

The @vanderLaanetal2020 extension of the nonparametric CoR threshold estimation method of @donovan2019 was applied to each D14, fold-rise, and cord blood antibody marker. This extension adjusts for the baseline covariates maternal baseline risk score and the number of days between vaccination and birth using targeted maximum likelihood estimation (TMLE). Results are reported as plots of point and simultaneous 95% confidence interval estimates of the risk of RSV endpoint 1 or 2 varying over subgroups of vaccine recipients defined by antibody marker above a given threshold v , and repeating the analysis over all possible thresholds v . The same analysis was done pooling over vaccine and placebo recipients.

For endpoint 1, Figures ?? and ?? show results for the vaccine arm, for each of the four antibody markers, as fold-rise, D14 values, and cord blood values. Figures ?? and ?? show the same results for the vaccine and placebo arms pooled. The results show that risk of RSV disease does not change markedly depending on threshold value of any of the antibody markers.

Figures ??–?? show the same analyses, except for endpoint 2. The results show that for fold rise of EIA and PCA, RSV risk sharply decreased across subgroups defined by increasing thresholds, approaching zero risk at highest thresholds. There were no RSV disease endpoint 2 cases above a log10 fold-rise of 1.3 for EIA or above log-10 fold-rise of 1.4 for PCA (fold-rises of about 20 and 25, respectively). Endpoint 2 RSV risk did not change much across subgroups defined by D14 marker thresholds for any of the markers, with possible exception of decreasing risk with the highest D14 RSVA and RSVB thresholds, though the estimated effect is smaller than for the fold-rise EIA and PCA results. RSV risk decreased with threshold of cord blood response for all four antibody markers, moreso for RSVA and RSVB, especially at highest antibody levels, than for EIA and PCA. Results were generally similar for the vaccine arm only or combining the vaccine and placebo arms.

In conclusion, the analyses did not support threshold CoPs for endpoint 1, and supported that fold rise EIA, PCA, RSVA, and RSVB all have utility as threshold CoPs for endpoint 2, and may potentially be absolute CoPs. Moreover, D14 RSVA and D14 RSVB show potential as threshold CoPs. Yet, the limited number of endpoint 2 cases limit precision about this inference.

Treatment arm, endpoint 1

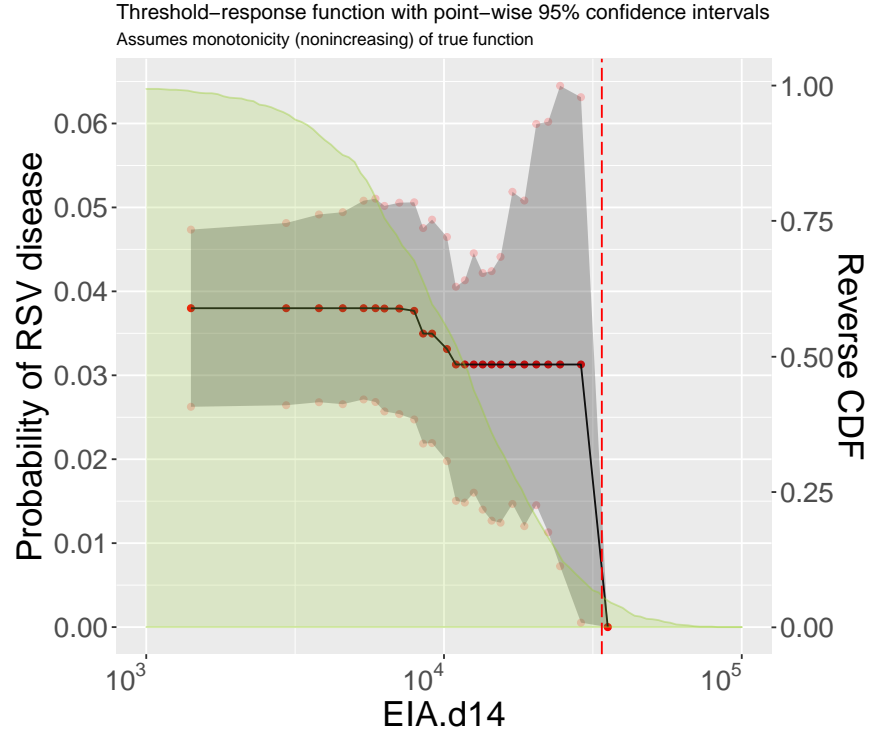


Figure 1: Marginalized risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia for those in vaccine arm with day 14 EIA greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

\log_{10} -Threshold	Threshold	Risk estimate	CI left	CI right
3.152	$1.42 \cdot 10^3$	0.03680	0.02625	0.04736
3.662	$4.59 \cdot 10^3$	0.03800	0.02656	0.04943
3.768	$5.86 \cdot 10^3$	0.03893	0.02682	0.05104
3.900	$7.94 \cdot 10^3$	0.03768	0.02474	0.05061
4.008	$1.02 \cdot 10^4$	0.03313	0.01978	0.04648
4.071	$1.18 \cdot 10^4$	0.02808	0.01484	0.04132
4.156	$1.43 \cdot 10^4$	0.02754	0.01268	0.04241
4.267	$1.85 \cdot 10^4$	0.03142	0.01203	0.05082
4.347	$2.22 \cdot 10^4$	0.03575	0.01130	0.06020
4.549	$3.54 \cdot 10^4$	0.00000	0.00000	1.00000

Table 1: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

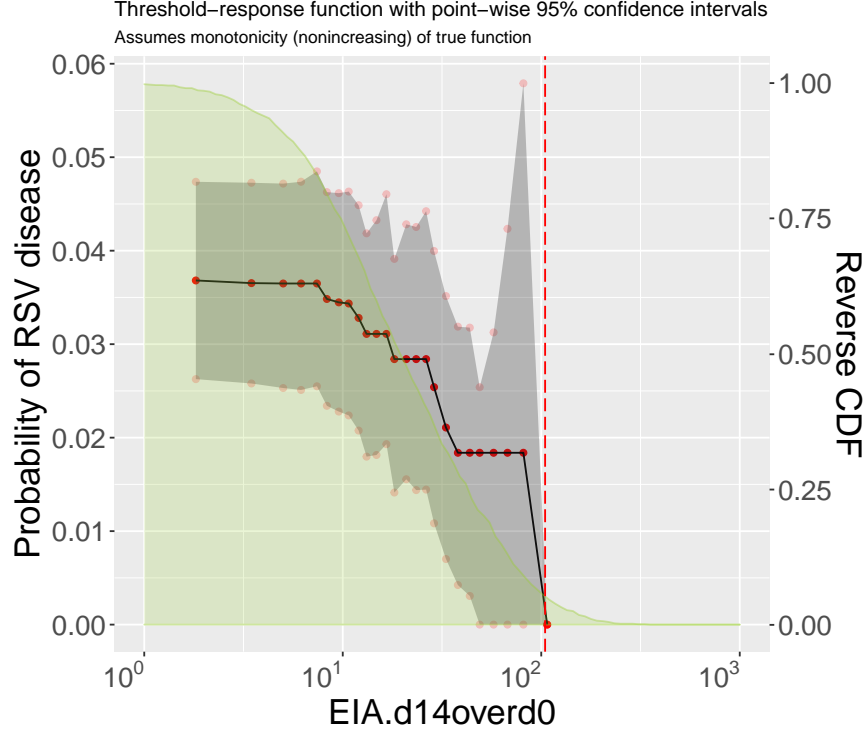


Figure 2: Conditional risk (\geq) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia for those in vaccine arm with fold increase in day 14 EIA relative to day 0 EIA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

\log_{10} -Threshold	Threshold	Risk estimate	CI left	CI right
0.259	$1.82 \cdot 10^0$	0.03682	0.02626	0.04737
0.792	$6.19 \cdot 10^0$	0.03624	0.02510	0.04738
0.921	$8.34 \cdot 10^0$	0.03484	0.02341	0.04627
1.083	$1.21 \cdot 10^1$	0.03281	0.02076	0.04487
1.221	$1.66 \cdot 10^1$	0.03267	0.01931	0.04604
1.315	$2.07 \cdot 10^1$	0.02919	0.01555	0.04282
1.464	$2.91 \cdot 10^1$	0.02540	0.01084	0.03997
1.638	$4.35 \cdot 10^1$	0.01742	0.00307	0.03177
1.764	$5.81 \cdot 10^1$	0.01492	0.00000	0.03126
2.025	$1.06 \cdot 10^2$	0.00000	0.00000	1.00000

Table 2: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

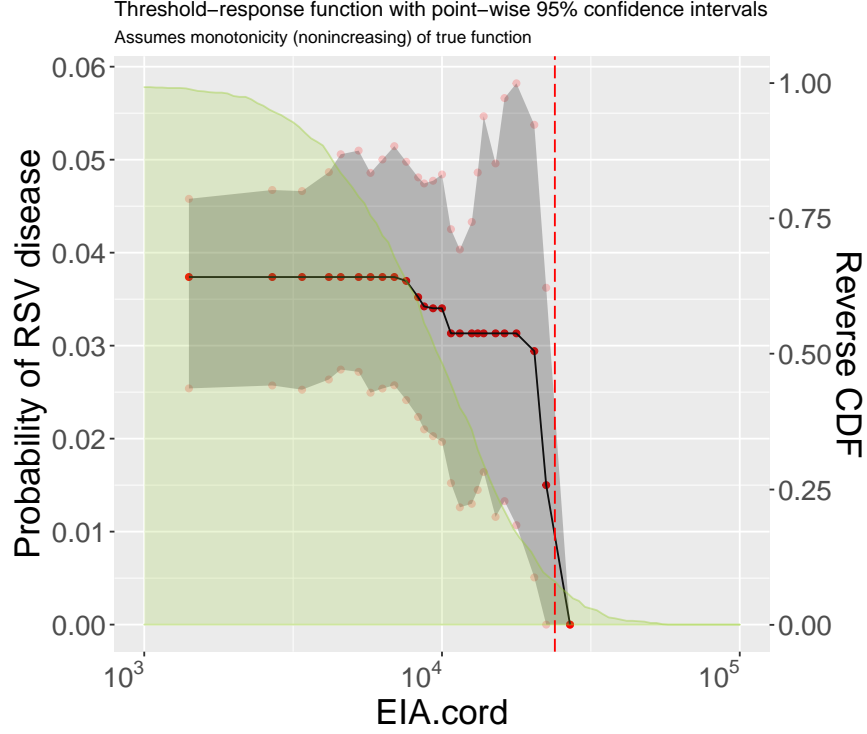


Figure 3: Conditional risk (\geq) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia for those in vaccine arm with EIA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

\log_{10} -Threshold	Threshold	Risk estimate	CI left	CI right
3.152	$1.42 \cdot 10^3$	0.03559	0.02540	0.04579
3.617	$4.14 \cdot 10^3$	0.03751	0.02636	0.04866
3.717	$5.21 \cdot 10^3$	0.03908	0.02718	0.05097
3.842	$6.95 \cdot 10^3$	0.03860	0.02574	0.05145
3.939	$8.69 \cdot 10^3$	0.03422	0.02100	0.04744
4.002	$1.00 \cdot 10^4$	0.03403	0.01966	0.04841
4.096	$1.25 \cdot 10^4$	0.02815	0.01299	0.04330
4.178	$1.51 \cdot 10^4$	0.03059	0.01158	0.04960
4.249	$1.77 \cdot 10^4$	0.03445	0.01069	0.05821
4.433	$2.71 \cdot 10^4$	0.00000	0.00000	1.00000

