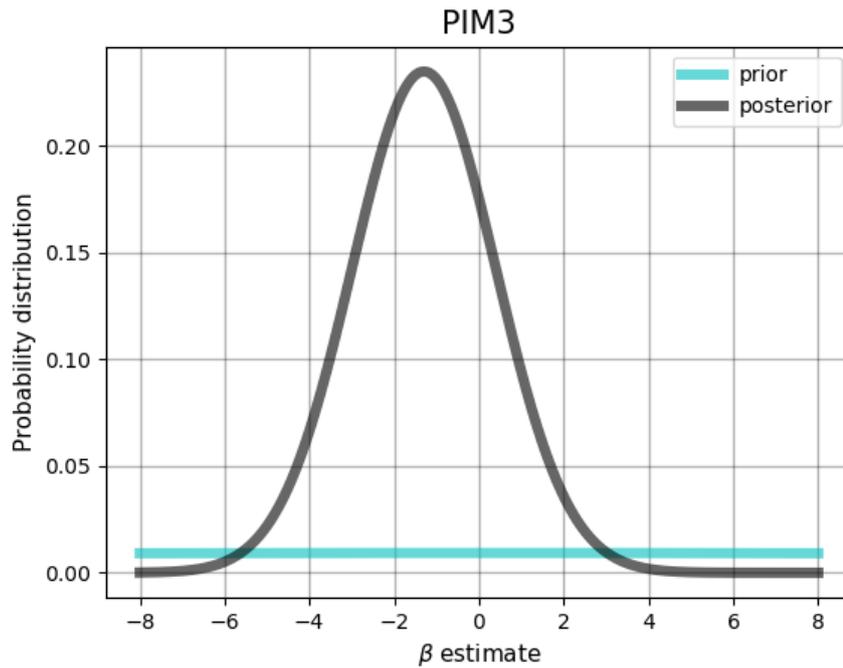


Figure 6 Comparison between the β priors and β posteriors probability distribution for the covariate nutritional strategy of the multivariable Bayesian model on the relation between mean SctO2 and total IQ (neutral prior, first 12 hours of monitoring time).

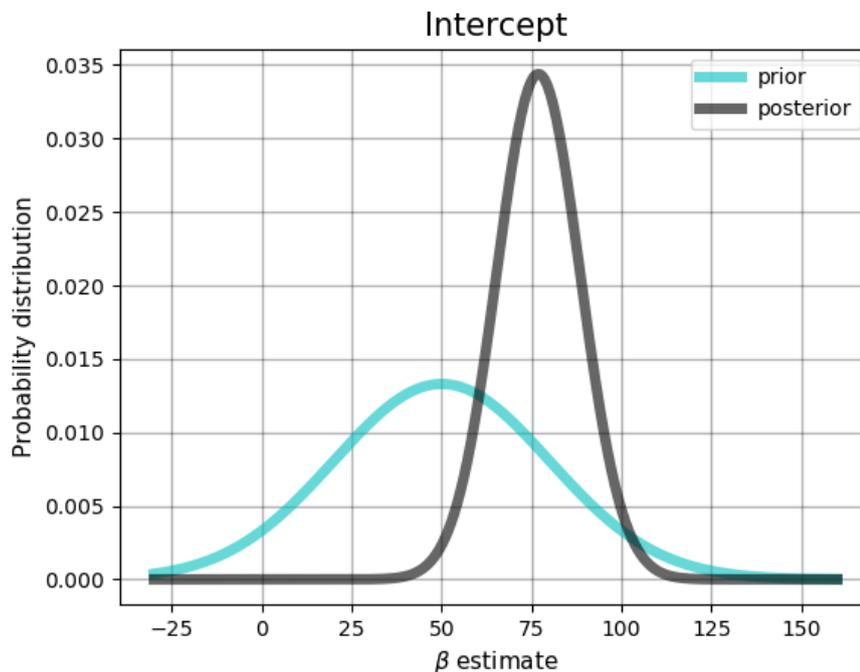


Figure 7 Comparison between the β priors and β posteriors probability distribution for the intercept of the multivariable Bayesian model on the relation between mean SctO2 and total IQ (neutral prior, first 12 hours of monitoring time).

Interaction analysis

No association was found between presence of cyanotic cardiopathy and dose of desaturation ($p=0.47$ and $p=0.22$ respectively for the first 12 hours and 24 hours of monitoring). Presence of cyanotic cardiopathy was associated with lower mean SctO₂ during the first 12 hours and 24 hours of monitoring time, p -values of respectively $p < 0.001$ and $p < 0.001$. However, no interaction effect was found between the presence of cyanotic cardiopathy and mean SctO₂ in relation with long-term total IQ. Results of the β estimates for the neutral prior are reported in Table 4 (first 12 hours).

