

Annex to: Update of the risk assessment of inorganic arsenic in food.
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Annex E2 Benchmark dose modelling reports

Relative increase of the background incidence after adjustment for confounders by 1%¹

Annex E2 provides a comprehensive overview of the benchmark dose (BMD) analyses carried out for the critical studies, employing the model averaging technique. The BMD analyses were conducted in accordance with the EFSA BMD guidance (EFSA Scientific Committee, 2022) and used in the uncertainty analysis.

E2.1 Selection of the BMR

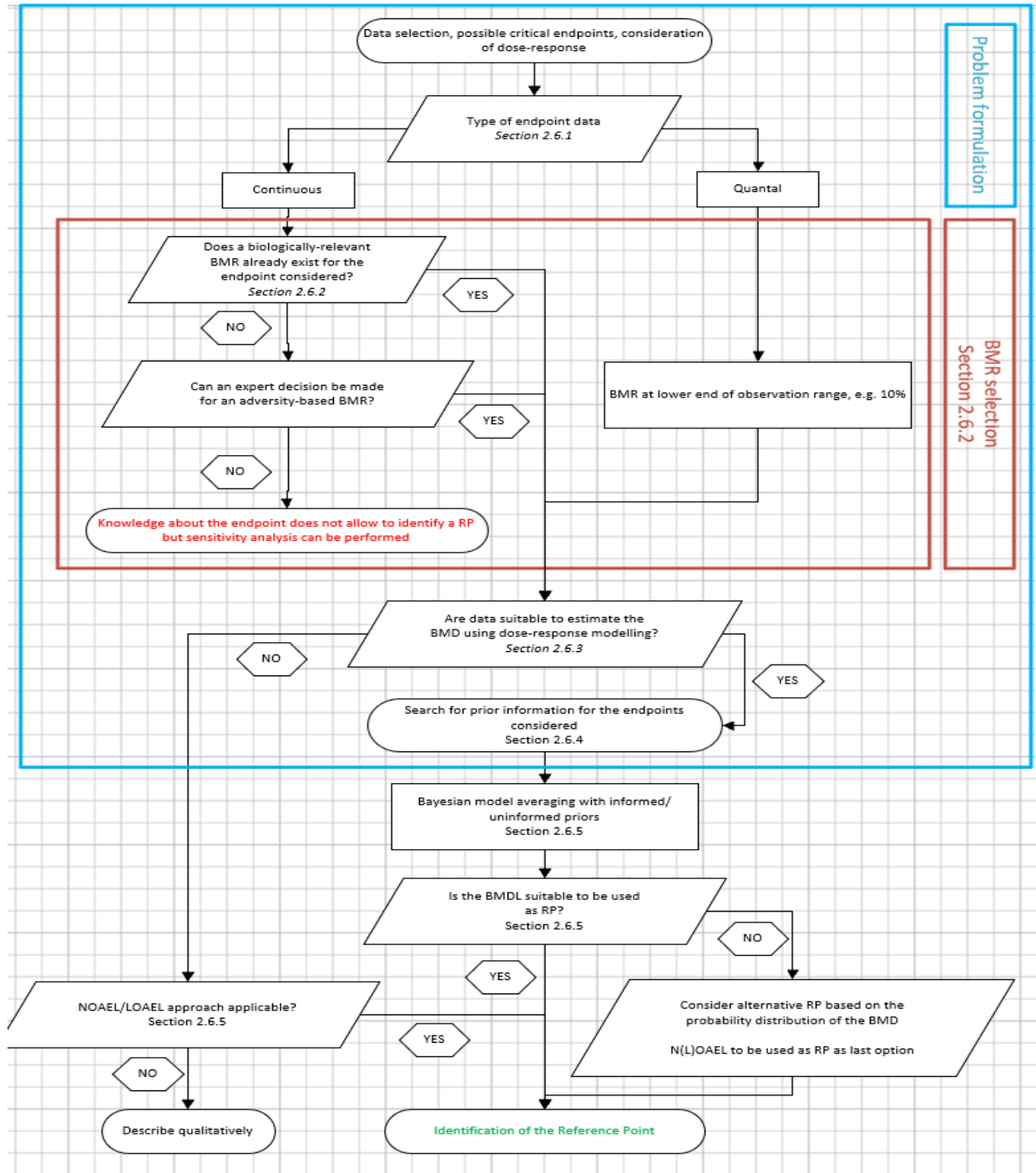
The BMD is identified as the specific dose that corresponds to the desired BMR level. To assess the uncertainty associated with the BMD, a 90% confidence interval is estimated, with the lower bound denoted as BMDL and the upper bound as BMDU. The BMDL and BMDU values help to quantify the range within which the true BMD value is expected to lie.

As BMR the CONTAM Panel decided to use a relative increase of the background incidence after adjustment for confounders by 1%¹.

E2.2 Software Used

Results are obtained using the EFSA web-tool for Bayesian BMD analysis, which uses the R-package [BMABMDR] version 0.0.0.9057/0.0.0.9060/0.0.0.9073 for the underlying calculations.

¹ Exceptions: For continuous endpoints including the studies of Parvez et al. (2013) on FEV1 and FVC, Siddique et al. (2020) on FEV1 and FEV6 and Vahter et al. (2020), an extra risk of 1% was applied.



Flowchart to derive a Reference Point (RP) from a dose-response dataset of a specified endpoint, using BMD analysis. Figure from EFSA BMD guidance (EFSA Scientific Committee, 2022).

E2.3 BMD modelling reports

Ahsan et al. (2006) skin lesions, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for skin lesions

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.22	51	2259
2.76	90	2122
5.60	143	2202
10.18	171	2185
19.64	239	2183

The 'Value for CES' is set to 0.00023098.

Extended dose range is applied.

Informative background prior: min: 0.02235060; the most likely: 0.02257636; max: 0.02280212. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.56e-03).

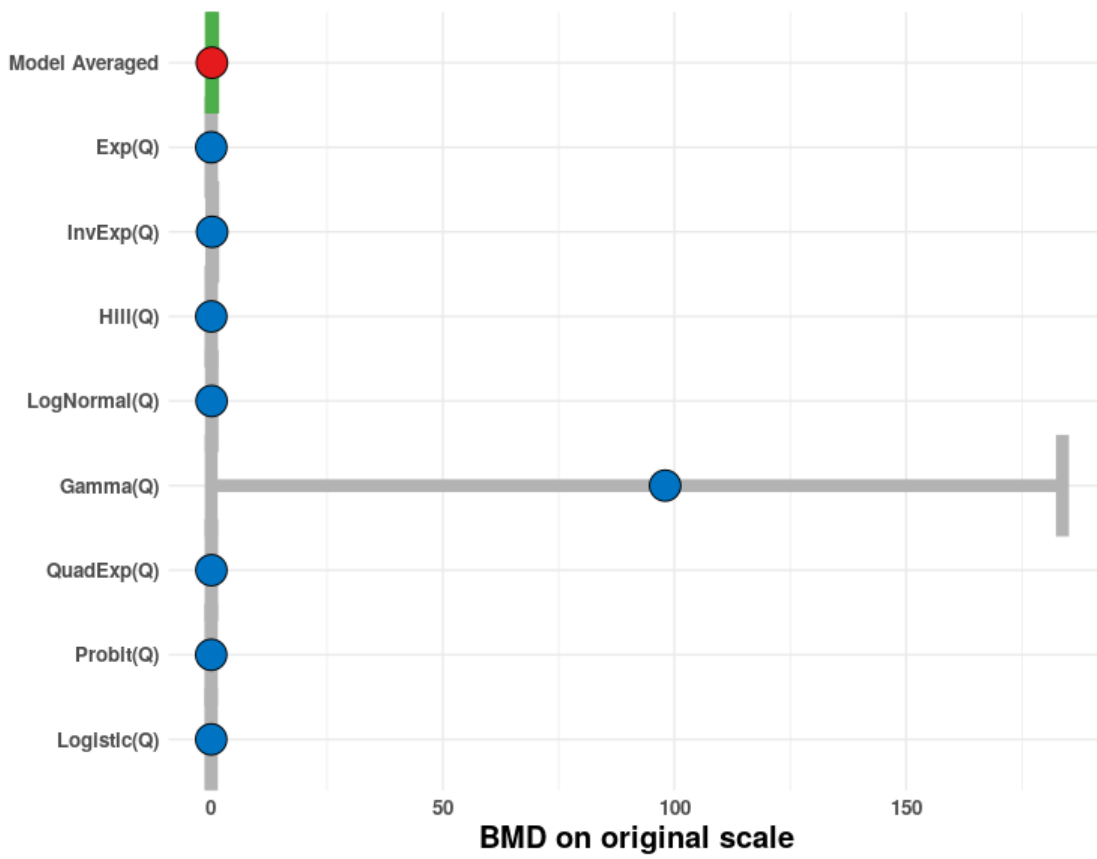
Model Averaged BMD

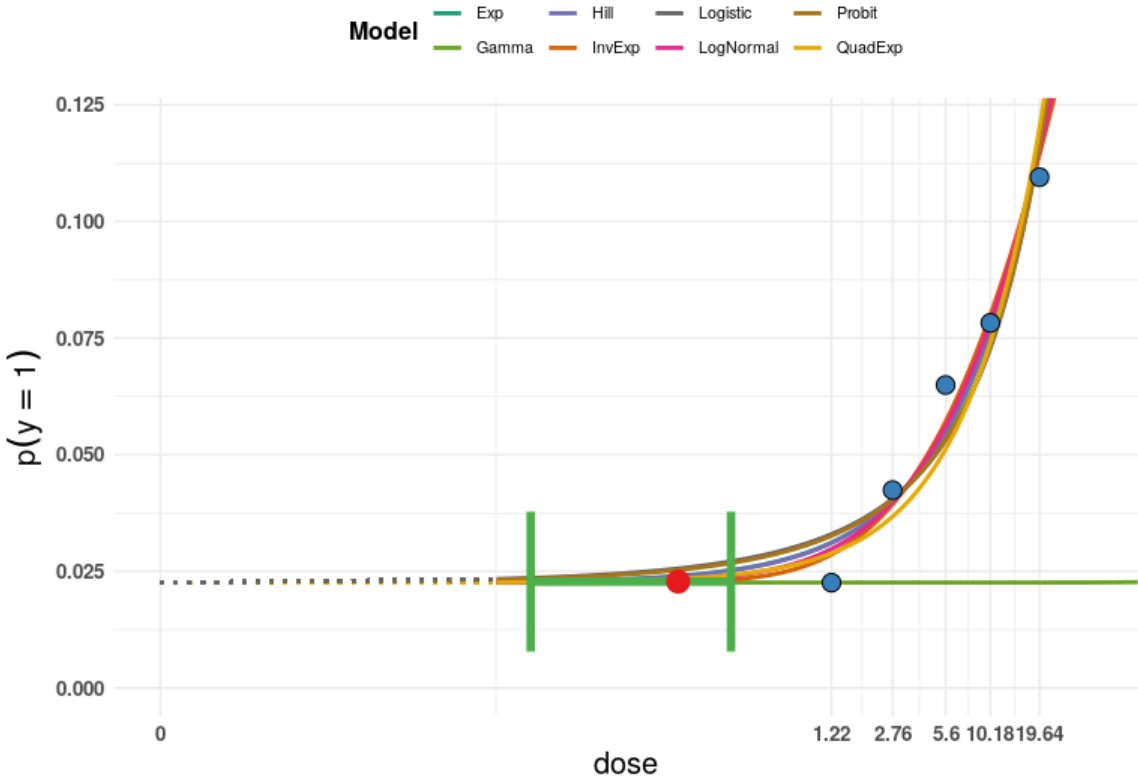
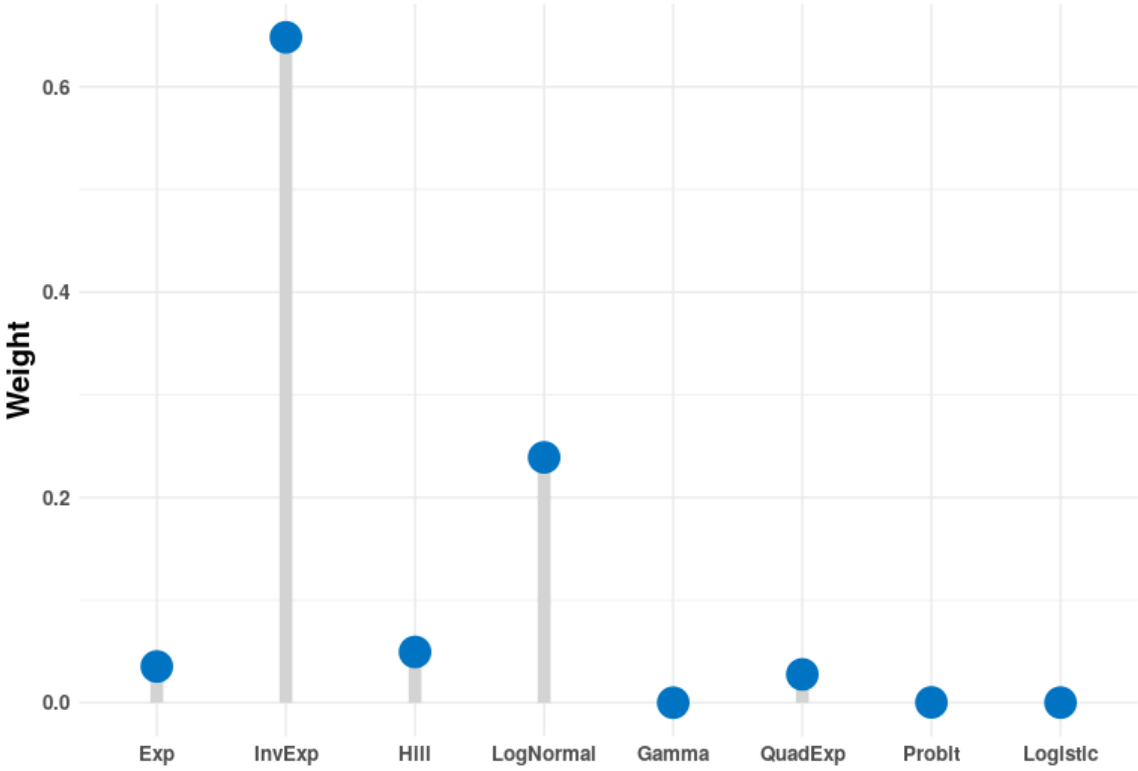
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.022	0.157	0.319