Table 3: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

Treatment arm, endpoint 2

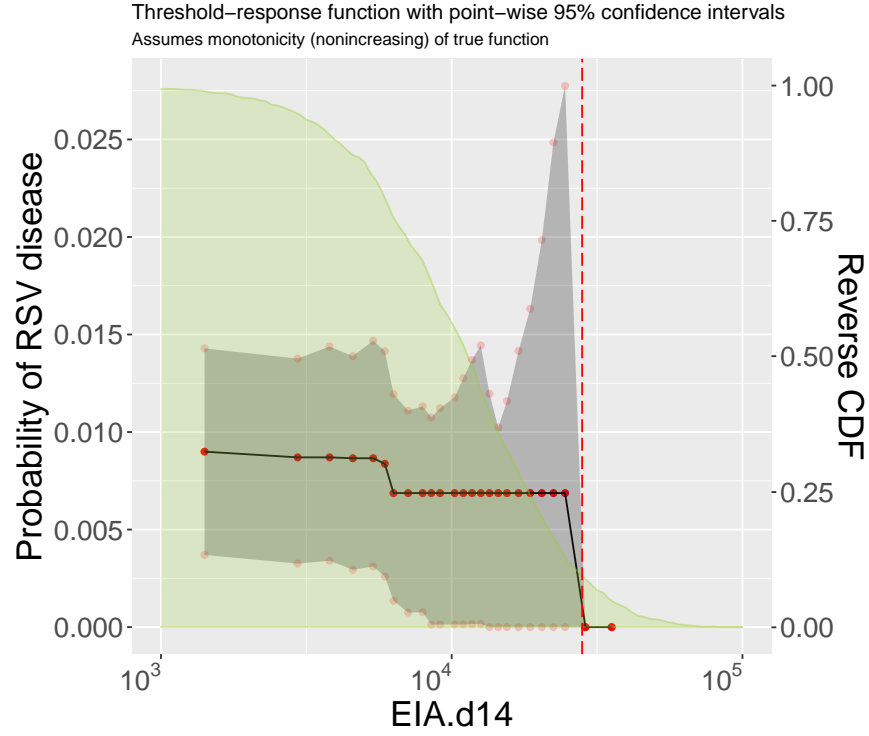


Figure 4: Marginalized risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia for those in vaccine arm with day 14 EIA greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

\log_{10} -Threshold	Threshold	Risk estimate	CI left	CI right
3.152	$1.42 \cdot 10^3$	0.00899	0.00370	0.01429
3.662	$4.59 \cdot 10^3$	0.00842	0.00294	0.01389
3.768	$5.86 \cdot 10^3$	0.00837	0.00260	0.01414
3.900	$7.94 \cdot 10^3$	0.00604	0.00076	0.01132
4.008	$1.02 \cdot 10^4$	0.00596	0.00014	0.01178
4.071	$1.18 \cdot 10^4$	0.00693	0.00016	0.01370
4.156	$1.43 \cdot 10^4$	0.00430	0.00000	0.01023
4.267	$1.85 \cdot 10^4$	0.00688	0.00000	0.01632
4.347	$2.22 \cdot 10^4$	0.01055	0.00000	0.02485
4.549	$3.54 \cdot 10^4$	0.00000	0.00000	1.00000

Table 4: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

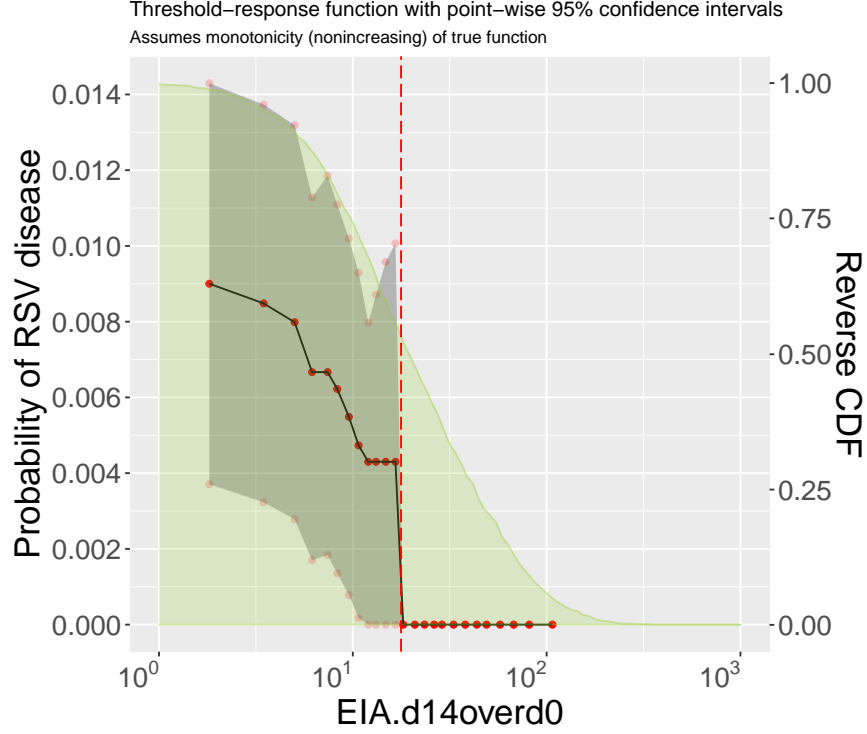


Figure 5: Conditional risk ($\geq s$) of RSV-associated lower respiratory tract infection with severe hypoxemia for those in vaccine arm with fold increase in day 14 EIA relative to day 0 EIA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

\log_{10} -Threshold	Threshold	Risk estimate	CI left	CI right
0.259	$1.82 \cdot 10^0$	0.00900	0.00371	0.01429
0.792	$6.19 \cdot 10^0$	0.00649	0.00170	0.01128
0.921	$8.34 \cdot 10^0$	0.00622	0.00135	0.01109
1.083	$1.21 \cdot 10^1$	0.00378	0.00000	0.00797
1.221	$1.66 \cdot 10^1$	0.00476	0.00000	0.01007
1.315	$2.07 \cdot 10^1$	0.00000	0.00000	1.00000
1.464	$2.91 \cdot 10^1$	0.00000	0.00000	1.00000
1.638	$4.35 \cdot 10^1$	0.00000	0.00000	1.00000
1.764	$5.81 \cdot 10^1$	0.00000	0.00000	1.00000
2.025	$1.06 \cdot 10^2$	0.00000	0.00000	1.00000

Table 5: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

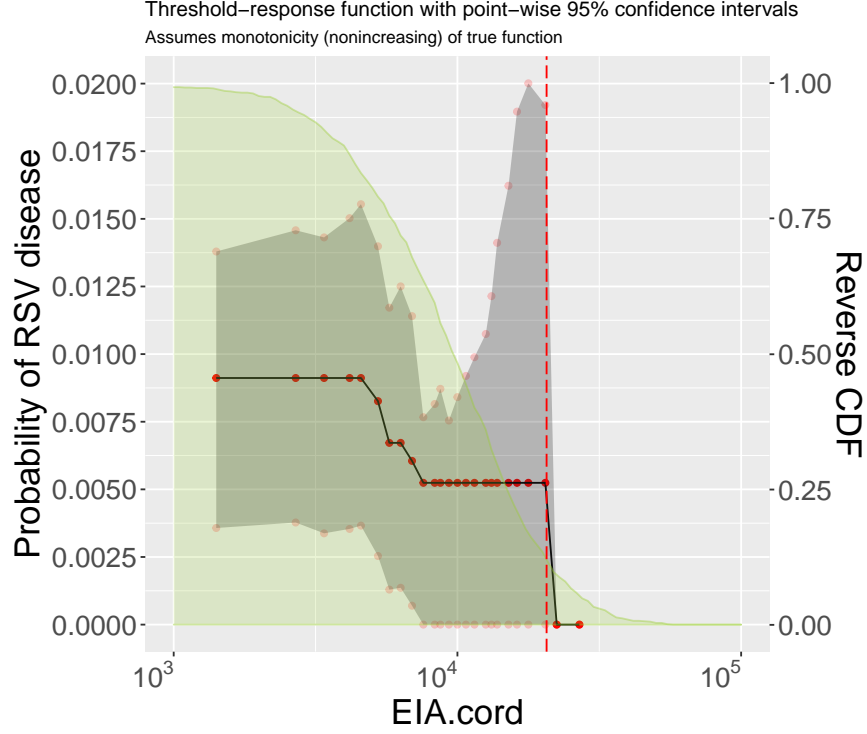


Figure 6: Conditional risk ($\geq s$) of RSV-associated lower respiratory tract infection with severe hypoxemia for those in vaccine arm with EIA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

\log_{10} -Threshold	Threshold	Risk estimate	CI left	CI right
3.152	$1.42 \cdot 10^3$	0.00868	0.00357	0.01379
3.617	$4.14 \cdot 10^3$	0.00928	0.00354	0.01503
3.717	$5.21 \cdot 10^3$	0.00826	0.00254	0.01398
3.842	$6.95 \cdot 10^3$	0.00605	0.00070	0.01140
3.939	$8.69 \cdot 10^3$	0.00413	0.00000	0.00872
4.002	$1.00 \cdot 10^4$	0.00357	0.00000	0.00841
4.096	$1.25 \cdot 10^4$	0.00452	0.00000	0.01074
4.178	$1.51 \cdot 10^4$	0.00685	0.00000	0.01622
4.249	$1.77 \cdot 10^4$	0.01001	0.00000	0.02362
4.433	$2.71 \cdot 10^4$	0.00000	0.00000	1.00000

Table 6: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

Pooled, endpoint 1

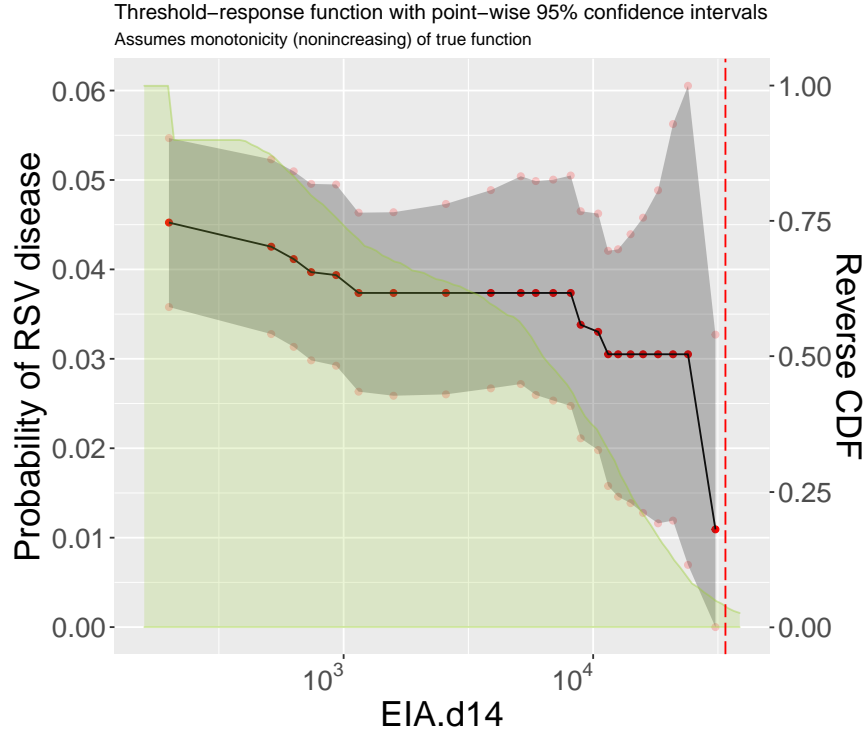


Figure 7: Marginalized risk (\geq s) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with day 14 EIA greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.301	$2.00 \cdot 10^2$	0.04524	0.03579	0.05468
2.801	$6.32 \cdot 10^2$	0.04115	0.03134	0.05097
3.062	$1.15 \cdot 10^3$	0.03634	0.02633	0.04634
3.415	$2.60 \cdot 10^3$	0.03667	0.02603	0.04732
3.772	$5.92 \cdot 10^3$	0.03792	0.02596	0.04988
3.909	$8.11 \cdot 10^3$	0.03761	0.02473	0.05050
4.064	$1.16 \cdot 10^4$	0.02893	0.01578	0.04208
4.150	$1.41 \cdot 10^4$	0.02890	0.01386	0.04393
4.316	$2.07 \cdot 10^4$	0.03408	0.01191	0.05626
4.487	$3.07 \cdot 10^4$	0.01093	0.00000	0.03270