Table 3 Results of the interaction term analysis for mean SctO₂ and total IQ

Covariates	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)
Mean SctO ₂	0.23 [0.13 to 0.36]	90% (+)
Age	-0.04 [-0.08 to 0.01]	75% (-)
Syndrome	-8.92 [-12.86 to -4.75]	95% (-)
Nutrition strategy	-5.33 [-7.68 to -2.95]	95% (-)
Cyanotic cardiopathy	-3.31 [-11.6 to 4.15]	65% (-)
PIM3	-1.36 [-2.76 to 0.09]	75% (-)
Mean SctO ₂ * cyanotic cardiopathy	-0.003 [-0.121 to 0.122]	50% (-)

Sensitivity analysis on the definition of desaturation

Given that Bayesian analyses using neutral, skeptical and enthusiastic priors provided consistent results, sensitivity analyses for different definitions of desaturation were performed only with the neutral prior. Desaturation was defined as SctO₂ below the thresholds of 60% and 55%. The results of the sensitivity analyses confirmed the robustness of the results of the main analysis, see Table 5 and Table 6 for desaturation defined as SctO₂ below 60% and 55% respectively.

Table 4 Results of a sensitivity analysis with desaturation defined as SctO₂ below 60%

	Desaturation dose (SctO₂ < 60%)	
	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)
First 12-hours of SctO₂ monitoring	-0.09 [-0.16 to -0.03]	95% (-)
First 24-hours of SctO₂ monitoring	-0.02 [-0.067 to 0.025]	85% (-)

Table 5 Results of a sensitivity analysis with desaturation defined as SctO₂ below 55%

	Desaturation dose (SctO₂ < 55%)	
	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)
First 12-hours of SctO₂ monitoring	-0.052 [-0.09 to -0.01]	95% (-)
First 24-hours of SctO₂ monitoring	-0.033 [-0.068 to 0.003]	85% (-)

Sensitivity analyses on the effect of additional adjusting factors

Sensitivity analyses were performed on the effect of additional adjusting factors on the results of the multivariable linear regression model. The multivariable linear regression model of the main analysis was additionally adjusted for the educational status of the parents and, in a separate analysis, for the duration of the cardiopulmonary bypass. The analyses were performed in two subsets of patients that had the required information, namely, in a subset of 76 patients for the additional adjusting factor “educational status of the parents” and a subset of 71 patients for the adjusting factor “duration of cardiopulmonary bypass”. The results remained consistent with the main analysis. In particular Table 6 reports the results of the linear regression model further adjusted for the educational status of the parents,

while Table 7 reports the results of the linear regression model further adjusted for the duration of cardiopulmonary bypass.

Table 6 Multivariable linear regression analysis for the association between SctO₂ features and total IQ. Additional adjusting factor: educational status parents. The analysis was performed on 76 children.

	Desaturation dose		Mean SctO ₂	
	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)
First 12-hours of SctO₂ monitoring				
Skeptical prior	-0.009 [-0.013 to -0.004]	90% (-)	0.224 [0.101 to 0.358]	90% (+)
Neutral prior	-0.011 [-0.016 to -0.006]	95% (-)	0.248 [0.125 to 0.372]	95% (+)
Enthusiastic prior	-0.013 [-0.017 to -0.009]	97.5% (+)	0.308 [0.220 to 0.396]	97.5% (+)
First 24-hours of SctO₂ monitoring				
Skeptical prior	-0.009 [-0.014 to -0.004]	90% (-)	0.254 [0.133 to 0.393]	90% (+)
Neutral prior	-0.011 [-0.017 to -0.007]	95% (-)	0.268 [0.147 to 0.389]	95% (+)
Enthusiastic prior	-0.013 [-0.17 to -0.009]	97.5% (-)	0.317 [0.233 to 0.402]	97.5% (+)

Table 7 Multivariable linear regression analysis for the association between SctO₂ features and total IQ. Additional adjusting factor: duration of CPB. The analysis was performed on 71 children.

	Desaturation dose		Mean SctO ₂	
	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)	Posterior β estimates [80% credible interval]	Probability that the posterior β estimate is strictly negative(-)/positive(+)
First 12-hours of SctO₂ monitoring				
Skeptical prior	-0.005 [-0.010 to 0.000]	80% (-)	0.169 [0.029 to 0.311]	85% (+)
Neutral prior	-0.007 [-0.013 to -0.002]	85% (-)	0.199 [0.074 to 0.332]	90% (+)
Enthusiastic prior	-0.011 [-0.016 to -0.007]	97.5% (-)	0.287 [0.200 to 0.406]	97.5% (+)
First 24-hours of SctO₂ monitoring				
Skeptical prior	-0.003[-0.009 to 0.003]	70% (-)	0.146 [0.006 to 0.291]	80% (+)
Neutral prior	-0.005 [-0.012 to 0.000]	80% (-)	0.179 [0.035 to 0.291]	85% (+)
Enthusiastic prior	-0.010[-0.015 to -0.050]	95% (-)	0.276 [0.188 to 0.373]	97.5% (+)