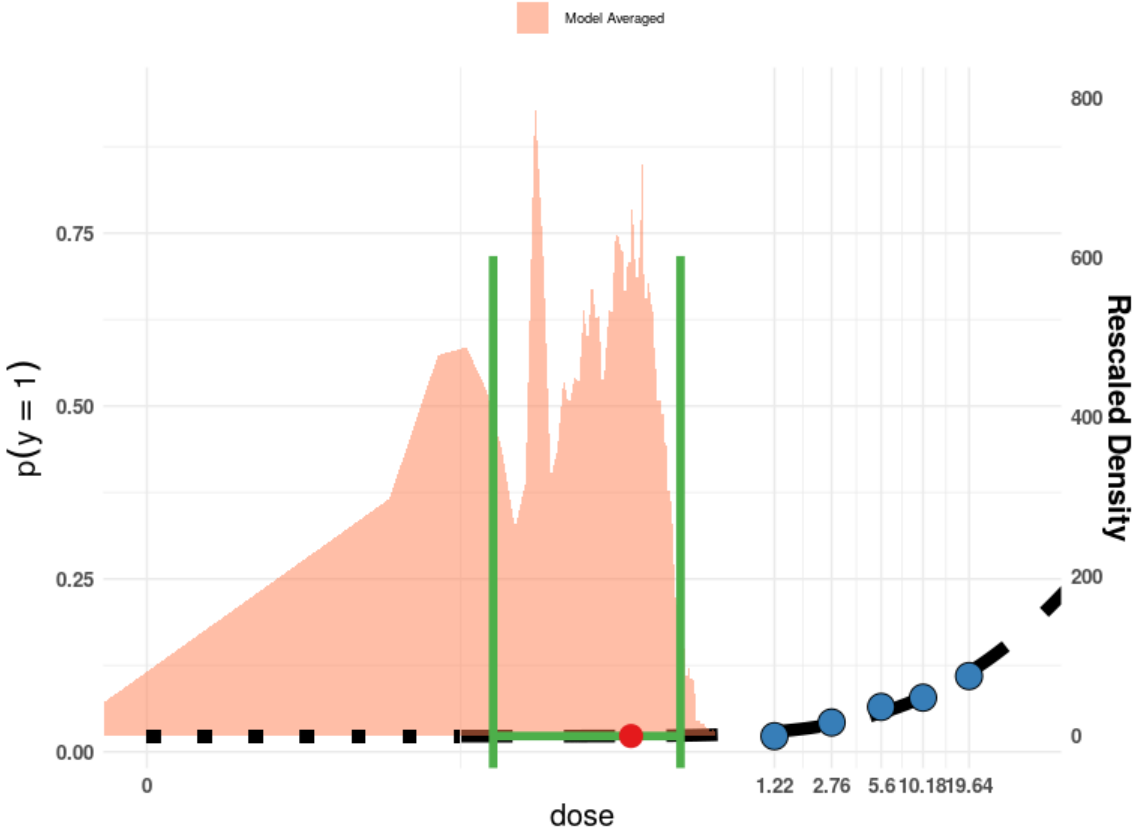
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.006	0.019	0.044	0.035	1
IE4_Q	0.104	0.200	0.340	0.648	1
H4_Q	0.008	0.021	0.048	0.049	1
LN4_Q	0.042	0.088	0.166	0.239	1
G4_Q	0.010	97.992	183.752	0.000	0
QE4_Q	0.039	0.044	0.049	0.028	1
P4_Q	0.001	0.002	0.008	0.000	1
L4_Q	0.000	0.001	0.005	0.000	1

Plots of Fitted Models







Chen et al. (2010a) lung cancer, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.927	48	2288
2.288	48	2093
4.743	19	907
11.561	29	909
17.018	33	691

The 'Value for CES' is set to 0.00021429.

Extended dose range is not applied.

Informative background prior: min: 0.01993007; the most likely: 0.02097902; max: 0.02202797. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.99e-04).

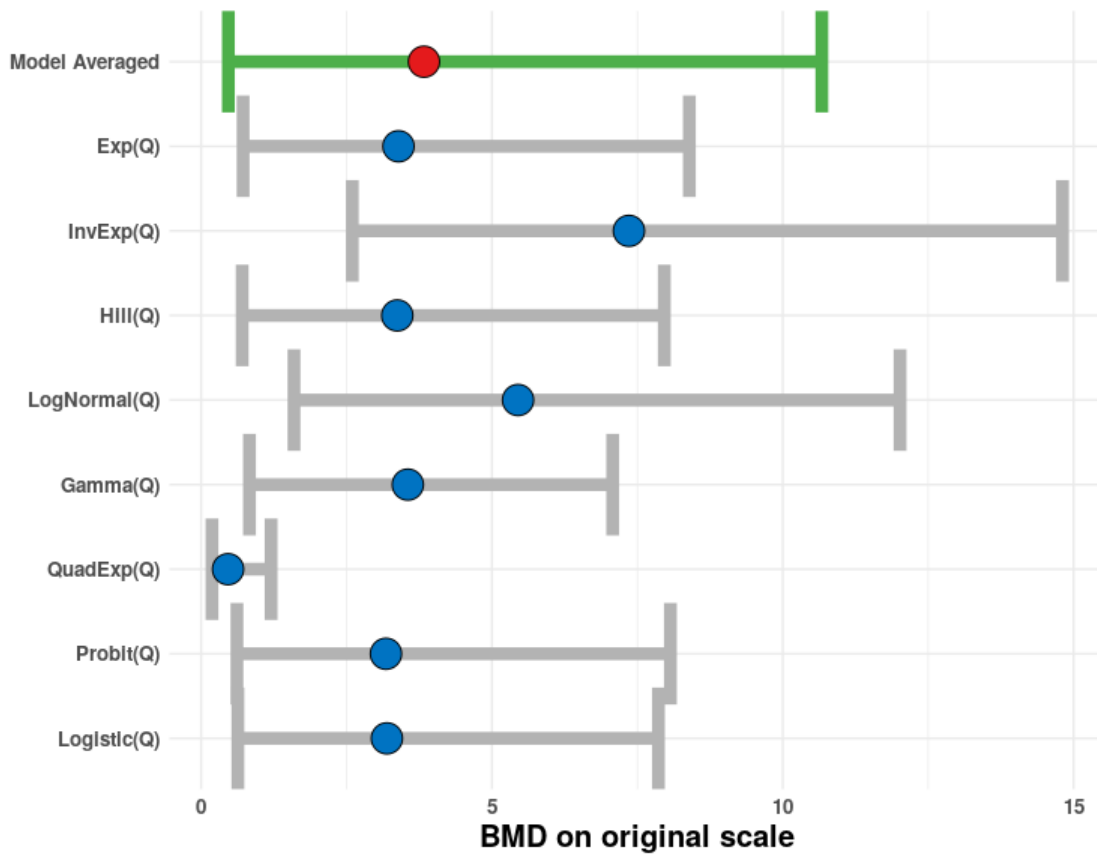
Model Averaged BMD

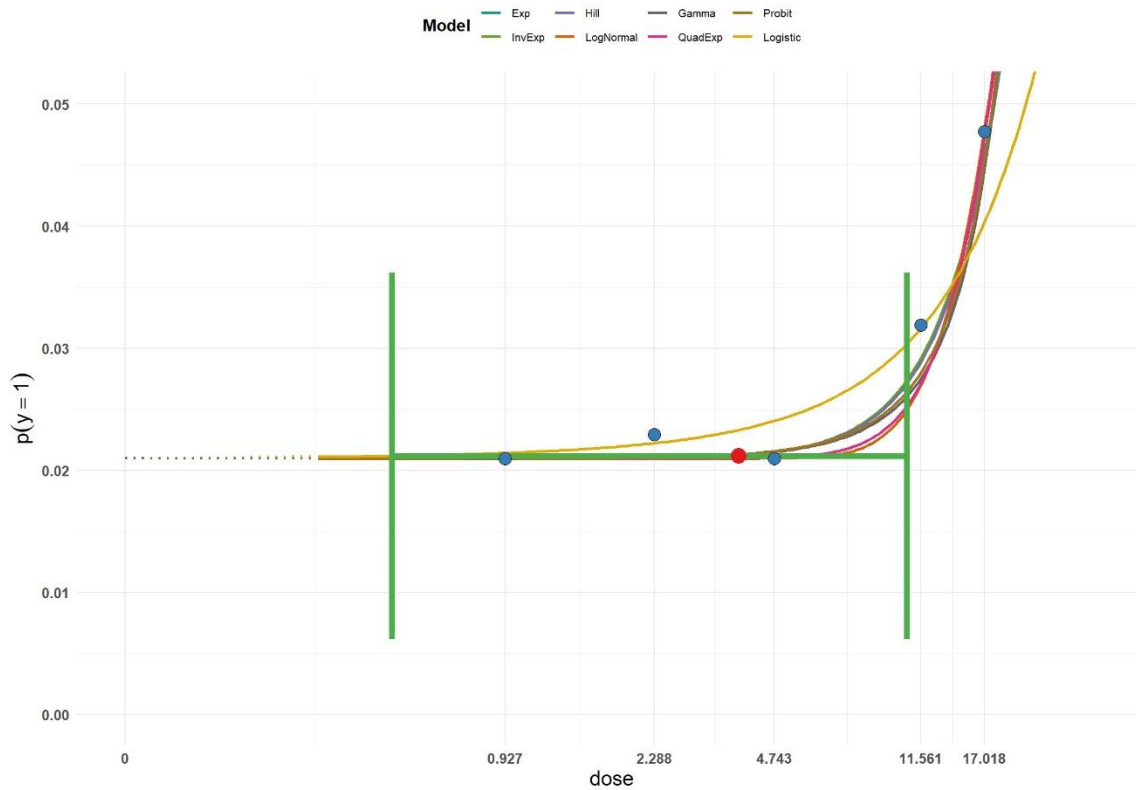
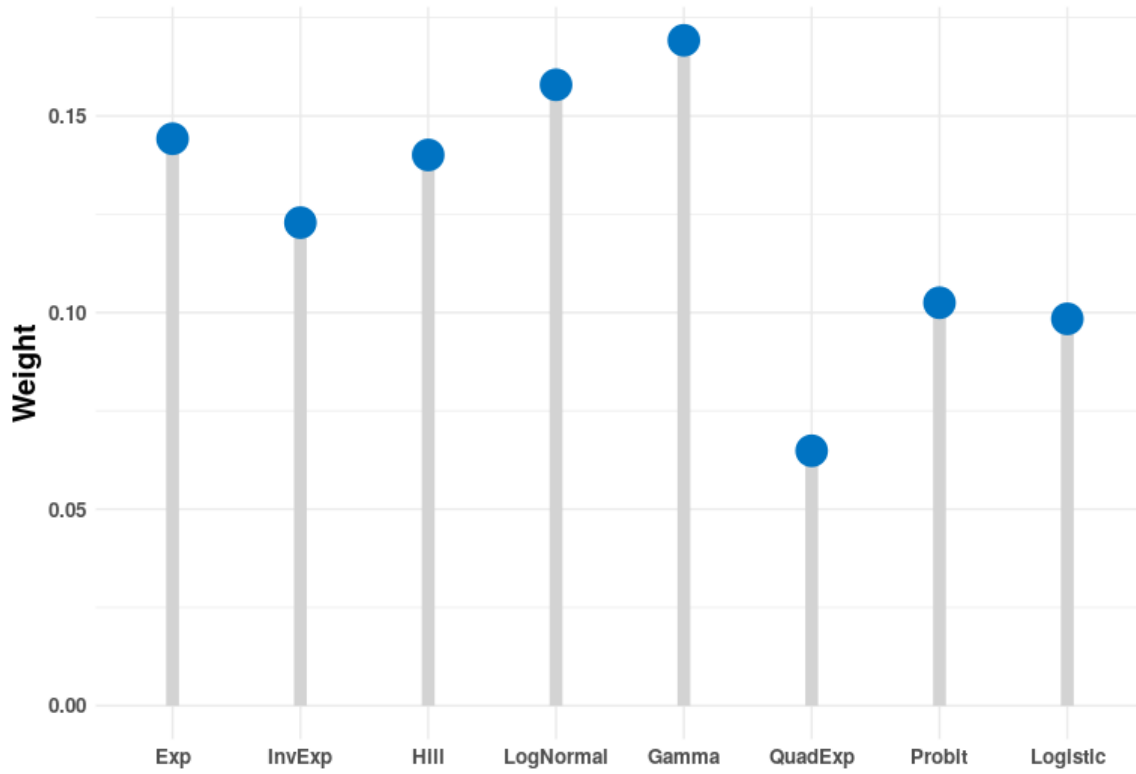
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.468	3.831	10.672

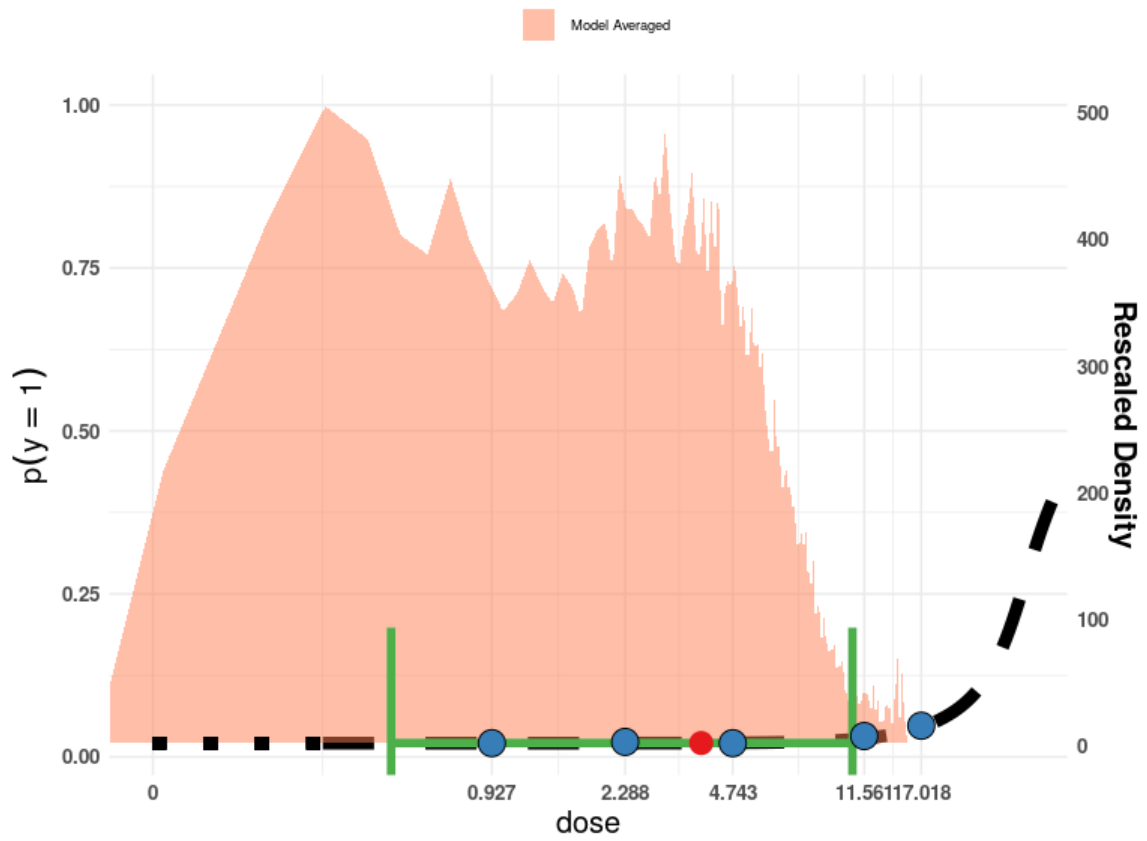
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.721	3.393	8.394	0.144	1
IE4_Q	2.600	7.355	14.810	0.123	1
H4_Q	0.706	3.372	7.964	0.140	1
LN4_Q	1.597	5.449	12.017	0.158	1
G4_Q	0.831	3.554	7.076	0.169	1
QE4_Q	0.187	0.463	1.203	0.065	1
P4_Q	0.616	3.178	8.068	0.102	1
L4_Q	0.631	3.194	7.862	0.098	1

Plots of Fitted Models







Chen et al. (2010b) bladder cancer, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for bladder cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.927	3	2288
2.288	5	2093
4.743	3	907
11.561	7	909
17.018	11	691

The 'Value for CES' is set to 1.313e-05.