Table 7: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

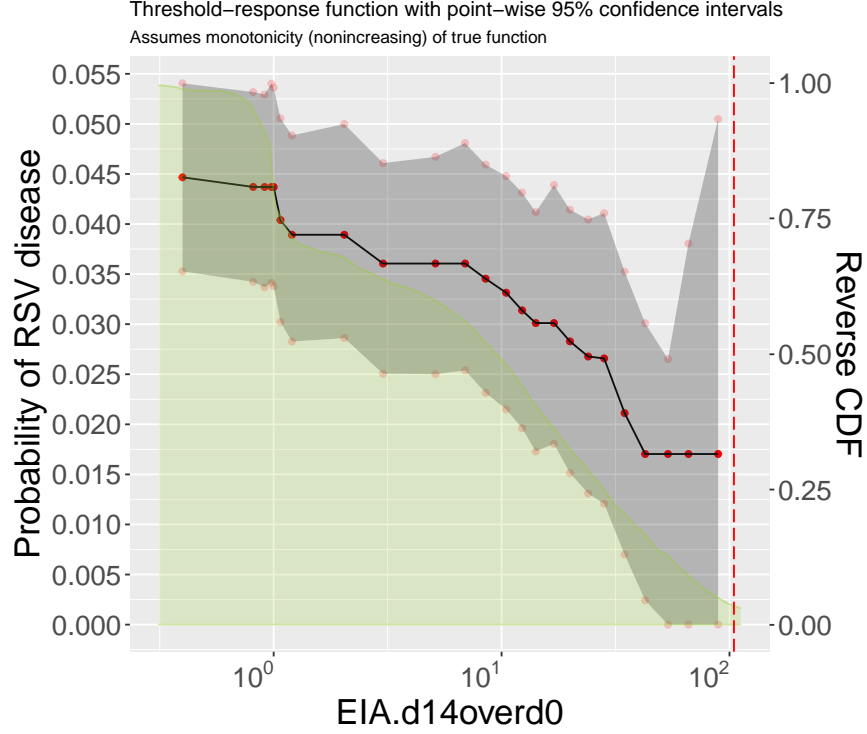


Figure 8: Conditional risk (\geq) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 EIA relative to day 0 EIA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.403	$3.95 \cdot 10^{-1}$	0.04467	0.03528	0.05405
-0.006	$9.86 \cdot 10^{-1}$	0.04408	0.03415	0.05401
0.030	$1.07 \cdot 10^0$	0.04039	0.03022	0.05057
0.482	$3.03 \cdot 10^0$	0.03557	0.02506	0.04609
0.842	$6.95 \cdot 10^0$	0.03673	0.02538	0.04809
1.092	$1.24 \cdot 10^1$	0.03138	0.01962	0.04315
1.229	$1.69 \cdot 10^1$	0.03098	0.01806	0.04389
1.455	$2.85 \cdot 10^1$	0.02658	0.01207	0.04109
1.627	$4.24 \cdot 10^1$	0.01626	0.00242	0.03010
1.948	$8.87 \cdot 10^1$	0.02134	0.00000	0.05049

Table 8: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

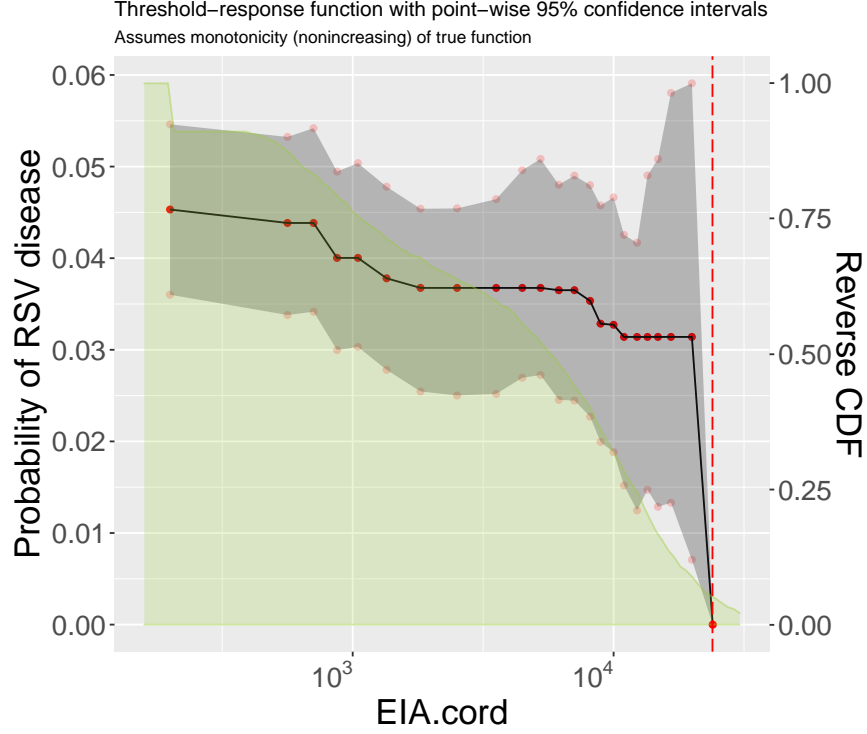


Figure 9: Conditional risk (\geq) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with EIA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.301	$2.00 \cdot 10^2$	0.04531	0.03601	0.05461
2.849	$7.06 \cdot 10^2$	0.04417	0.03416	0.05419
3.128	$1.34 \cdot 10^3$	0.03780	0.02781	0.04780
3.403	$2.53 \cdot 10^3$	0.03523	0.02502	0.04543
3.724	$5.30 \cdot 10^3$	0.03904	0.02725	0.05083
3.848	$7.05 \cdot 10^3$	0.03674	0.02446	0.04902
3.996	$9.91 \cdot 10^3$	0.03273	0.01882	0.04664
4.091	$1.23 \cdot 10^4$	0.02708	0.01247	0.04169
4.223	$1.67 \cdot 10^4$	0.03567	0.01330	0.05804
4.384	$2.42 \cdot 10^4$	0.00000	0.00000	1.00000

Table 9: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

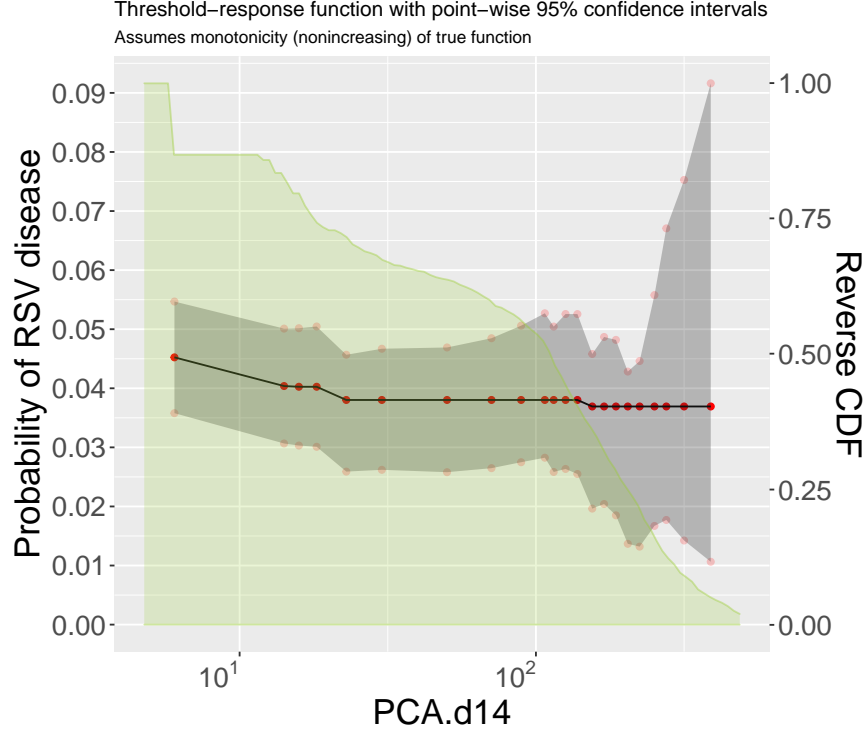


Figure 10: Marginalized risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with day 14 PCA greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.778	$6.00 \cdot 10^0$	0.04524	0.03579	0.05468
1.204	$1.60 \cdot 10^1$	0.04024	0.03031	0.05017
1.477	$3.00 \cdot 10^1$	0.03645	0.02620	0.04669
1.845	$7.00 \cdot 10^1$	0.03748	0.02648	0.04847
2.029	$1.07 \cdot 10^2$	0.04047	0.02825	0.05270
2.140	$1.38 \cdot 10^2$	0.03903	0.02549	0.05256
2.228	$1.69 \cdot 10^2$	0.03455	0.02042	0.04869
2.314	$2.06 \cdot 10^2$	0.02825	0.01368	0.04283
2.439	$2.75 \cdot 10^2$	0.04239	0.01771	0.06707
2.588	$3.87 \cdot 10^2$	0.05113	0.01063	0.09162

Table 10: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

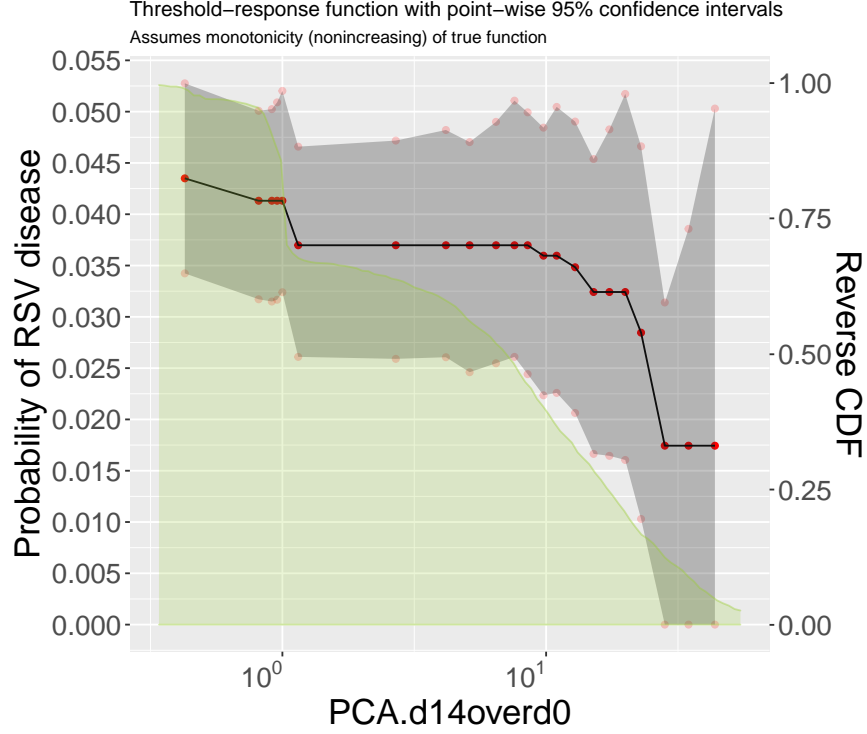


Figure 11: Conditional risk (\geq) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 PCA relative to day 0 PCA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.368	$4.29 \cdot 10^{-1}$	0.04350	0.03424	0.05276
-0.040	$9.12 \cdot 10^{-1}$	0.04087	0.03149	0.05024
0.063	$1.16 \cdot 10^0$	0.03634	0.02610	0.04659
0.619	$4.16 \cdot 10^0$	0.03714	0.02606	0.04821
0.809	$6.44 \cdot 10^0$	0.03724	0.02547	0.04900
0.990	$9.77 \cdot 10^0$	0.03540	0.02235	0.04844
1.112	$1.29 \cdot 10^1$	0.03483	0.02063	0.04903
1.235	$1.72 \cdot 10^1$	0.03236	0.01645	0.04827
1.447	$2.80 \cdot 10^1$	0.01478	0.00000	0.03140
1.637	$4.34 \cdot 10^1$	0.02147	0.00000	0.05030

Table 11: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

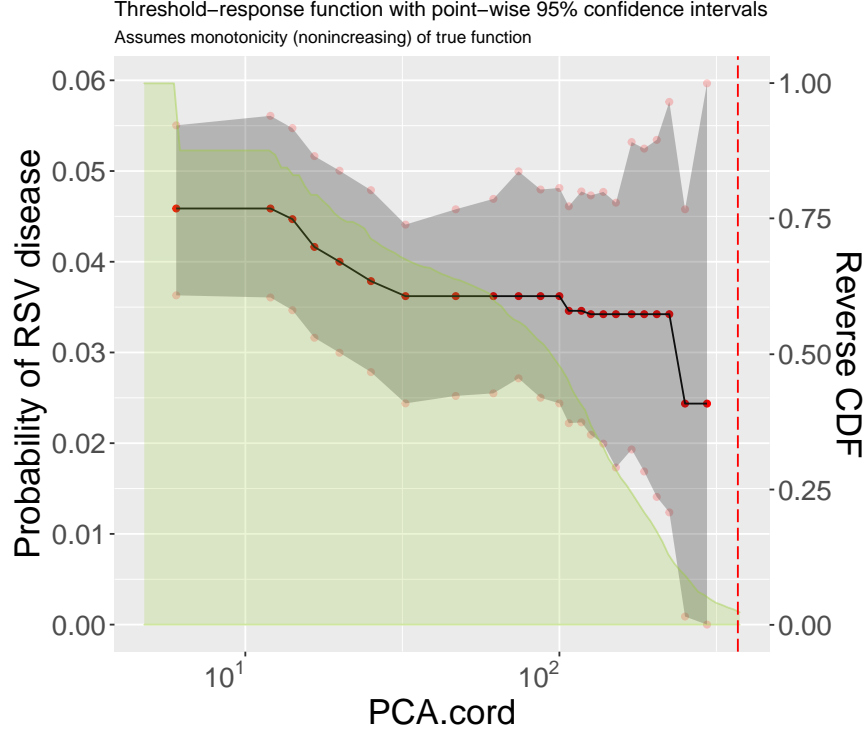


Figure 12: Conditional risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with PCA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.778	$6.00 \cdot 10^0$	0.04567	0.03630	0.05504
1.146	$1.40 \cdot 10^1$	0.04470	0.03466	0.05473
1.398	$2.50 \cdot 10^1$	0.03786	0.02784	0.04789
1.674	$4.72 \cdot 10^1$	0.03550	0.02521	0.04578
1.942	$8.75 \cdot 10^1$	0.03648	0.02501	0.04796
2.033	$1.08 \cdot 10^2$	0.03416	0.02220	0.04611
2.143	$1.39 \cdot 10^2$	0.03382	0.01995	0.04770
2.225	$1.68 \cdot 10^2$	0.03625	0.01931	0.05319
2.348	$2.23 \cdot 10^2$	0.03500	0.01237	0.05762
2.474	$2.98 \cdot 10^2$	0.02539	0.00000	0.05967

Table 12: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

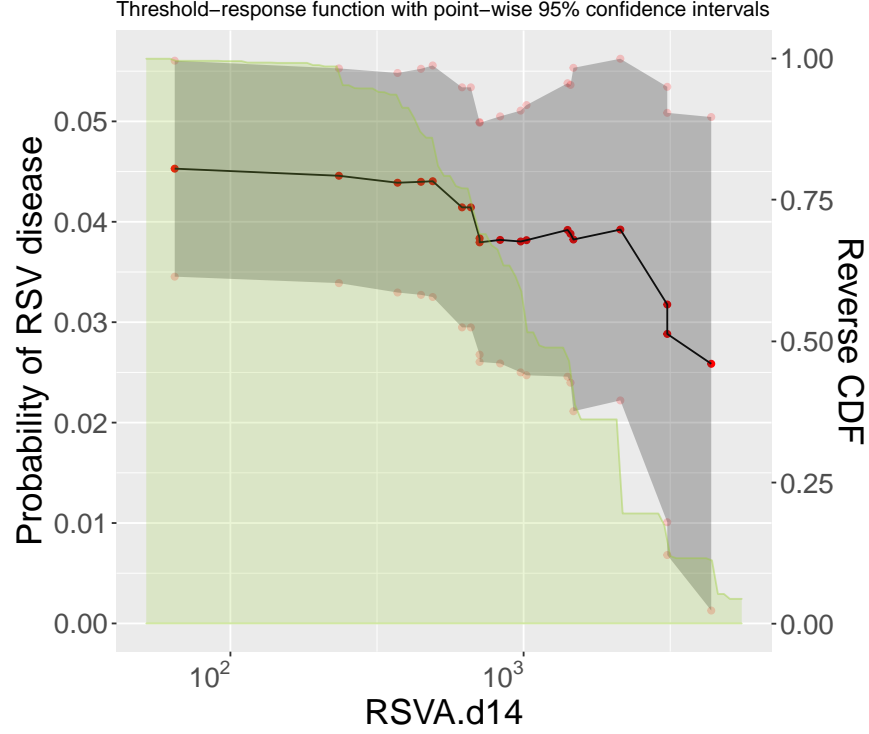


Figure 13: Marginalized risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with day 14 RSVA greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.813	$6.50 \cdot 10^1$	0.04529	0.03454	0.05605
2.574	$3.75 \cdot 10^2$	0.04389	0.03296	0.05482
2.691	$4.91 \cdot 10^2$	0.04404	0.03251	0.05557
2.822	$6.64 \cdot 10^2$	0.04144	0.02948	0.05339
2.851	$7.10 \cdot 10^2$	0.03795	0.02605	0.04986
2.990	$9.77 \cdot 10^2$	0.03804	0.02500	0.05107
3.148	$1.41 \cdot 10^3$	0.03919	0.02457	0.05380
3.167	$1.47 \cdot 10^3$	0.03823	0.02113	0.05533
3.485	$3.05 \cdot 10^3$	0.03176	0.01008	0.05344
3.644	$4.41 \cdot 10^3$	0.02586	0.00128	0.05043

Table 13: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

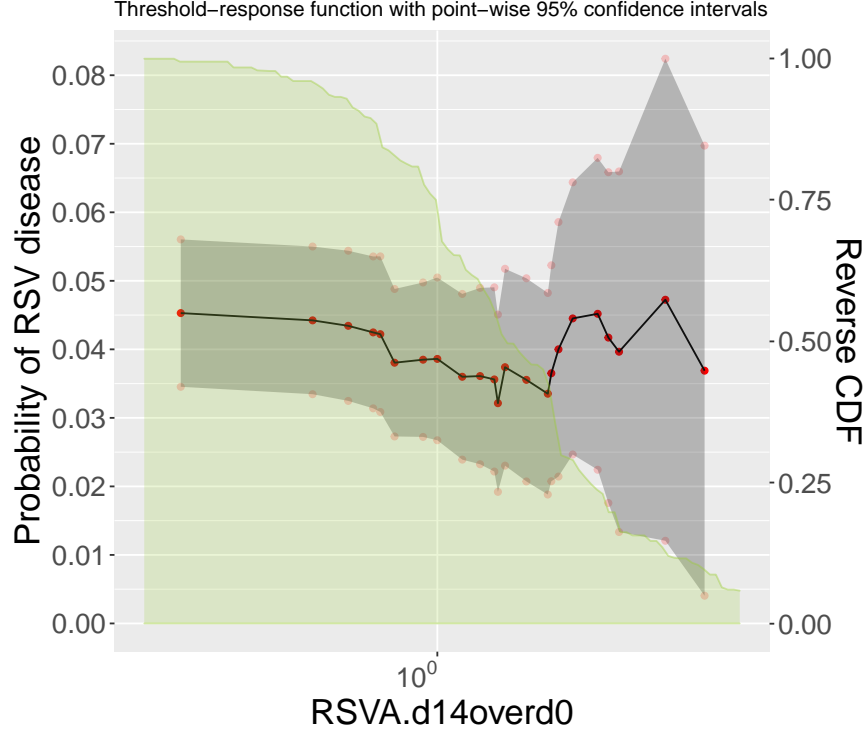


Figure 14: Conditional risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 RSVA relative to day 0 RSVA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.722	$1.90 \cdot 10^{-1}$	0.04529	0.03454	0.05605
-0.252	$5.60 \cdot 10^{-1}$	0.04343	0.03248	0.05439
-0.121	$7.57 \cdot 10^{-1}$	0.03805	0.02729	0.04881
0.000	$1.00 \cdot 10^0$	0.03861	0.02673	0.05048
0.159	$1.44 \cdot 10^0$	0.03561	0.02217	0.04905
0.190	$1.55 \cdot 10^0$	0.03739	0.02303	0.05176
0.318	$2.08 \cdot 10^0$	0.03651	0.02075	0.05227
0.381	$2.40 \cdot 10^0$	0.04451	0.02465	0.06437
0.512	$3.25 \cdot 10^0$	0.03965	0.01334	0.06596
0.749	$5.61 \cdot 10^0$	0.03689	0.00405	0.06973

Table 14: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

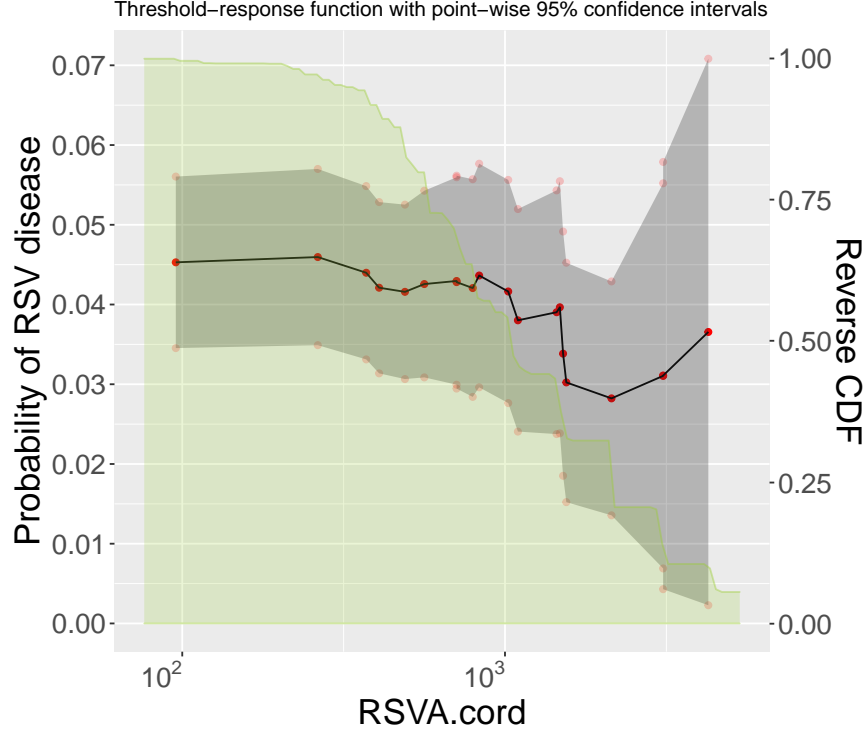


Figure 15: Conditional risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with RSVA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.982	$9.59 \cdot 10^1$	0.04529	0.03454	0.05605
2.574	$3.75 \cdot 10^2$	0.04398	0.03312	0.05485
2.691	$4.91 \cdot 10^2$	0.04159	0.03065	0.05253
2.849	$7.06 \cdot 10^2$	0.04295	0.02994	0.05596
2.898	$7.91 \cdot 10^2$	0.04206	0.02841	0.05571
3.040	$1.10 \cdot 10^3$	0.03802	0.02406	0.05197
3.167	$1.47 \cdot 10^3$	0.03965	0.02384	0.05546
3.190	$1.55 \cdot 10^3$	0.03023	0.01522	0.04524
3.485	$3.05 \cdot 10^3$	0.03105	0.00690	0.05520
3.627	$4.24 \cdot 10^3$	0.03656	0.00229	0.07083