Extended dose range is not applied.

Informative background prior: min: 0.00129808; the most likely; 0.00131119; max: 0.00132430. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since BMD/BMDL > 20 and BMDU/BMDL > 50.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.92e-04).

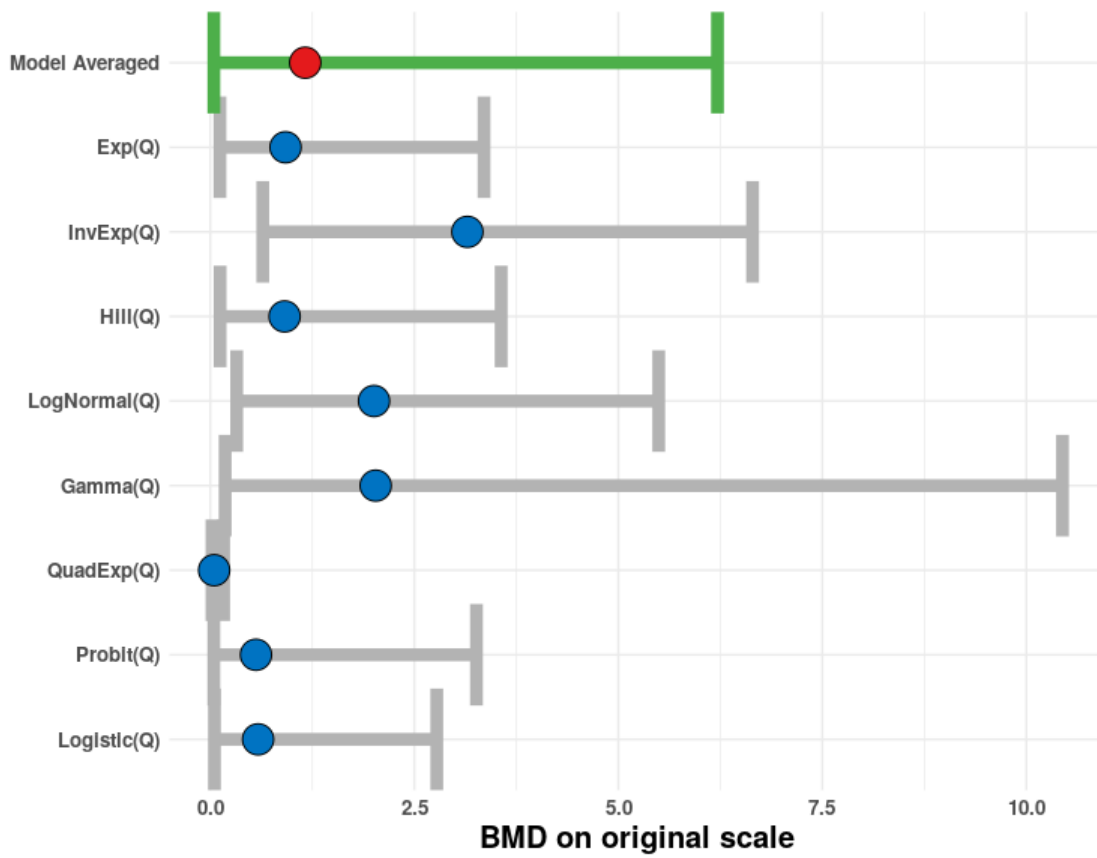
Model Averaged BMD

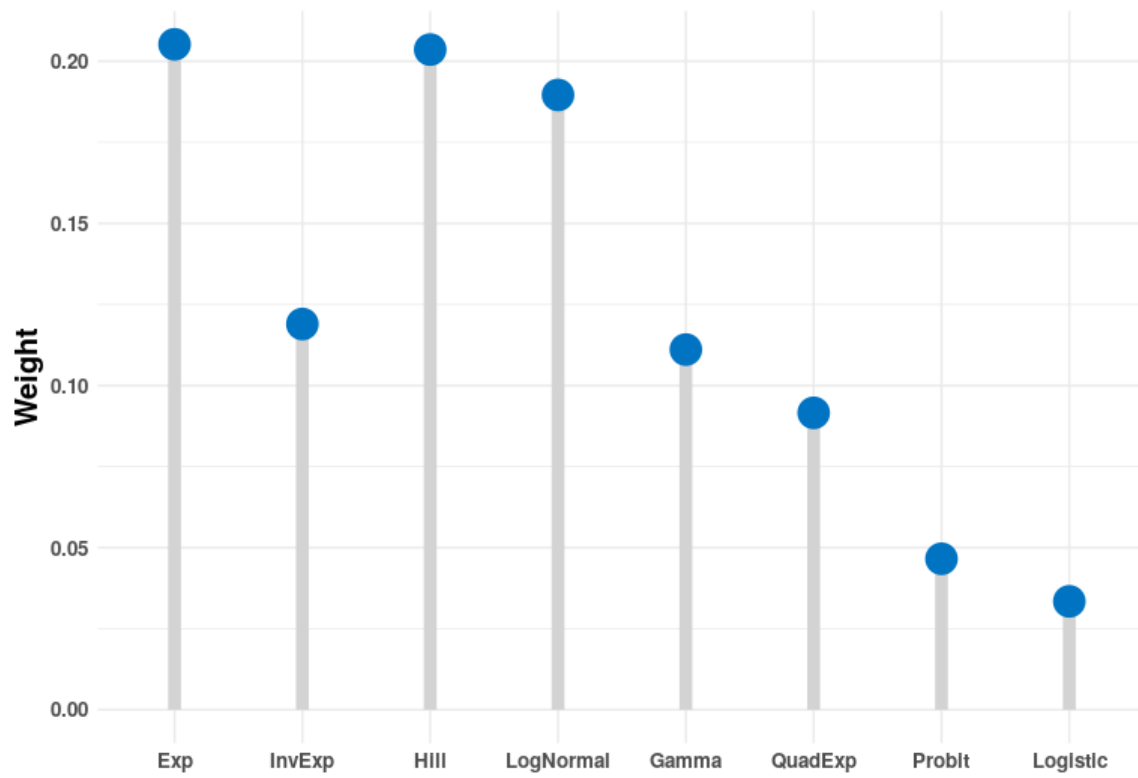
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.043	1.163	6.215

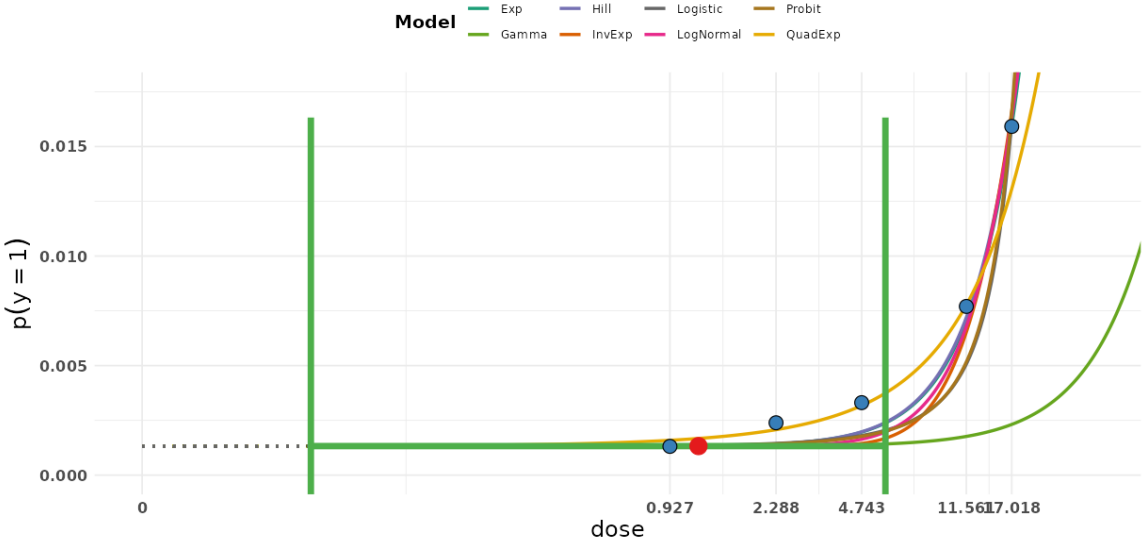
Estimated BMDs per model

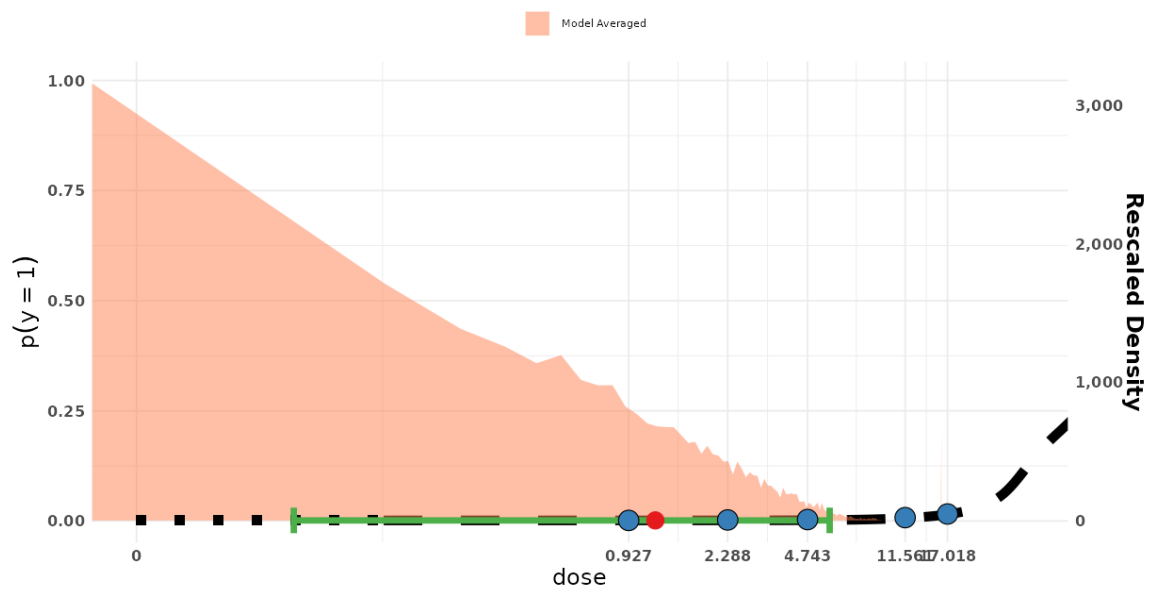
Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.118	0.922	3.354	0.205	1
IE4_Q	0.643	3.150	6.645	0.119	1
H4_Q	0.120	0.911	3.564	0.204	1
LN4_Q	0.323	2.006	5.495	0.190	1
G4_Q	0.182	2.026	10.443	0.111	0
QE4_Q	0.021	0.047	0.163	0.092	1
P4_Q	0.043	0.560	3.261	0.047	1
L4_Q	0.051	0.585	2.775	0.033	1

Plots of Fitted Models









Cherry et al. (2008) stillbirth, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for stillbirth

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.45	492	16860
3.24	386	10669
4.73	177	3455

The 'Value for CES' is set to 0.00030059.

Extended dose range is applied.

Informative background prior: min: 0.02888968; the most likely: 0.02918149; max: 0.02947331. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.09e+00).

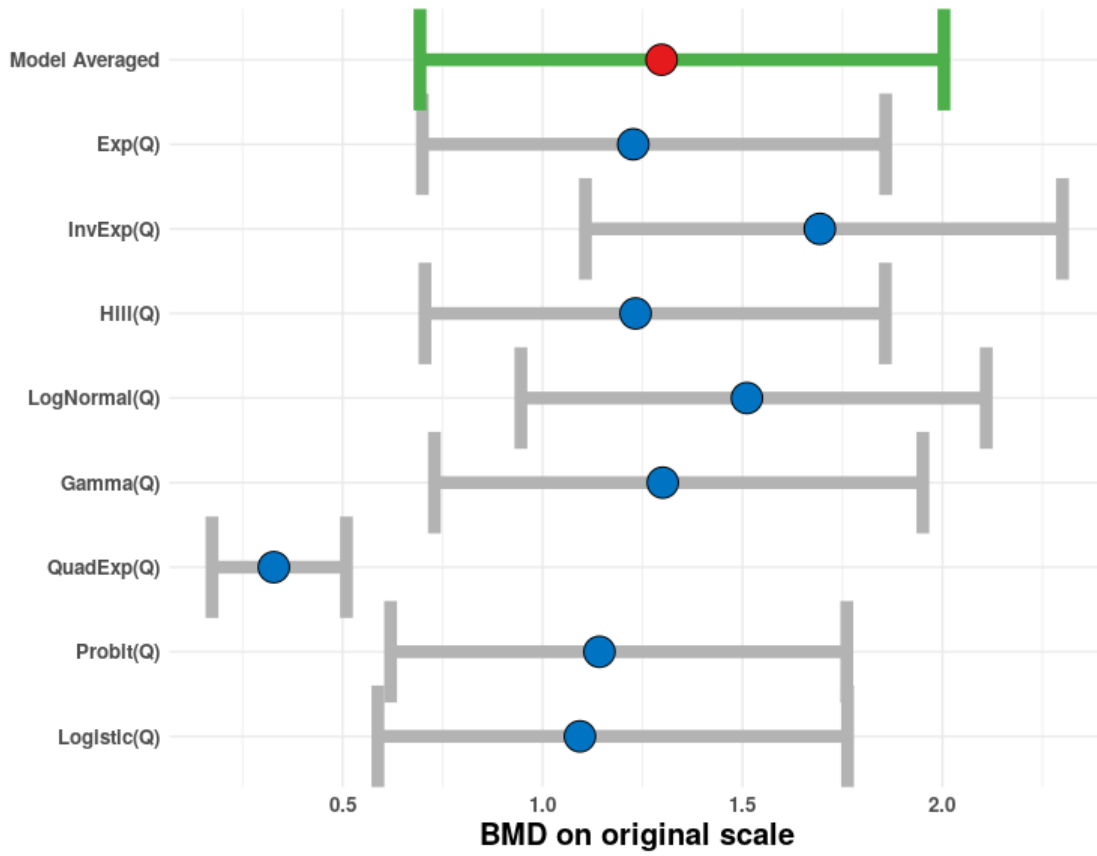
Model Averaged BMD

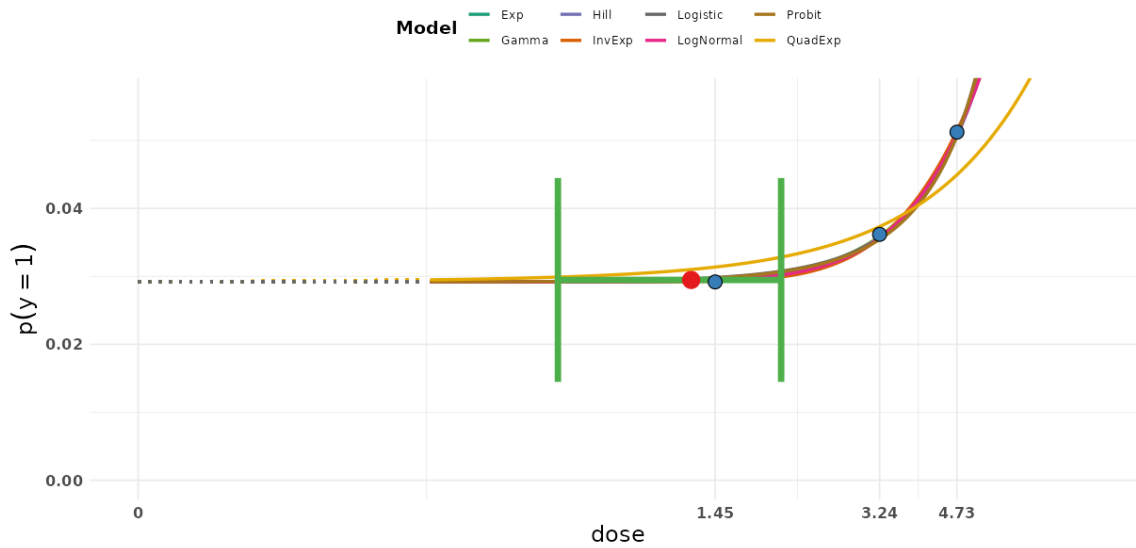
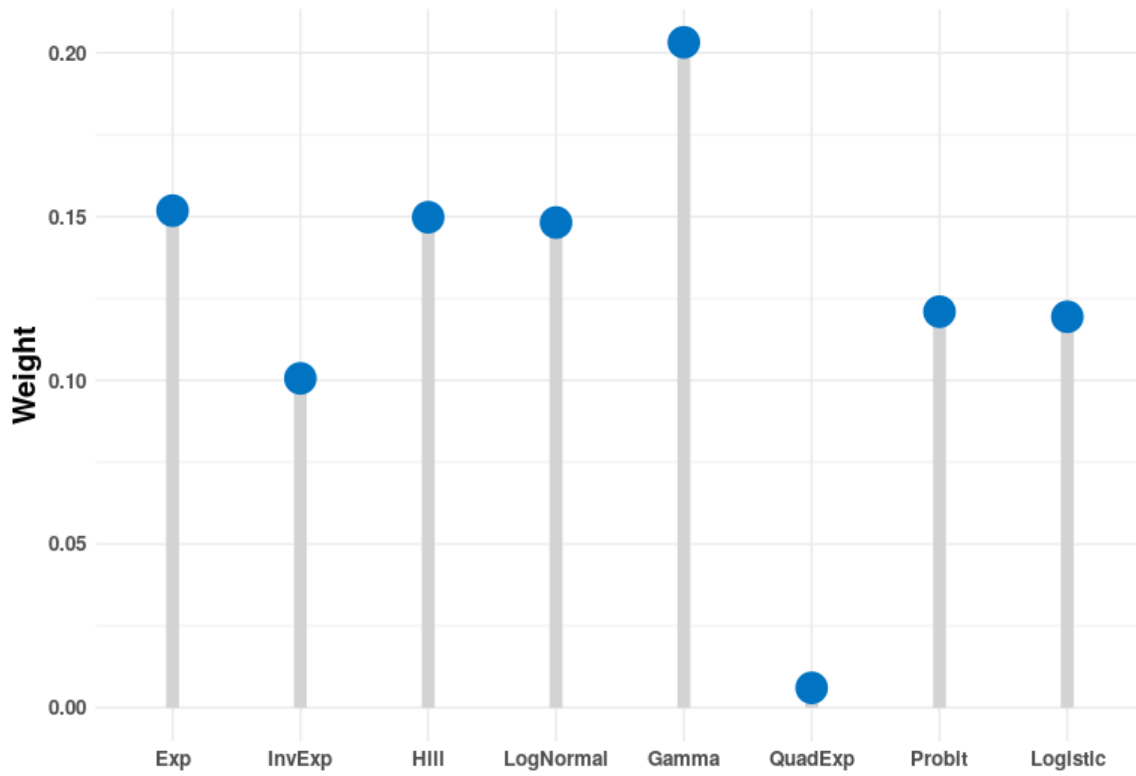
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.694	1.298	2.004

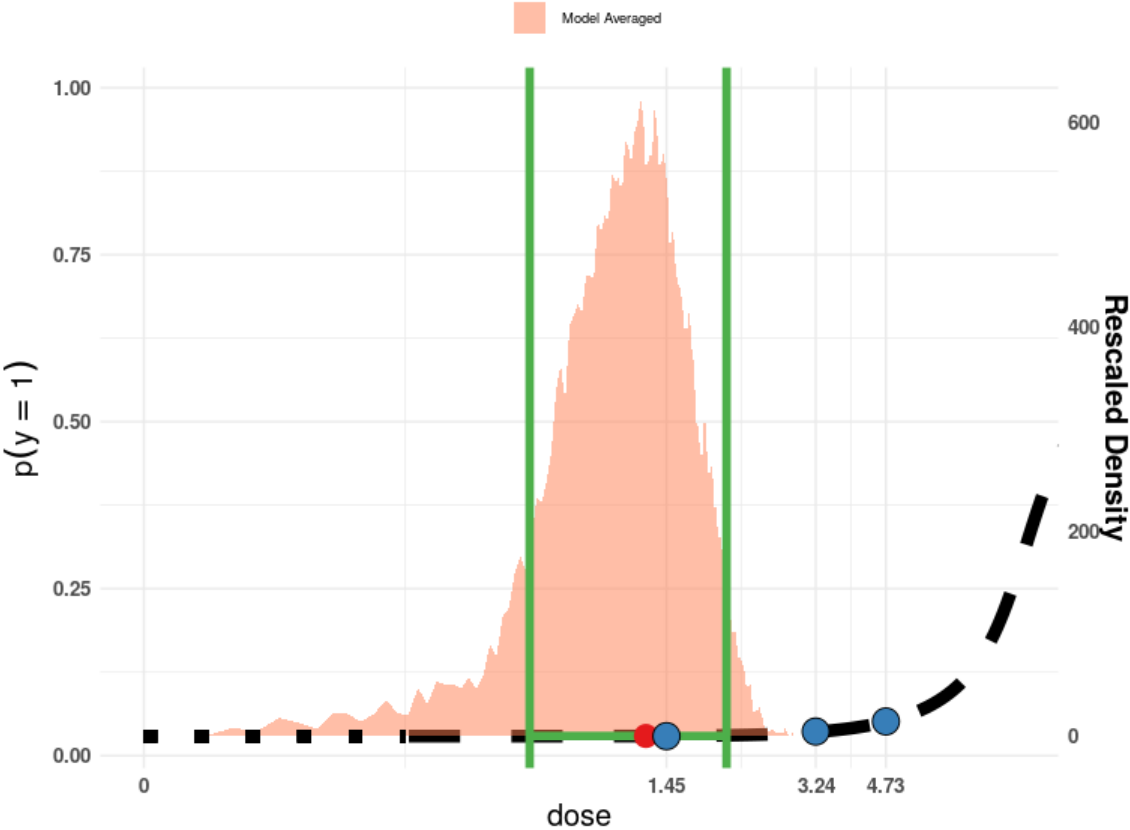
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.700	1.227	1.858	0.152	1
IE4_Q	1.107	1.693	2.300	0.101	1
H4_Q	0.706	1.233	1.857	0.150	1
LN4_Q	0.946	1.511	2.110	0.148	1
G4_Q	0.730	1.301	1.951	0.203	1
QE4_Q	0.174	0.328	0.510	0.006	1
P4_Q	0.620	1.142	1.761	0.121	1
L4_Q	0.588	1.094	1.763	0.119	1

Plots of Fitted Models







Gilbert-Diamond et al. (2013) skin cancer, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for skin cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.063	96	263307
0.120	90	260846
0.230	137	260846

The 'Value for CES' is set to 3.65e-06.

Extended dose range is not applied.

Informative background prior: min: 0.00036095; the most likely: 0.00036459; max: 0.00036824. Shape parameter is applied:

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.33e+00).