Table 15: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

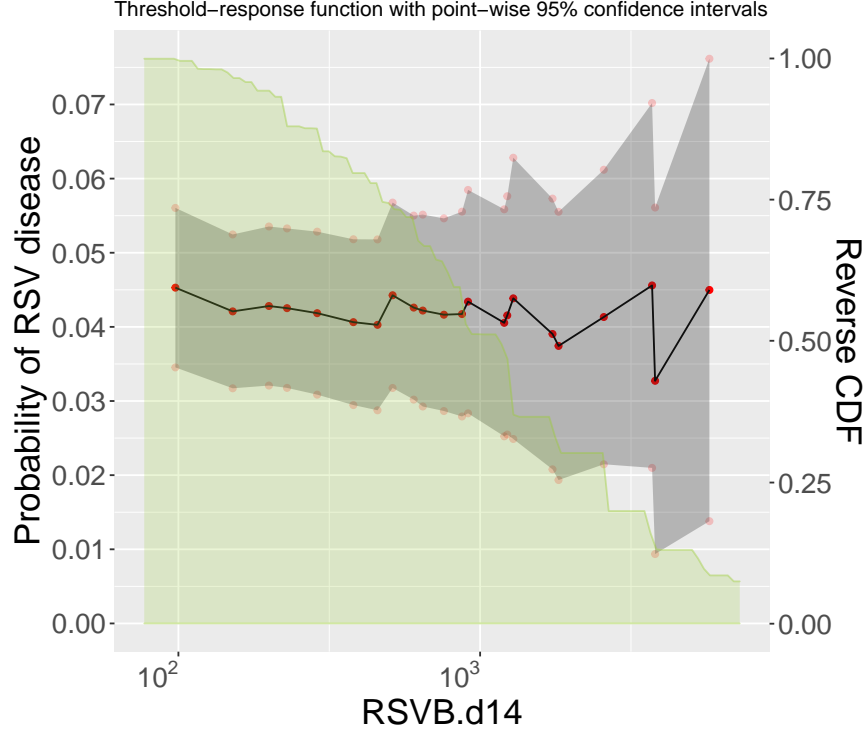


Figure 16: Marginalized risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with day 14 RSVB greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.987	$9.71 \cdot 10^1$	0.04529	0.03453	0.05605
2.303	$2.01 \cdot 10^2$	0.04281	0.03209	0.05354
2.577	$3.78 \cdot 10^2$	0.04064	0.02946	0.05182
2.707	$5.09 \cdot 10^2$	0.04426	0.03176	0.05676
2.808	$6.43 \cdot 10^2$	0.04220	0.02926	0.05514
2.958	$9.08 \cdot 10^2$	0.04341	0.02834	0.05847
3.093	$1.24 \cdot 10^3$	0.04155	0.02548	0.05762
3.243	$1.75 \cdot 10^3$	0.03904	0.02079	0.05730
3.566	$3.68 \cdot 10^3$	0.04559	0.02098	0.07020
3.761	$5.77 \cdot 10^3$	0.04498	0.01379	0.07617

Table 16: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

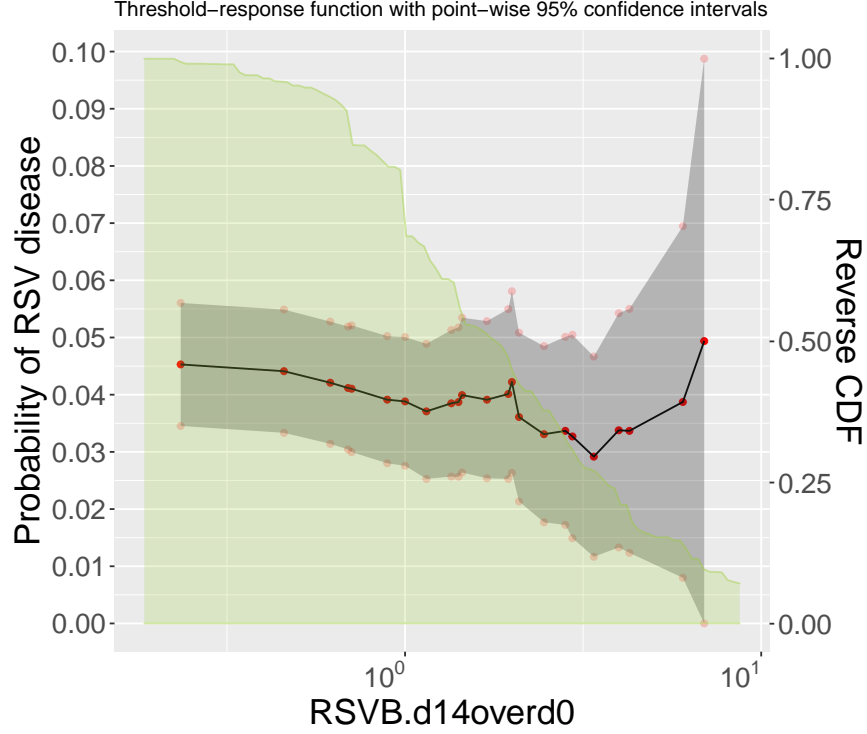


Figure 17: Conditional risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 RSVB relative to day 0 RSVB above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.632	$2.33 \cdot 10^{-1}$	0.04529	0.03454	0.05605
-0.207	$6.21 \cdot 10^{-1}$	0.04210	0.03141	0.05278
-0.053	$8.85 \cdot 10^{-1}$	0.03913	0.02801	0.05025
0.057	$1.14 \cdot 10^0$	0.03708	0.02528	0.04889
0.158	$1.44 \cdot 10^0$	0.03993	0.02640	0.05347
0.287	$1.94 \cdot 10^0$	0.04013	0.02528	0.05497
0.387	$2.44 \cdot 10^0$	0.03309	0.01769	0.04849
0.473	$2.97 \cdot 10^0$	0.03270	0.01492	0.05048
0.632	$4.29 \cdot 10^0$	0.03368	0.01235	0.05500
0.840	$6.92 \cdot 10^0$	0.04937	0.00000	0.11483

Table 17: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

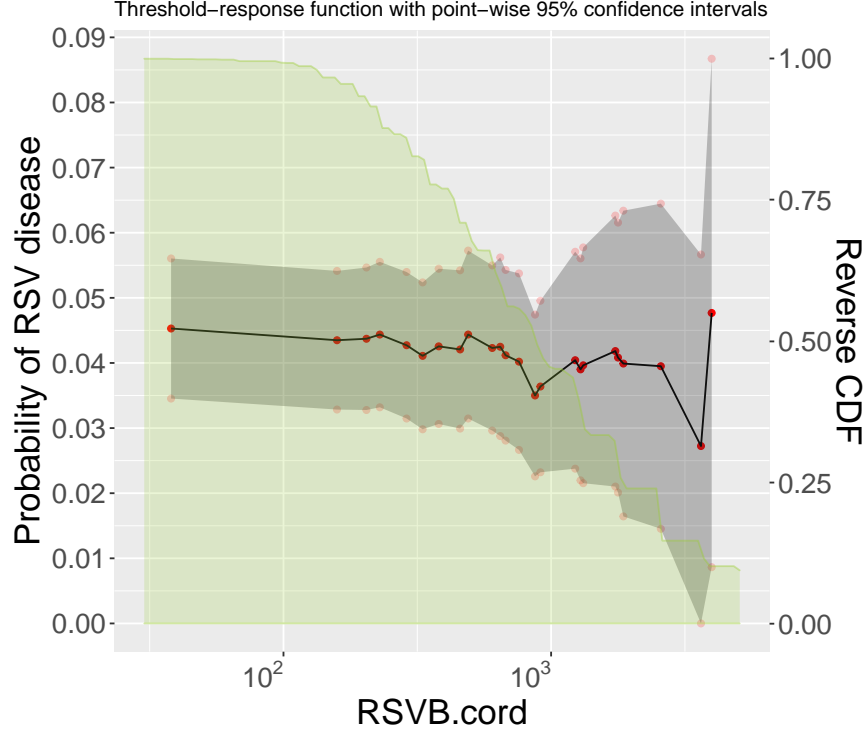


Figure 18: Conditional risk ($\geq s$) of RSV LRTI MS, RSV LRTI with hospitalization, or RSV LRTI with severe hypoxemia pooled across the treatment and placebo arms with RSVB measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.580	$3.80 \cdot 10^1$	0.04529	0.03453	0.05605
2.356	$2.27 \cdot 10^2$	0.04436	0.03319	0.05553
2.516	$3.28 \cdot 10^2$	0.04109	0.02981	0.05237
2.691	$4.91 \cdot 10^2$	0.04436	0.03147	0.05726
2.808	$6.43 \cdot 10^2$	0.04249	0.02877	0.05620
2.936	$8.63 \cdot 10^2$	0.03500	0.02259	0.04742
3.093	$1.24 \cdot 10^3$	0.04042	0.02377	0.05708
3.235	$1.72 \cdot 10^3$	0.04183	0.02102	0.06264
3.266	$1.85 \cdot 10^3$	0.03991	0.01644	0.06338
3.605	$4.03 \cdot 10^3$	0.04768	0.00864	0.08672