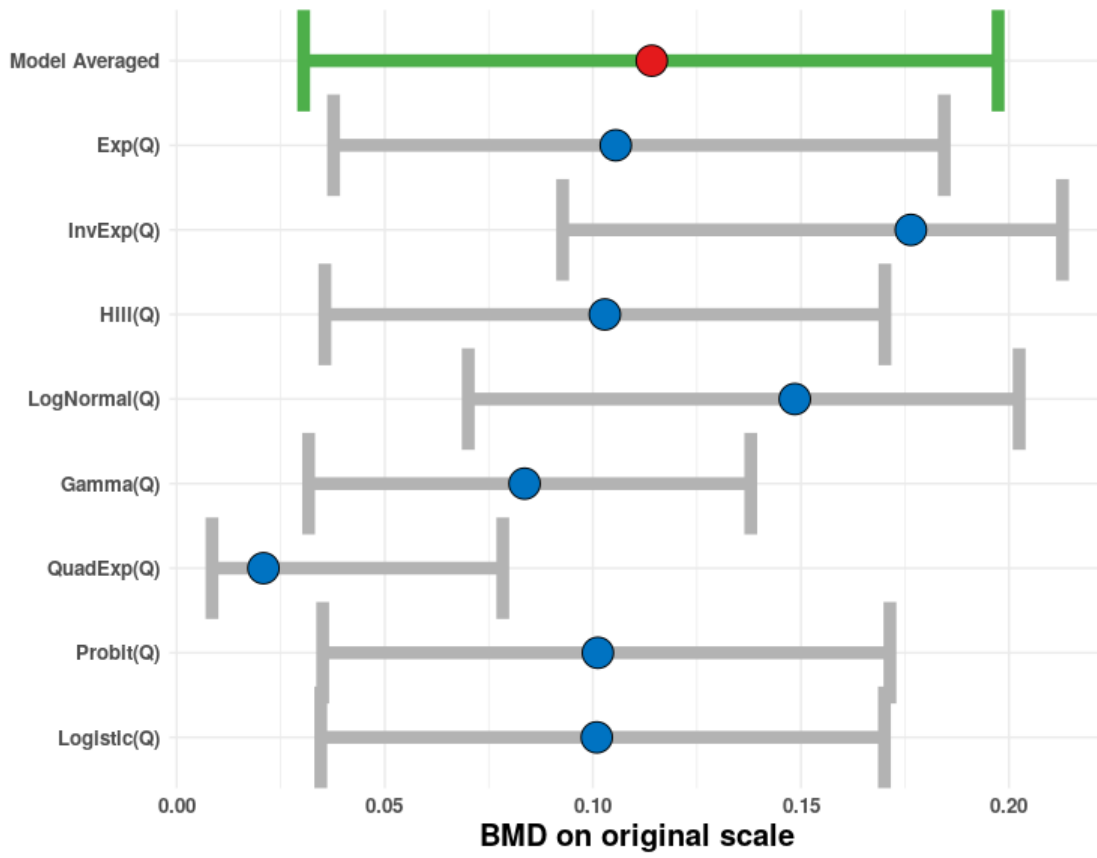
Model Averaged BMD

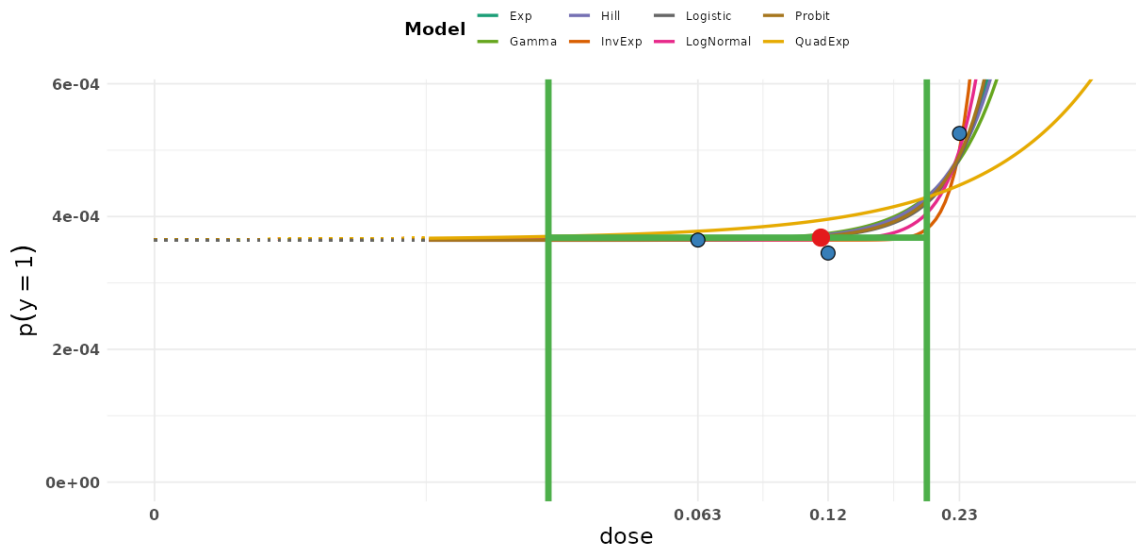
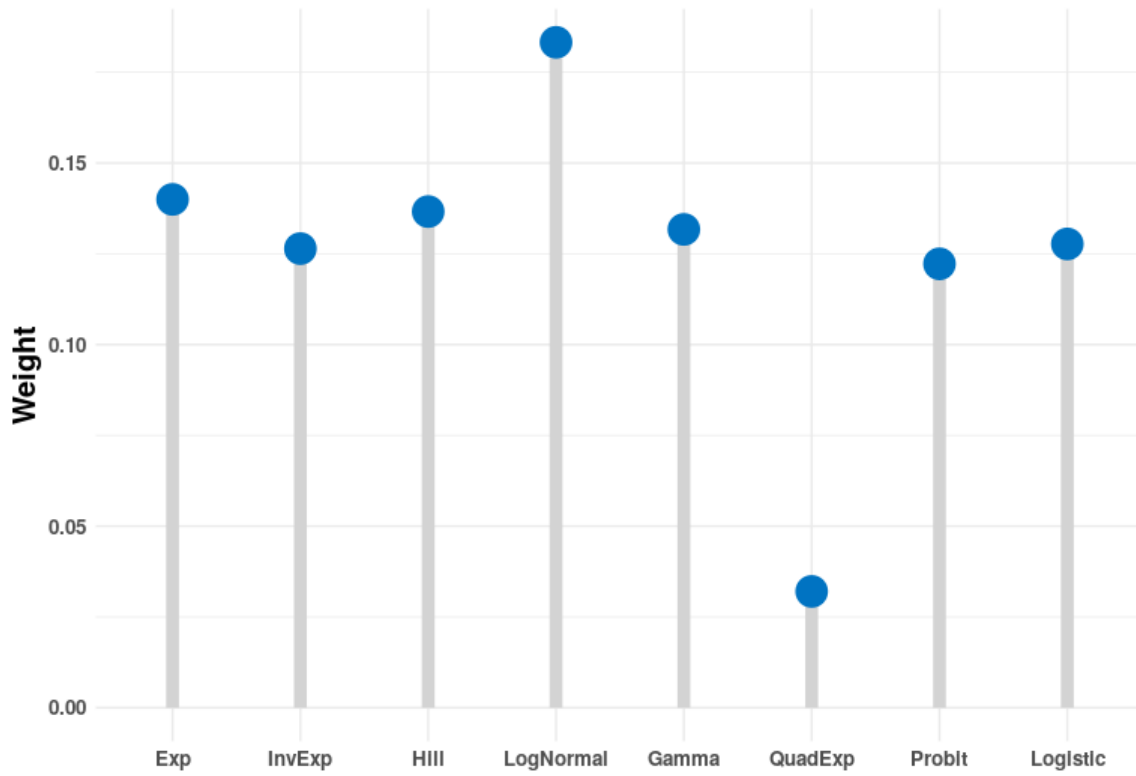
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.031	0.114	0.197

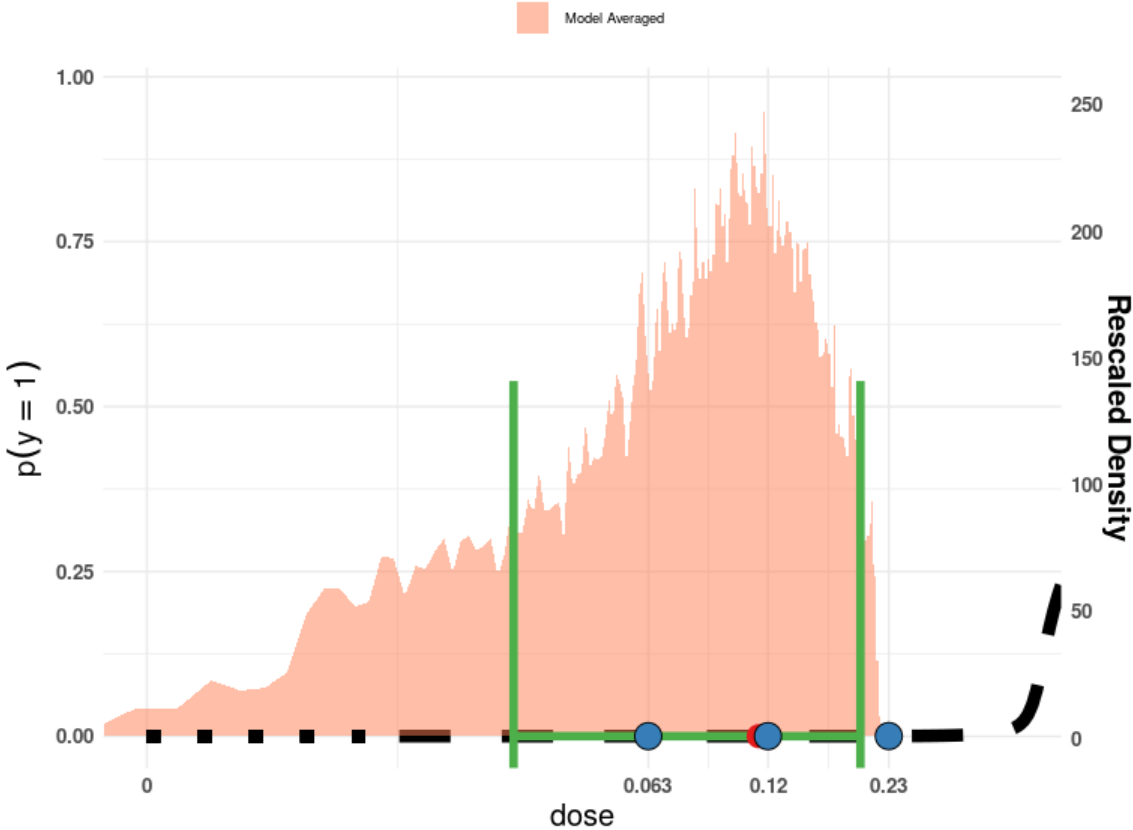
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.038	0.106	0.184	0.140	1
IE4_Q	0.093	0.176	0.213	0.126	0
H4_Q	0.036	0.103	0.170	0.137	1
LN4_Q	0.070	0.149	0.202	0.183	1
G4_Q	0.032	0.084	0.138	0.132	0
QE4_Q	0.008	0.021	0.078	0.032	1
P4_Q	0.035	0.101	0.171	0.122	1
L4_Q	0.035	0.101	0.170	0.128	1

Plots of Fitted Models







Hsueh et al. (2009) chronic kidney disease, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for chronic kidney disease

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.13	18	655022
0.36	27	681223
0.46	80	663755

The 'Value for CES' is set to 2.7e-07.

Extended dose range is not applied.

Informative background prior: min: 0.00002473; the most likely: 0.00002748; max: 0.00003023. Shape parameter applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 4.53e-01).

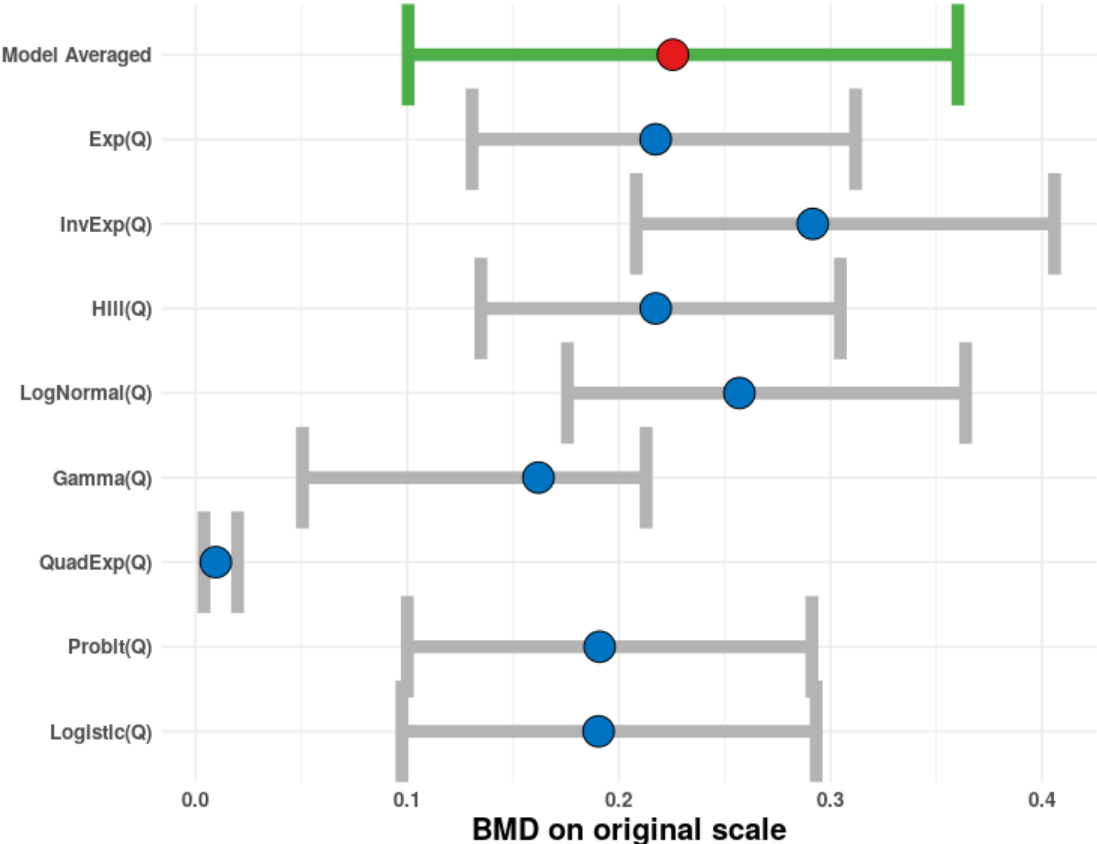
Model Averaged BMD

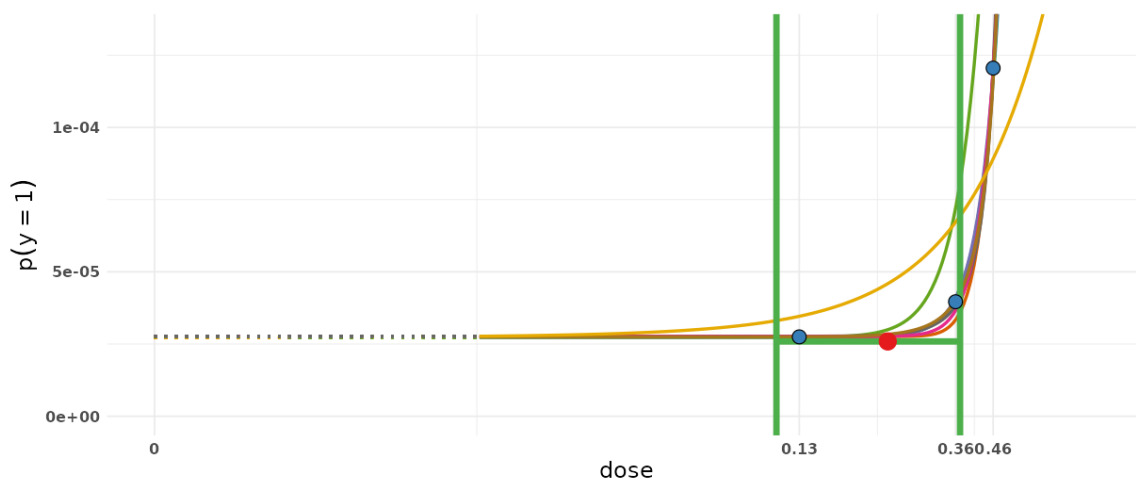
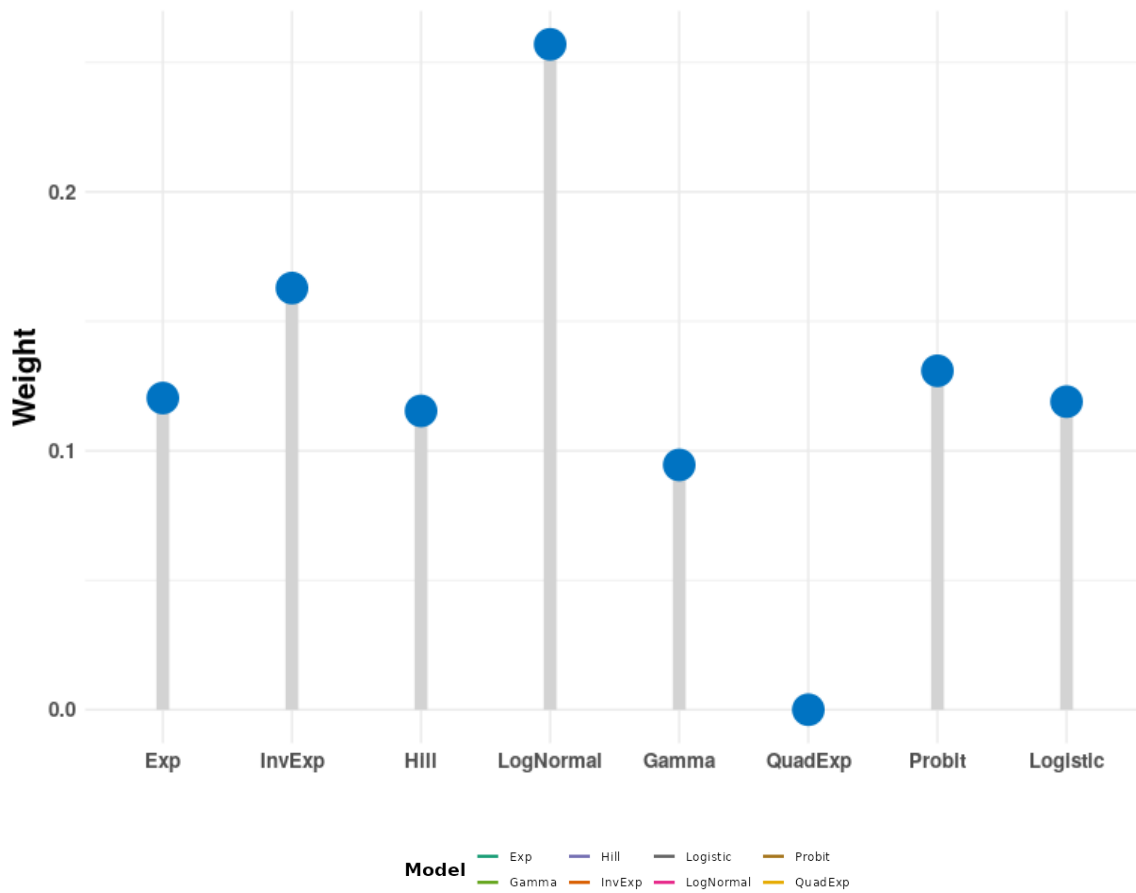
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.1	0.226	0.36