Table 18: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

Pooled, endpoint 2

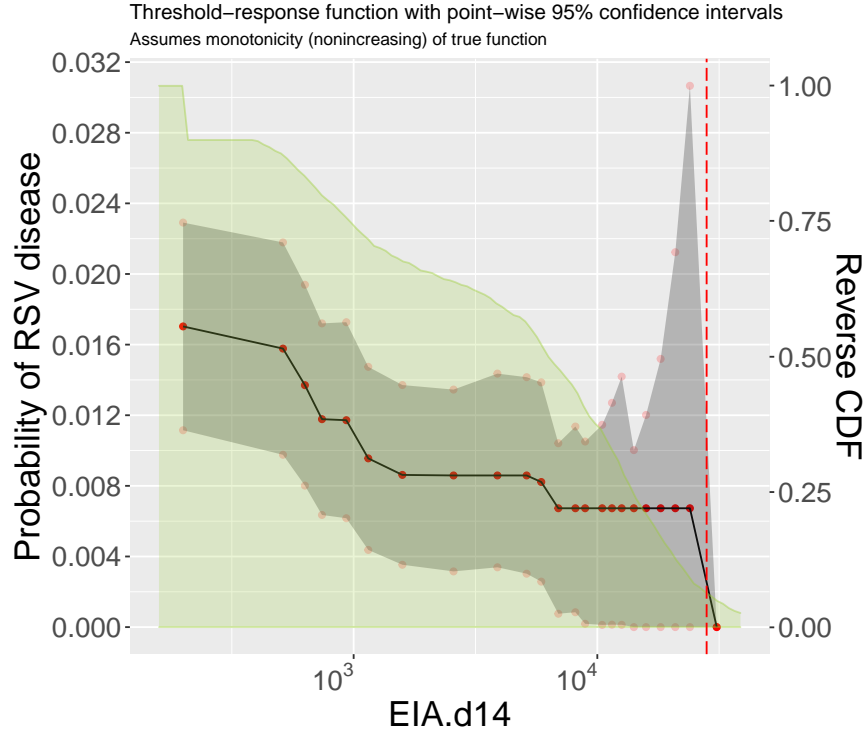


Figure 19: Marginalized risk ($\geq s$) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with day 14 EIA greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.301	$2.00 \cdot 10^2$	0.01703	0.01115	0.02291
2.801	$6.32 \cdot 10^2$	0.01370	0.00801	0.01939
3.062	$1.15 \cdot 10^3$	0.00956	0.00437	0.01474
3.415	$2.60 \cdot 10^3$	0.00830	0.00316	0.01345
3.772	$5.92 \cdot 10^3$	0.00822	0.00258	0.01386
3.909	$8.11 \cdot 10^3$	0.00610	0.00084	0.01136
4.064	$1.16 \cdot 10^4$	0.00642	0.00014	0.01270
4.150	$1.41 \cdot 10^4$	0.00422	0.00000	0.01002
4.316	$2.07 \cdot 10^4$	0.00898	0.00000	0.02123
4.487	$3.07 \cdot 10^4$	0.00000	0.00000	1.00000

Table 19: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

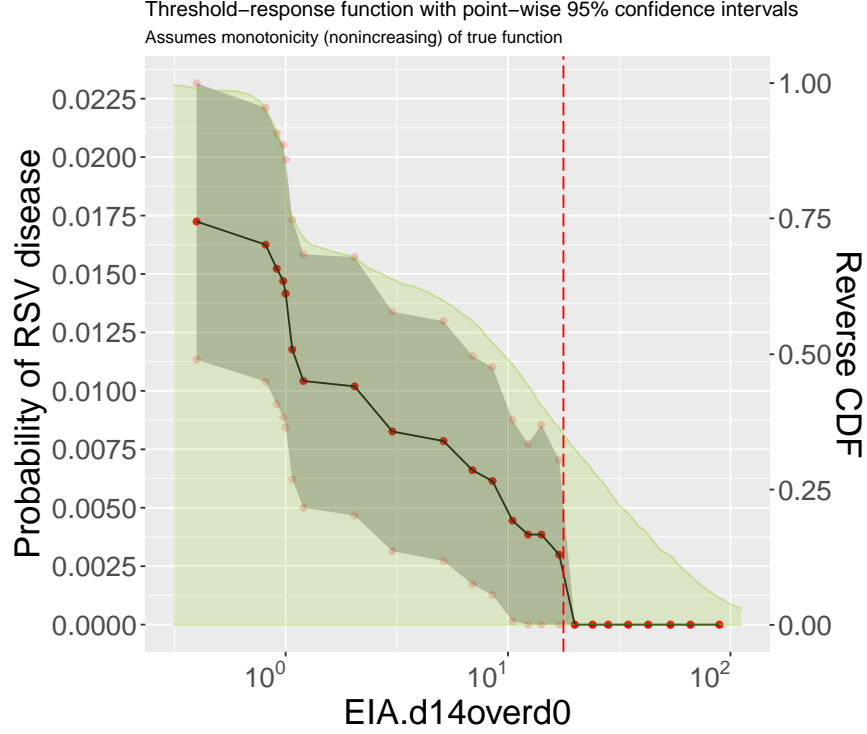


Figure 20: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 EIA relative to day 0 EIA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.403	$3.95 \cdot 10^{-1}$	0.01724	0.01133	0.02316
-0.006	$9.86 \cdot 10^{-1}$	0.01470	0.00888	0.02052
0.030	$1.07 \cdot 10^0$	0.01177	0.00622	0.01732
0.482	$3.03 \cdot 10^0$	0.00826	0.00314	0.01338
0.842	$6.95 \cdot 10^0$	0.00661	0.00172	0.01149
1.092	$1.24 \cdot 10^1$	0.00366	0.00000	0.00773
1.229	$1.69 \cdot 10^1$	0.00299	0.00000	0.00704
1.455	$2.85 \cdot 10^1$	0.00000	0.00000	1.00000
1.627	$4.24 \cdot 10^1$	0.00000	0.00000	1.00000
1.948	$8.87 \cdot 10^1$	0.00000	0.00000	1.00000

Table 20: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

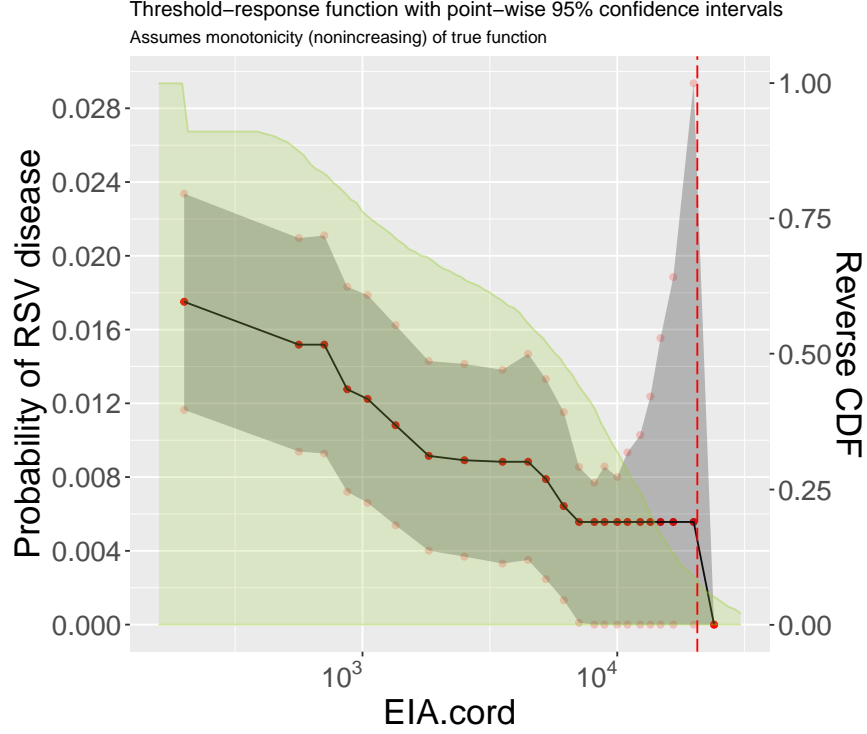


Figure 21: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with EIA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.301	$2.00 \cdot 10^2$	0.01751	0.01164	0.02337
2.849	$7.06 \cdot 10^2$	0.01519	0.00928	0.02110
3.128	$1.34 \cdot 10^3$	0.01081	0.00539	0.01624
3.403	$2.53 \cdot 10^3$	0.00891	0.00369	0.01414
3.724	$5.30 \cdot 10^3$	0.00789	0.00247	0.01332
3.848	$7.05 \cdot 10^3$	0.00432	0.00010	0.00854
3.996	$9.91 \cdot 10^3$	0.00336	0.00000	0.00800
4.091	$1.23 \cdot 10^4$	0.00433	0.00000	0.01028
4.223	$1.67 \cdot 10^4$	0.00793	0.00000	0.01885
4.384	$2.42 \cdot 10^4$	0.00000	0.00000	1.00000

Table 21: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

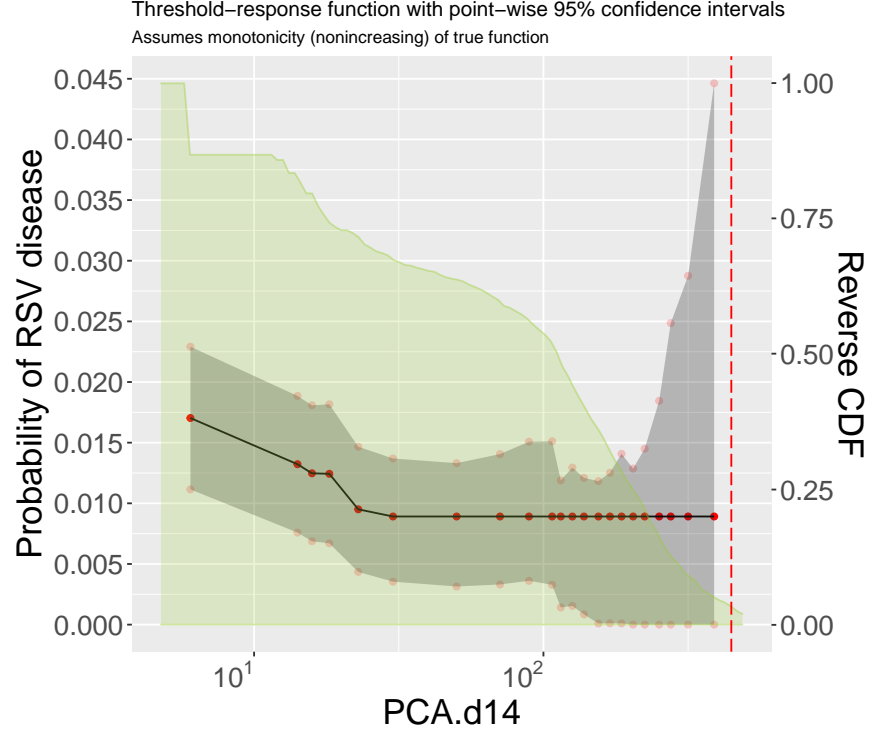


Figure 22: Marginalized risk ($\geq s$) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with day 14 PCA greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.778	$6.00 \cdot 10^0$	0.01703	0.01115	0.02291
1.204	$1.60 \cdot 10^1$	0.01248	0.00687	0.01808
1.477	$3.00 \cdot 10^1$	0.00862	0.00354	0.01370
1.845	$7.00 \cdot 10^1$	0.00868	0.00331	0.01406
2.029	$1.07 \cdot 10^2$	0.00920	0.00329	0.01511
2.140	$1.38 \cdot 10^2$	0.00647	0.00084	0.01210
2.228	$1.69 \cdot 10^2$	0.00631	0.00011	0.01252
2.314	$2.06 \cdot 10^2$	0.00609	0.00000	0.01286
2.439	$2.75 \cdot 10^2$	0.01171	0.00000	0.02485
2.588	$3.87 \cdot 10^2$	0.02231	0.00000	0.05149

Table 22: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

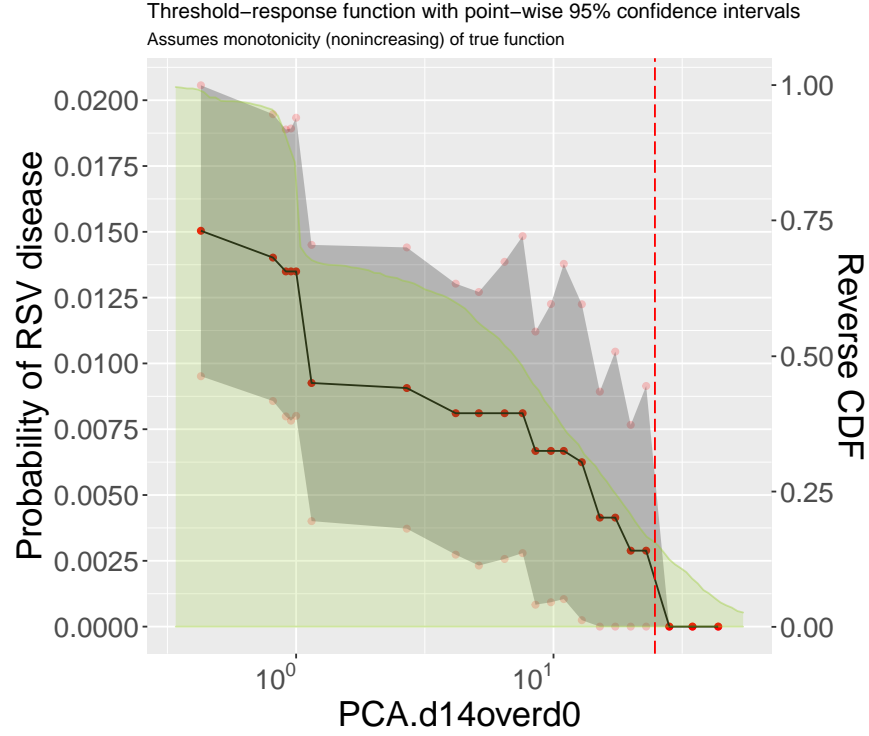


Figure 23: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 PCA relative to day 0 PCA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.368	$4.29 \cdot 10^{-1}$	0.01504	0.00951	0.02057
-0.040	$9.12 \cdot 10^{-1}$	0.01344	0.00799	0.01889
0.063	$1.16 \cdot 10^0$	0.00926	0.00401	0.01450
0.619	$4.16 \cdot 10^0$	0.00788	0.00273	0.01303
0.809	$6.44 \cdot 10^0$	0.00822	0.00257	0.01386
0.990	$9.77 \cdot 10^0$	0.00659	0.00093	0.01226
1.112	$1.29 \cdot 10^1$	0.00625	0.00025	0.01225
1.235	$1.72 \cdot 10^1$	0.00448	0.00000	0.01045
1.447	$2.80 \cdot 10^1$	0.00000	0.00000	1.00000
1.637	$4.34 \cdot 10^1$	0.00000	0.00000	1.00000

Table 23: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

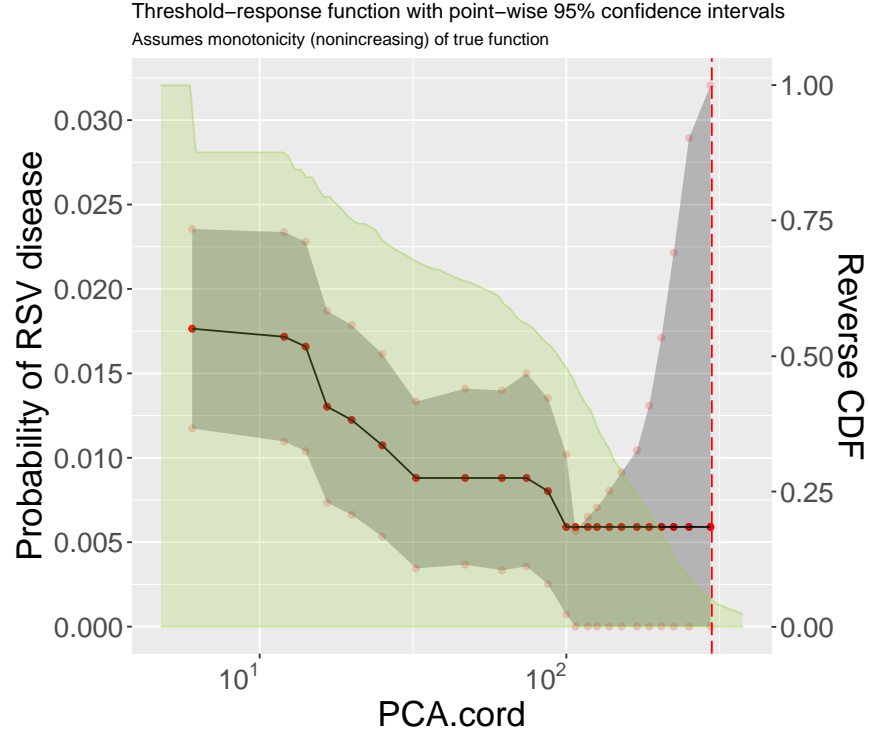


Figure 24: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with PCA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.778	$6.00 \cdot 10^0$	0.01764	0.01173	0.02355
1.146	$1.40 \cdot 10^1$	0.01659	0.01038	0.02279
1.398	$2.50 \cdot 10^1$	0.01074	0.00533	0.01615
1.674	$4.72 \cdot 10^1$	0.00888	0.00367	0.01409
1.942	$8.75 \cdot 10^1$	0.00803	0.00252	0.01353
2.033	$1.08 \cdot 10^2$	0.00240	0.00000	0.00568
2.143	$1.39 \cdot 10^2$	0.00339	0.00000	0.00806
2.225	$1.68 \cdot 10^2$	0.00440	0.00000	0.01043
2.348	$2.23 \cdot 10^2$	0.00941	0.00000	0.02215
2.474	$2.98 \cdot 10^2$	0.01114	0.00000	0.03206

Table 24: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

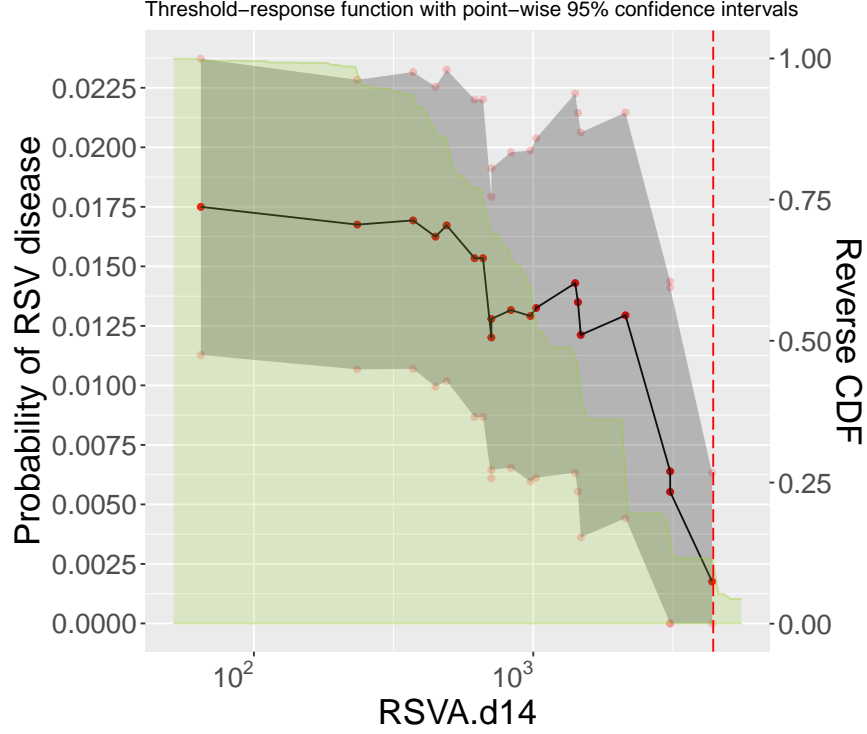


Figure 25: Marginalized risk ($\geq s$) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with day 14 RSV.d14 greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.813	$6.50 \cdot 10^1$	0.01750	0.01128	0.02372
2.574	$3.75 \cdot 10^2$	0.01693	0.01070	0.02316
2.691	$4.91 \cdot 10^2$	0.01672	0.01019	0.02326
2.822	$6.64 \cdot 10^2$	0.01534	0.00868	0.02201
2.851	$7.10 \cdot 10^2$	0.01279	0.00646	0.01912
2.990	$9.77 \cdot 10^2$	0.01291	0.00596	0.01987
3.148	$1.41 \cdot 10^3$	0.01429	0.00633	0.02226
3.167	$1.47 \cdot 10^3$	0.01212	0.00362	0.02063
3.485	$3.05 \cdot 10^3$	0.00639	0.00000	0.01437
3.644	$4.41 \cdot 10^3$	0.00176	0.00000	0.00633

Table 25: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

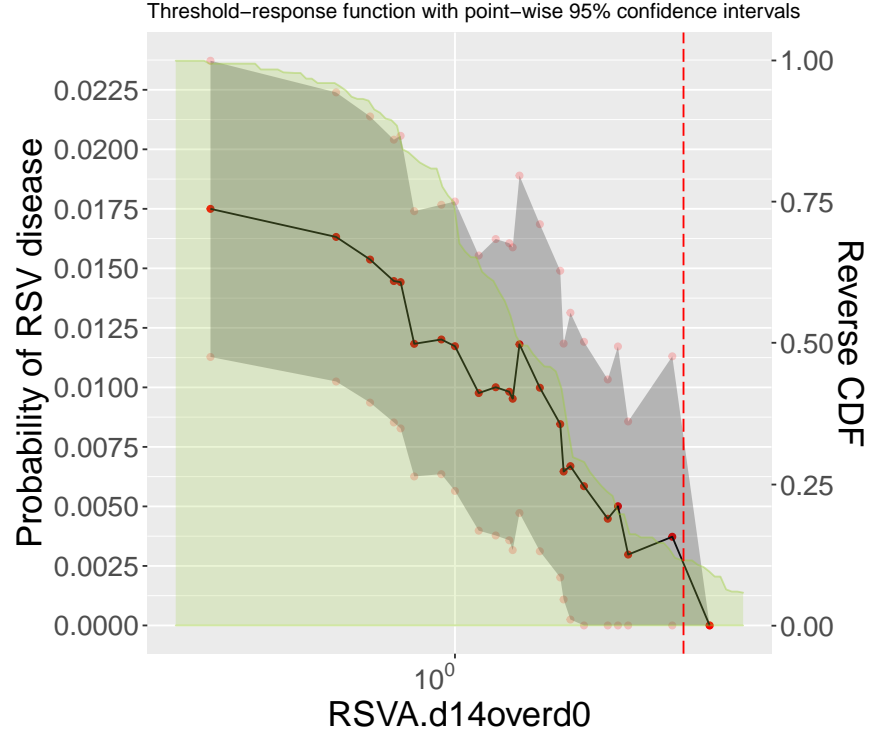


Figure 26: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 RSVA relative to day 0 RSVA above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.722	$1.90 \cdot 10^{-1}$	0.01750	0.01128	0.02372
-0.252	$5.60 \cdot 10^{-1}$	0.01537	0.00936	0.02138
-0.121	$7.57 \cdot 10^{-1}$	0.01183	0.00626	0.01740
0.000	$1.00 \cdot 10^0$	0.01173	0.00565	0.01781
0.159	$1.44 \cdot 10^0$	0.00982	0.00358	0.01606
0.190	$1.55 \cdot 10^0$	0.01181	0.00472	0.01890
0.318	$2.08 \cdot 10^0$	0.00646	0.00109	0.01184
0.381	$2.40 \cdot 10^0$	0.00585	0.00000	0.01191
0.512	$3.25 \cdot 10^0$	0.00298	0.00000	0.00857
0.749	$5.61 \cdot 10^0$	0.00000	0.00000	1.00000