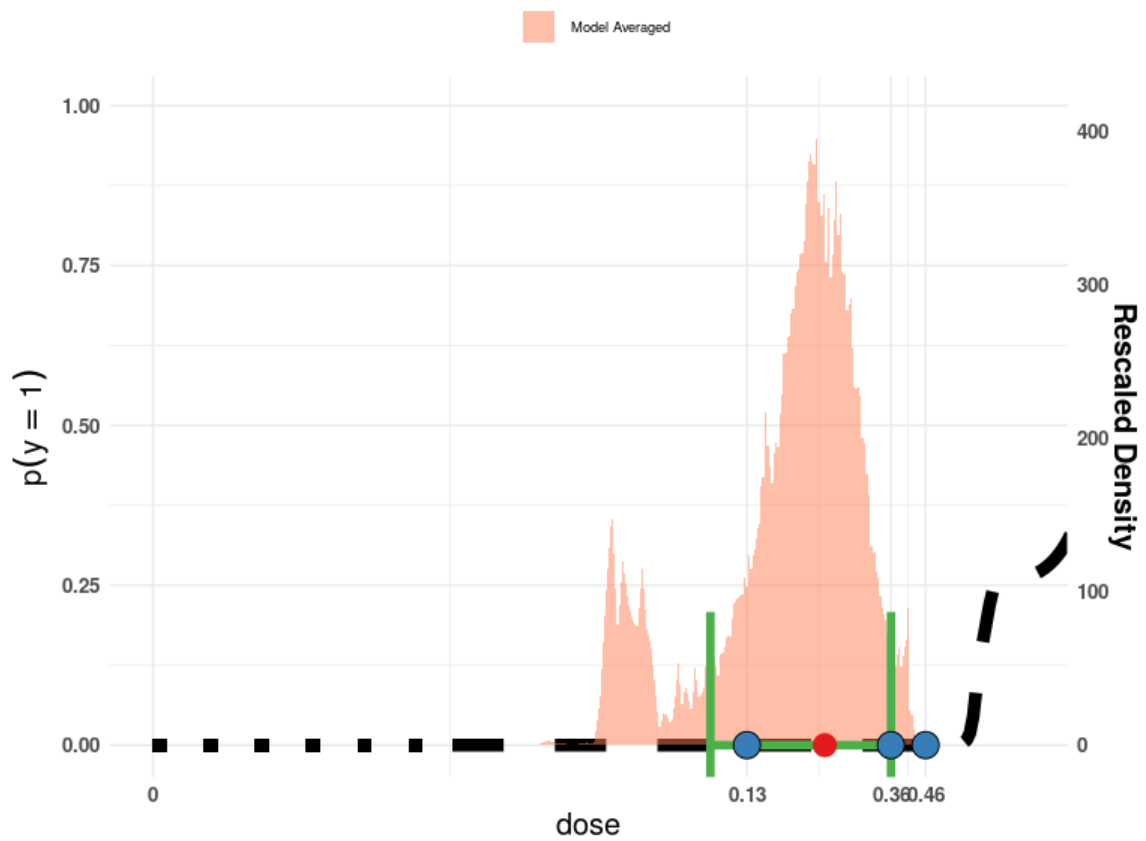
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.131	0.217	0.312	0.120	1
IE4_Q	0.208	0.292	0.406	0.163	1
H4_Q	0.135	0.217	0.305	0.115	1
LN4_Q	0.176	0.257	0.364	0.257	1
G4_Q	0.050	0.162	0.213	0.095	0
QE4_Q	0.004	0.009	0.020	0.000	1
P4_Q	0.100	0.191	0.291	0.131	1
L4_Q	0.097	0.190	0.293	0.119	1

Plots of Fitted Models







James et al. (2015) ischemic heart disease, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for ischemic heart disease

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	Person.years
0.34	58	4806
0.76	20	1335
0.97	14	534
1.30	4	98

The 'Value for CES' is set to 0.00012216.

Extended dose range is not applied.

Informative background prior: min: 0.01194757; the most likely: 0.01206825; max: 0.01218893. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.99e-02).

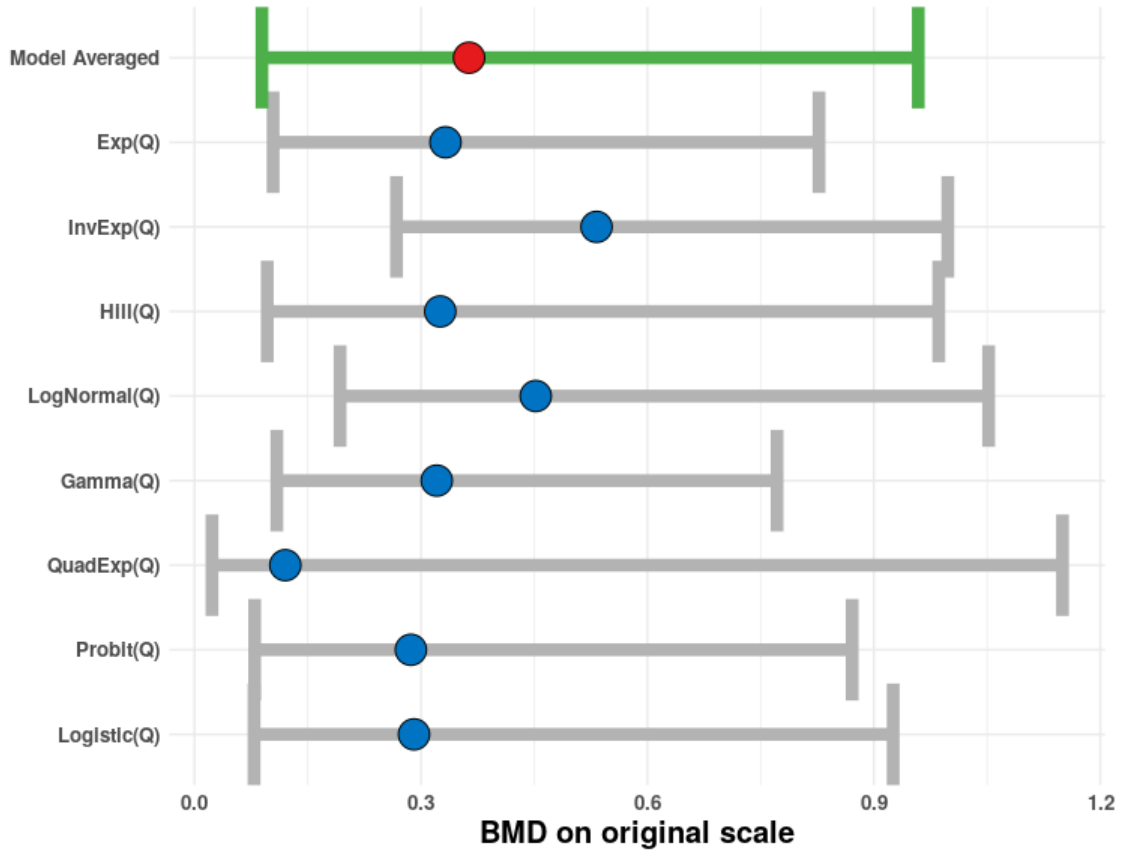
Model Averaged BMD

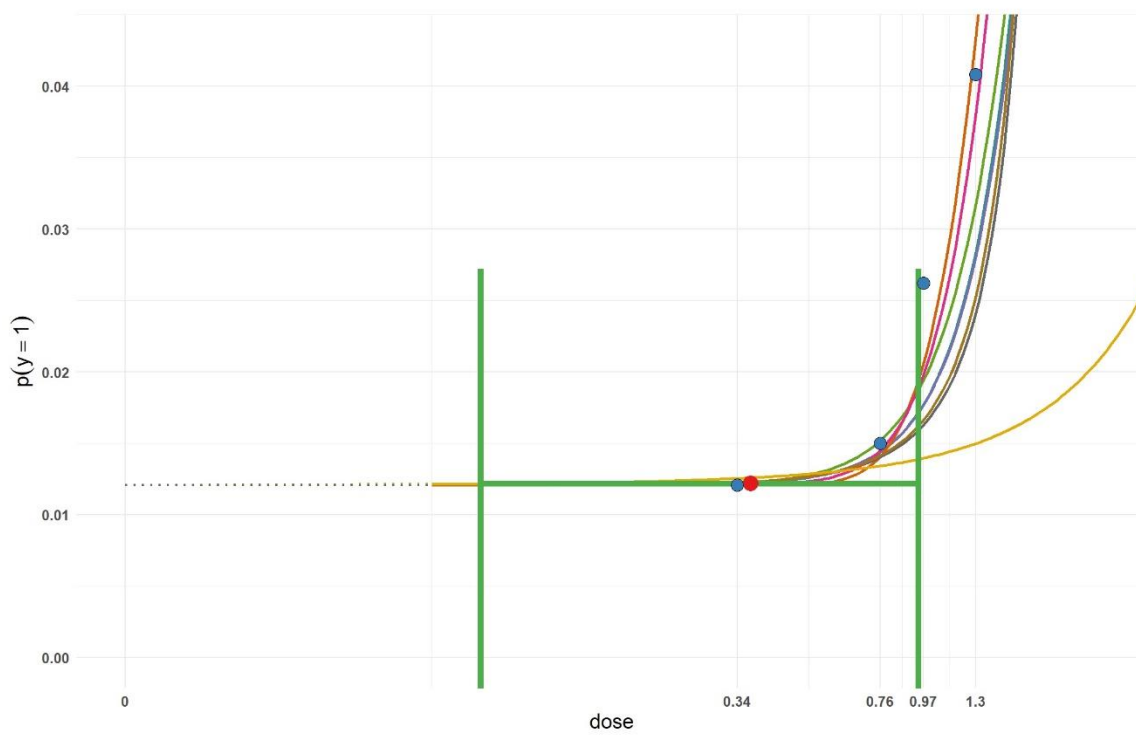
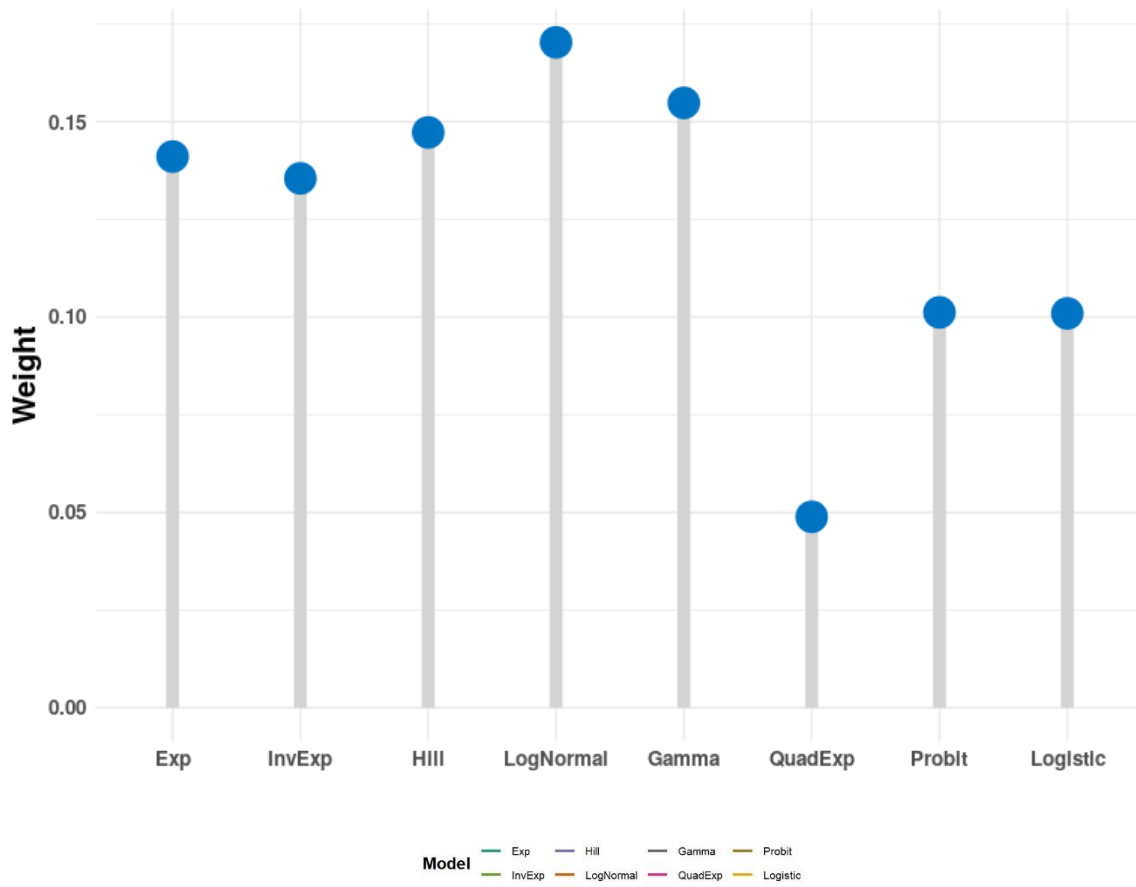
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.089	0.364	0.959