Table 26: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

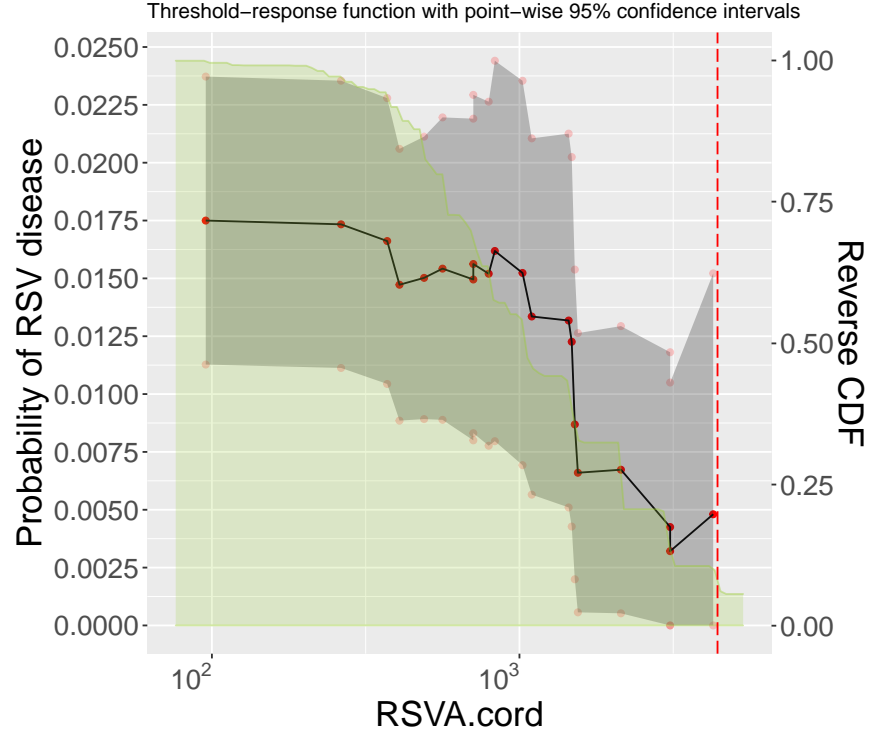


Figure 27: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with RSVA measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.982	9.59×10^1	0.01750	0.01128	0.02372
2.574	3.75×10^2	0.01661	0.01044	0.02279
2.691	4.91×10^2	0.01502	0.00892	0.02112
2.849	7.06×10^2	0.01495	0.00800	0.02190
2.898	7.91×10^2	0.01520	0.00777	0.02264
3.040	1.10×10^3	0.01335	0.00565	0.02105
3.167	1.47×10^3	0.01226	0.00428	0.02024
3.190	1.55×10^3	0.00660	0.00057	0.01263
3.485	3.05×10^3	0.00425	0.00000	0.01181
3.627	4.24×10^3	0.00480	0.00000	0.01522

Table 27: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

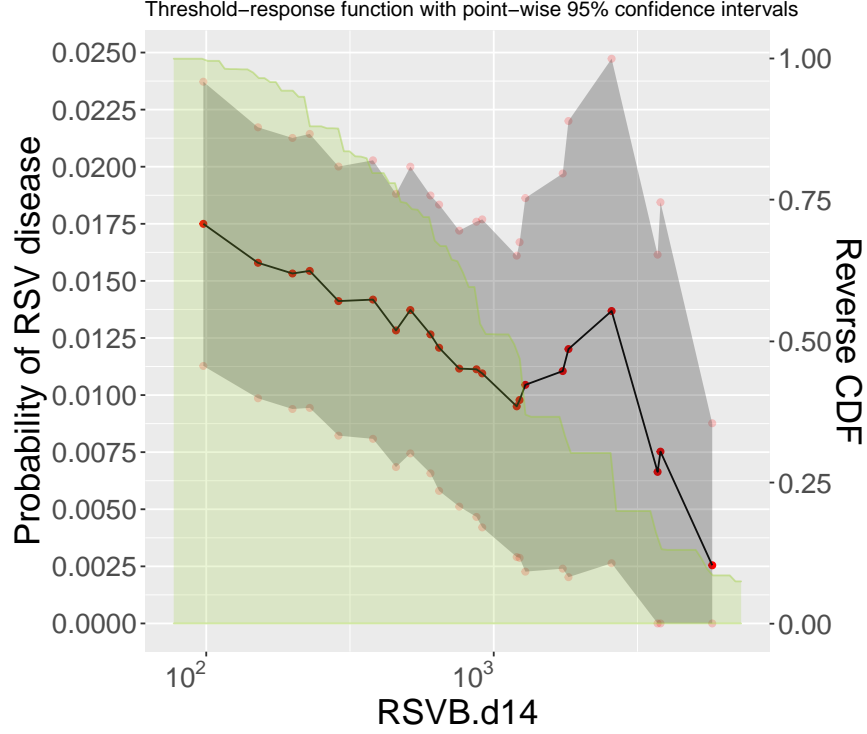


Figure 28: Marginalized risk ($\geq s$) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with day 14 RSVB greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.987	$9.71 \cdot 10^1$	0.01750	0.01128	0.02372
2.303	$2.01 \cdot 10^2$	0.01533	0.00939	0.02126
2.577	$3.78 \cdot 10^2$	0.01418	0.00808	0.02028
2.707	$5.09 \cdot 10^2$	0.01372	0.00745	0.02000
2.808	$6.43 \cdot 10^2$	0.01207	0.00581	0.01834
2.958	$9.08 \cdot 10^2$	0.01095	0.00421	0.01769
3.093	$1.24 \cdot 10^3$	0.00978	0.00287	0.01669
3.243	$1.75 \cdot 10^3$	0.01105	0.00240	0.01970
3.566	$3.68 \cdot 10^3$	0.00664	0.00000	0.01615
3.761	$5.77 \cdot 10^3$	0.00255	0.00000	0.00877

Table 28: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

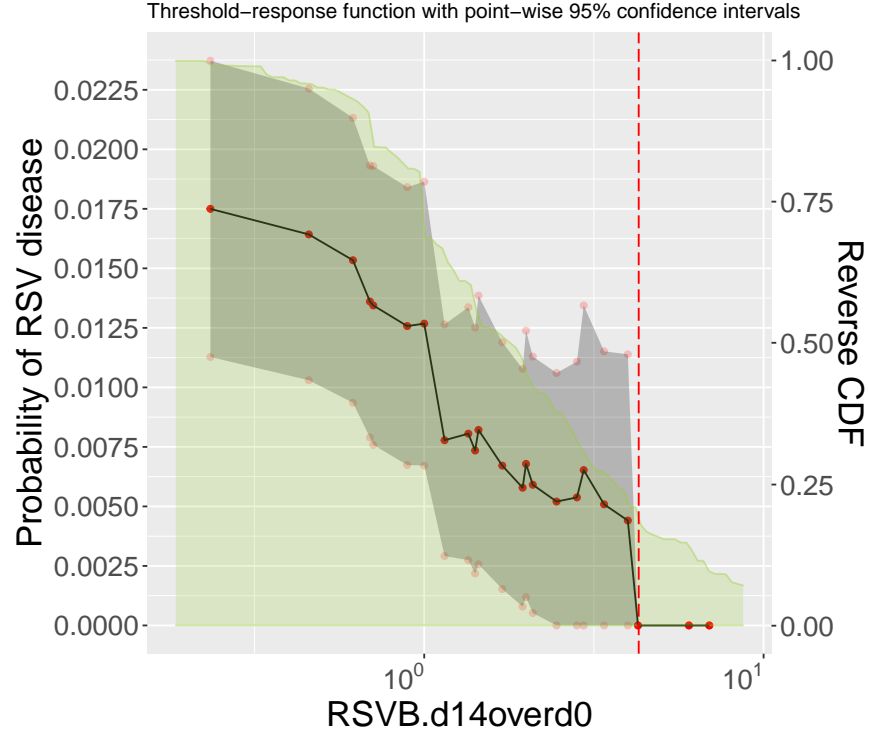


Figure 29: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with fold increase in day 14 RSVB relative to day 0 RSVB above a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
-0.632	$2.33 \cdot 10^{-1}$	0.01750	0.01128	0.02372
-0.207	$6.21 \cdot 10^{-1}$	0.01534	0.00936	0.02132
-0.053	$8.85 \cdot 10^{-1}$	0.01257	0.00674	0.01841
0.057	$1.14 \cdot 10^0$	0.00778	0.00292	0.01265
0.158	$1.44 \cdot 10^0$	0.00821	0.00257	0.01386
0.287	$1.94 \cdot 10^0$	0.00578	0.00079	0.01078
0.387	$2.44 \cdot 10^0$	0.00520	0.00000	0.01061
0.473	$2.97 \cdot 10^0$	0.00653	0.00000	0.01344
0.632	$4.29 \cdot 10^0$	0.00000	0.00000	1.00000
0.840	$6.92 \cdot 10^0$	0.00000	0.00000	1.00000

Table 29: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.

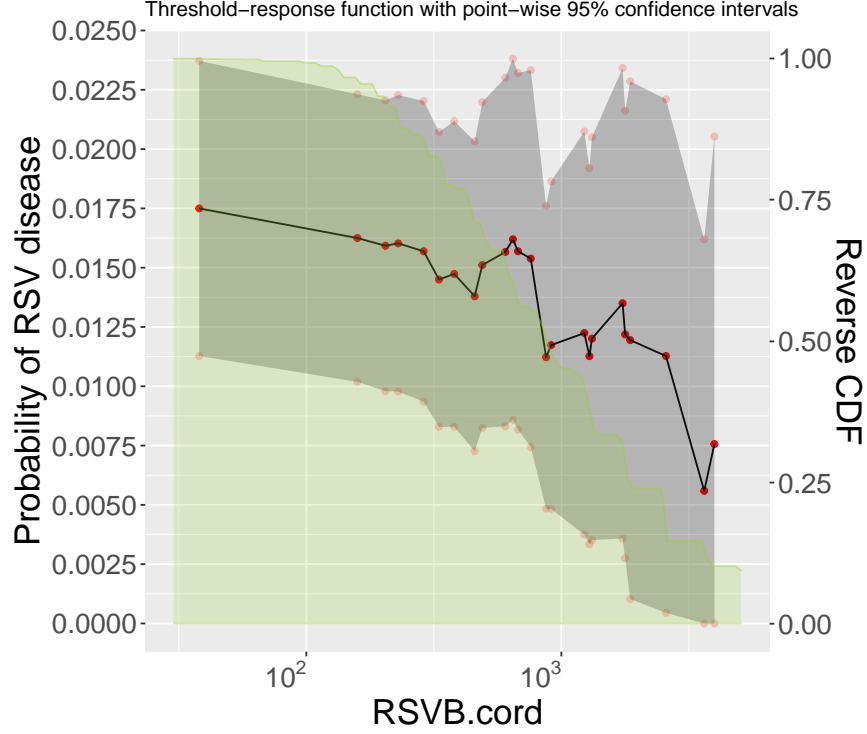


Figure 30: Conditional risk (\geq) of RSV-associated lower respiratory tract infection with severe hypoxemia pooled across the treatment and placebo arms with RSVB measured in infant cord blood greater than a given threshold. The plot shows point-wise 95% confidence intervals. The dashed red line marks the threshold of zero risk.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.580	$3.80 \cdot 10^1$	0.01750	0.01128	0.02372
2.356	$2.27 \cdot 10^2$	0.01603	0.00977	0.02228
2.516	$3.28 \cdot 10^2$	0.01450	0.00828	0.02072
2.691	$4.91 \cdot 10^2$	0.01511	0.00824	0.02198
2.808	$6.43 \cdot 10^2$	0.01620	0.00858	0.02381
2.936	$8.63 \cdot 10^2$	0.01122	0.00484	0.01761
3.093	$1.24 \cdot 10^3$	0.01224	0.00374	0.02074
3.235	$1.72 \cdot 10^3$	0.01350	0.00358	0.02342
3.266	$1.85 \cdot 10^3$	0.01195	0.00103	0.02286
3.605	$4.03 \cdot 10^3$	0.00757	0.00000	0.02053

Table 30: The table shows the non-monotone corrected estimates for the Marginalized risk of RSV disease by threshold.