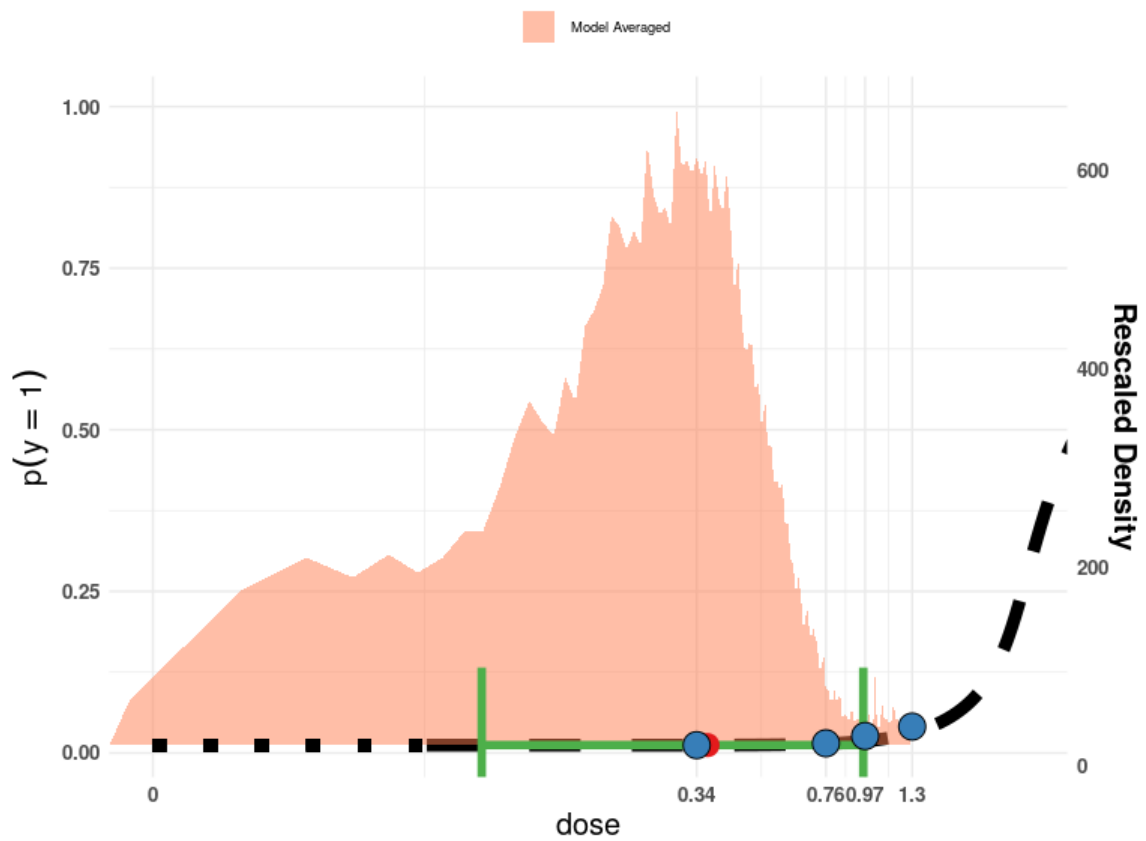
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.104	0.332	0.827	0.141	1
IE4_Q	0.268	0.533	0.998	0.135	1
H4_Q	0.096	0.325	0.986	0.147	0
LN4_Q	0.193	0.452	1.052	0.170	1
G4_Q	0.109	0.321	0.772	0.155	1
QE4_Q	0.023	0.120	1.150	0.049	1
P4_Q	0.080	0.287	0.871	0.101	1
L4_Q	0.079	0.291	0.926	0.101	1

Plots of Fitted Models







Leonardi et al. (2012) skin cancer, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for skin cancer

Data used for analysis:

Exposure	Adj.cases	N
0.12	59	4e+05
0.13	82	4e+05
0.20	70	4e+05
0.39	101	4e+05
2.11	179	4e+05

The 'Value for CES' is set to 1.48e-06.

Extended dose range is not applied.

Informative background prior: min: 0.00014603; the most likely: 0.00014750; max: 0.00014898. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since the lowest non-zero dose/BMD > 10.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 9.64e-06).

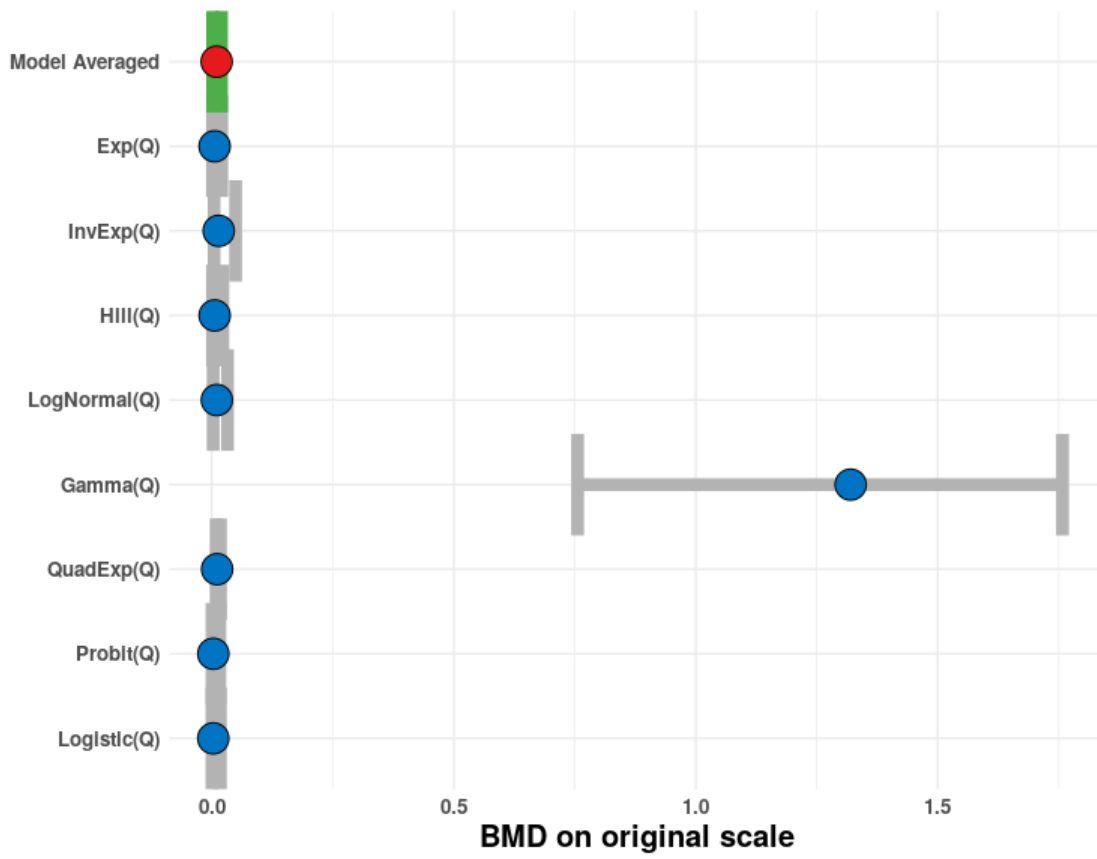
Model Averaged BMD

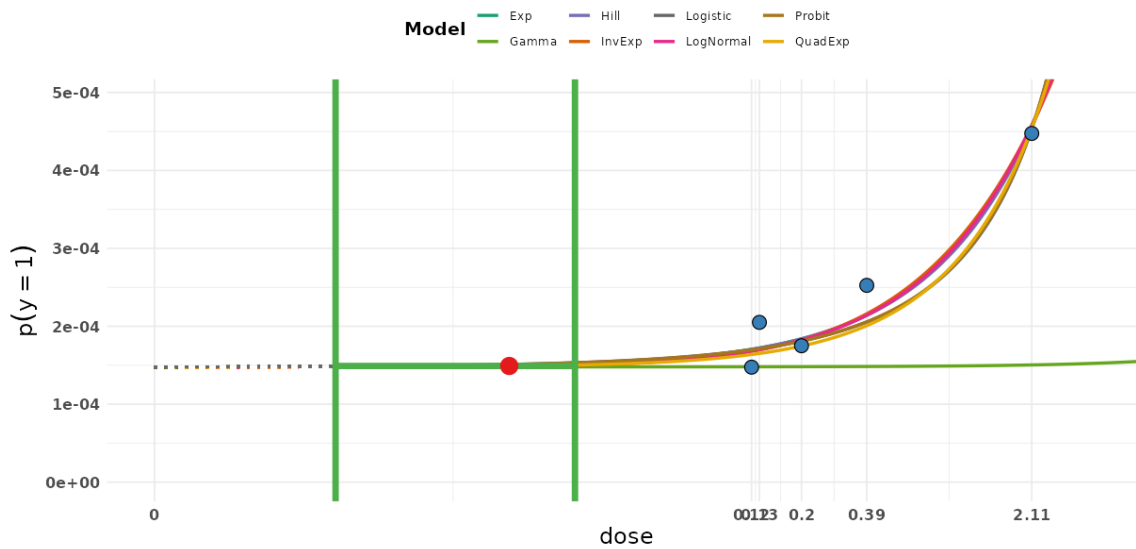
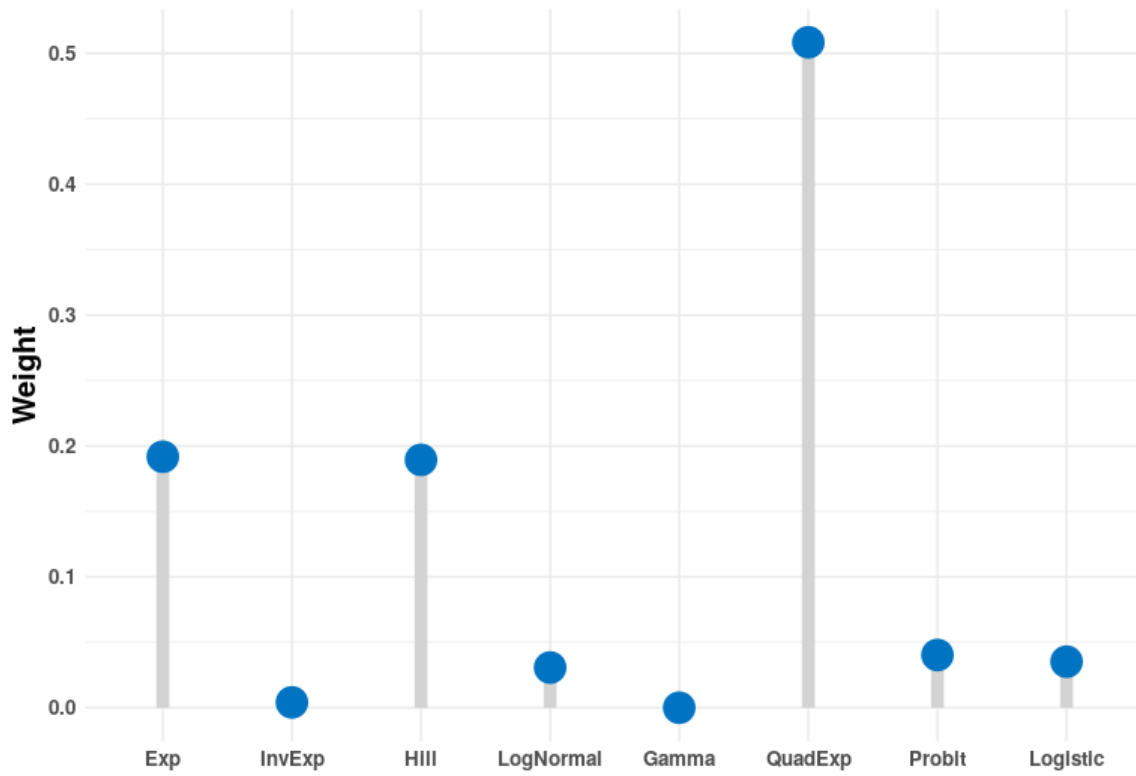
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.002	0.01	0.02

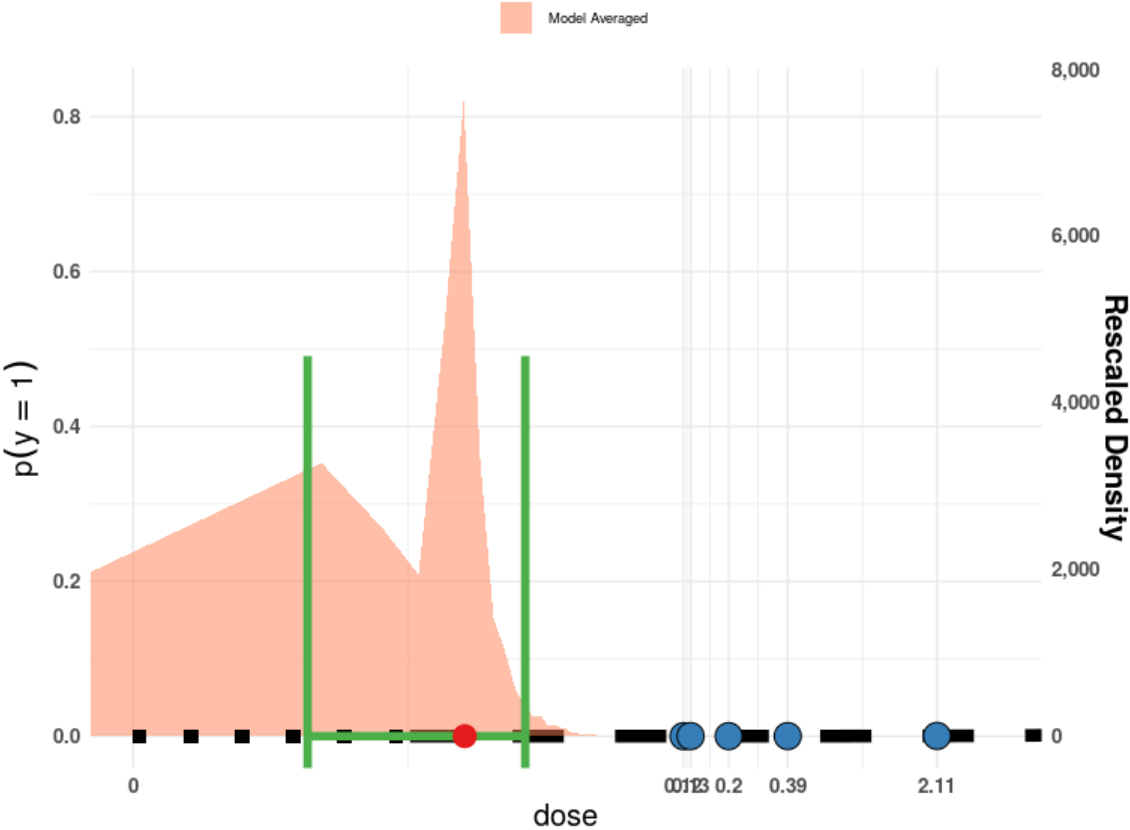
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.001	0.006	0.021	0.192	1
IE4_Q	0.005	0.014	0.049	0.004	1
H4_Q	0.001	0.006	0.023	0.189	1
LN4_Q	0.003	0.010	0.032	0.031	1
G4_Q	0.756	1.320	1.758	0.000	0
QE4_Q	0.009	0.011	0.018	0.508	1
P4_Q	0.001	0.003	0.017	0.040	1
L4_Q	0.000	0.003	0.018	0.035	1

Plots of Fitted Models







Milton et al. (2005) neonatal death, relative BMR 1%**Data Description**

The endpoint to be analyzed is: Adj.cases for neonatal death

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
2.91	19	176
6.58	14	53
8.36	53	304

The 'Value for CES' is set to 0.00121019.

Extended dose range is not applied.

Informative background prior: min: 0.10687500; the most likely: 0.10795455; max: 0.10903409. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) criteria since none of the candidate models fit the data sufficiently well.

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 1.25e+01).

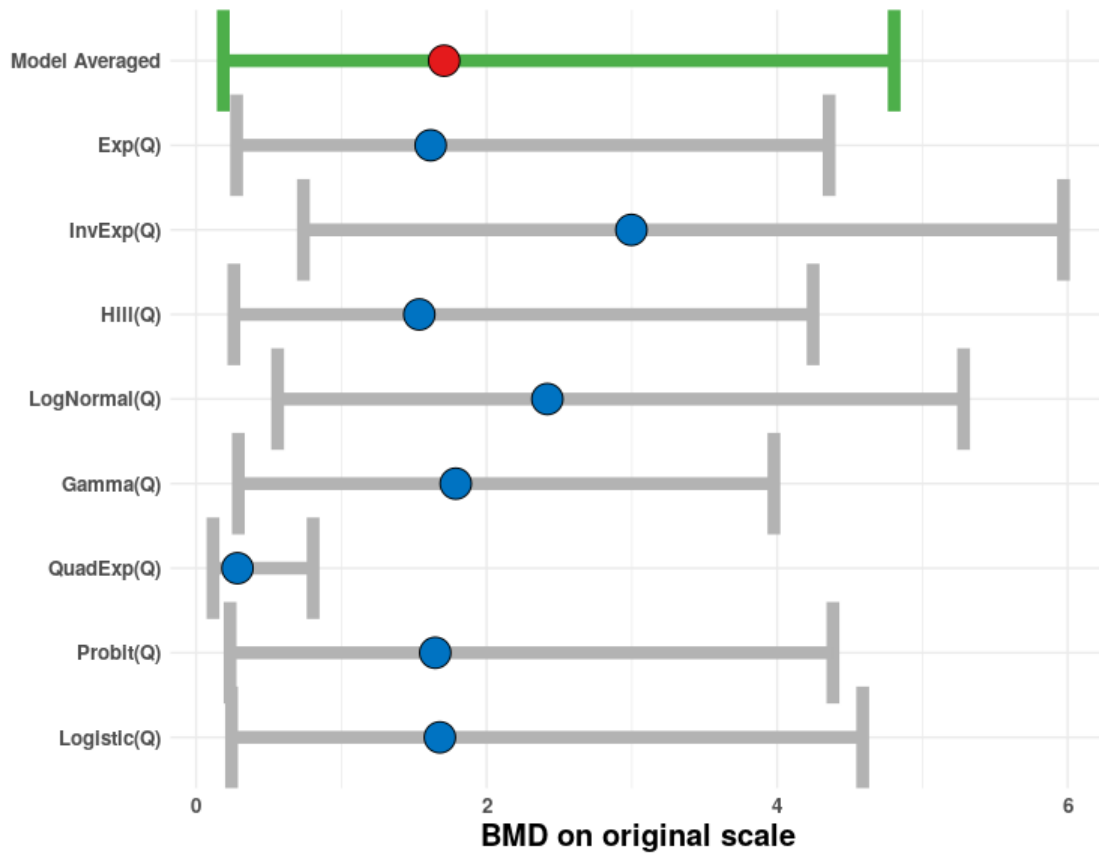
Model Averaged BMD

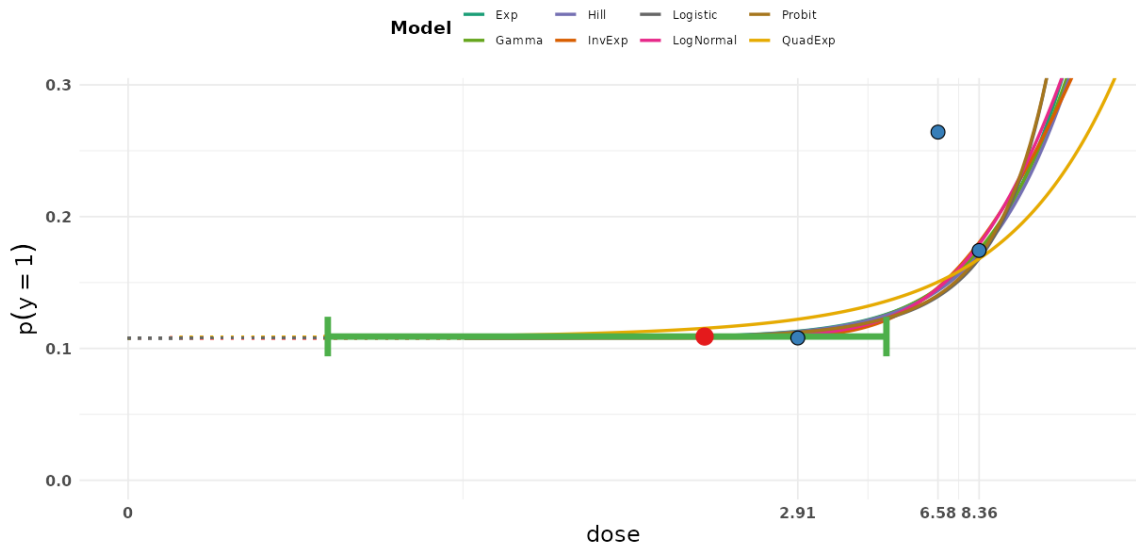
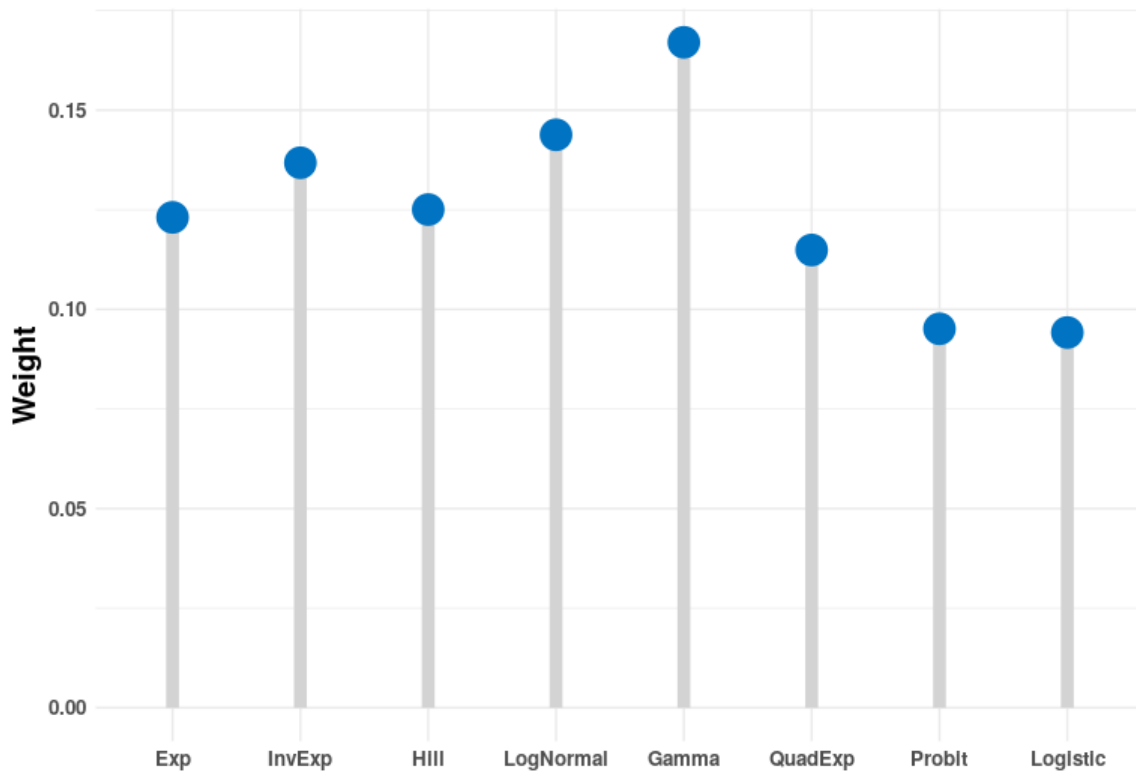
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.187	1.708	4.806

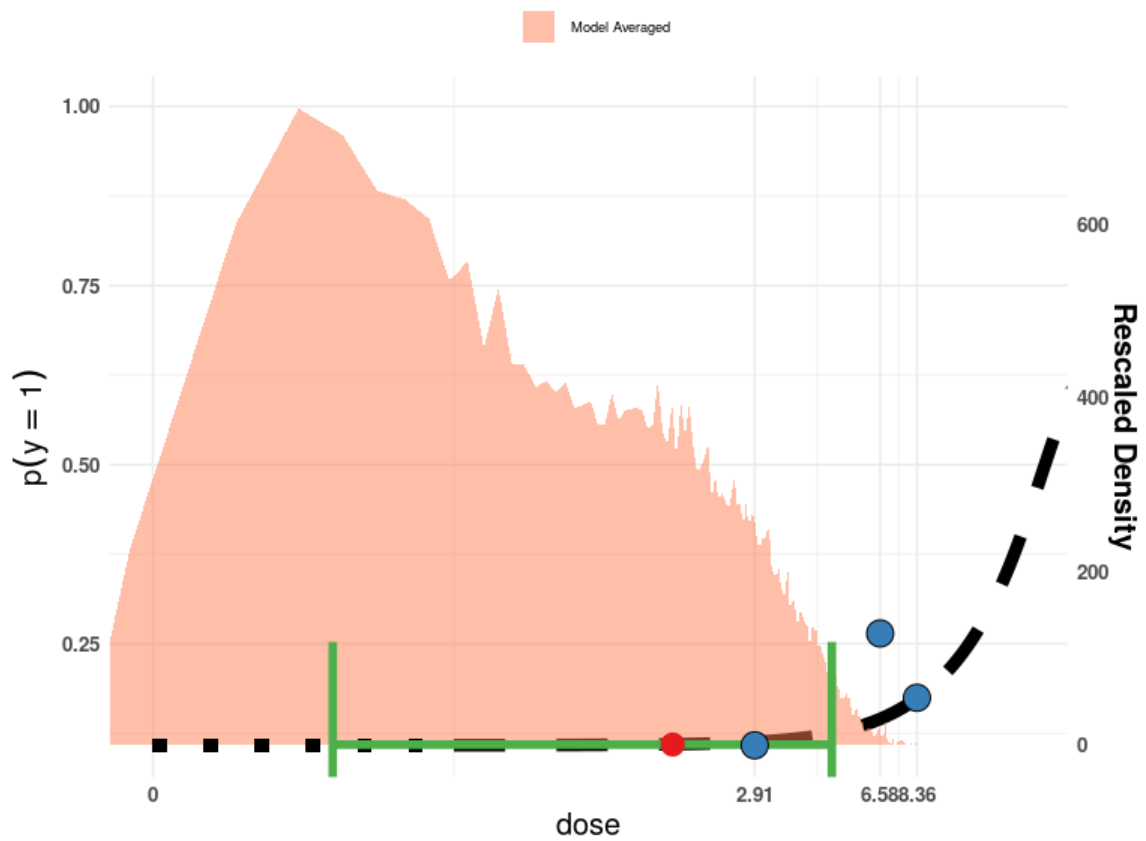
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.279	1.615	4.358	0.123	1
IE4_Q	0.739	2.996	5.971	0.137	1
H4_Q	0.260	1.537	4.247	0.125	1
LN4_Q	0.561	2.418	5.283	0.144	1
G4_Q	0.291	1.788	3.978	0.167	1
QE4_Q	0.116	0.285	0.806	0.115	1
P4_Q	0.234	1.646	4.384	0.095	1
L4_Q	0.244	1.678	4.589	0.094	1

Plots of Fitted Models







Milton et al. (2005) spontaneous abortion, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for spontaneous abortion

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
2.91	17	176
6.58	11	53
8.36	63	304

The 'Value for CES' is set to 0.00106918.

Extended dose range is not applied.

Informative background prior: min: 0.09562500; the most likely; 0.09659091; max: 0.09755682. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.77e+00).

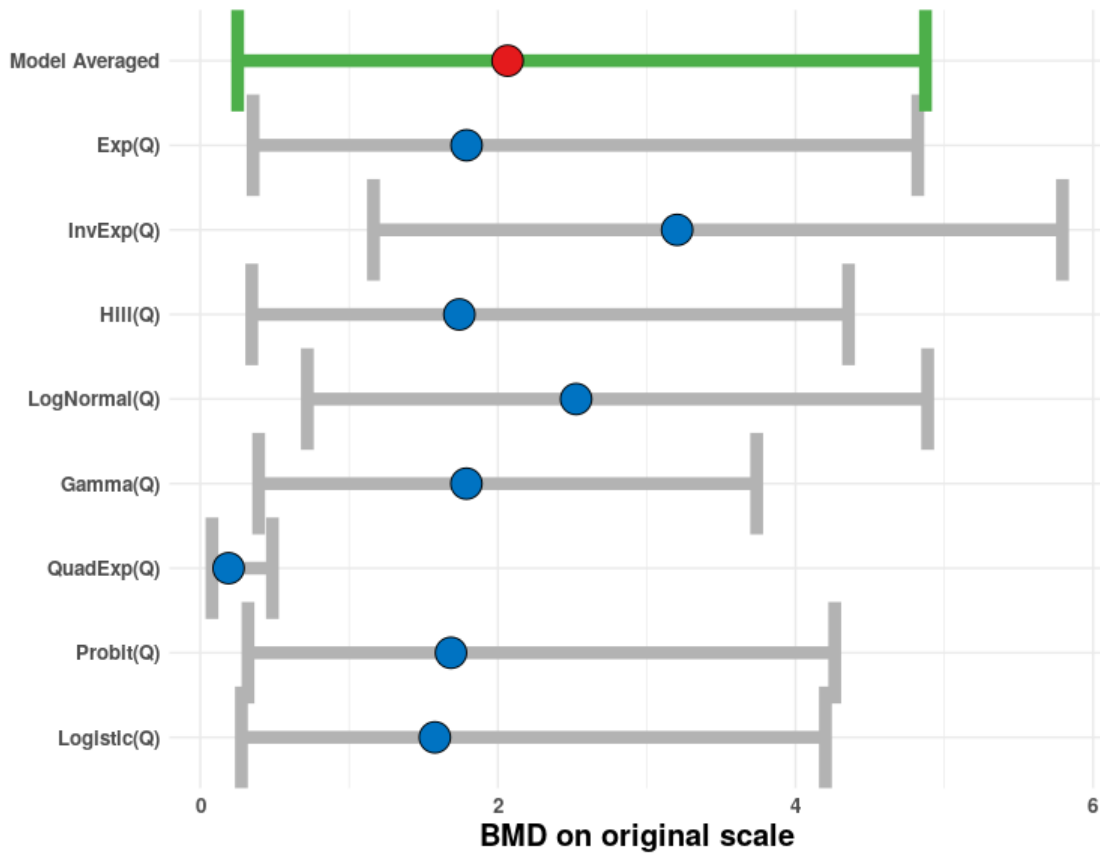
Model Averaged BMD

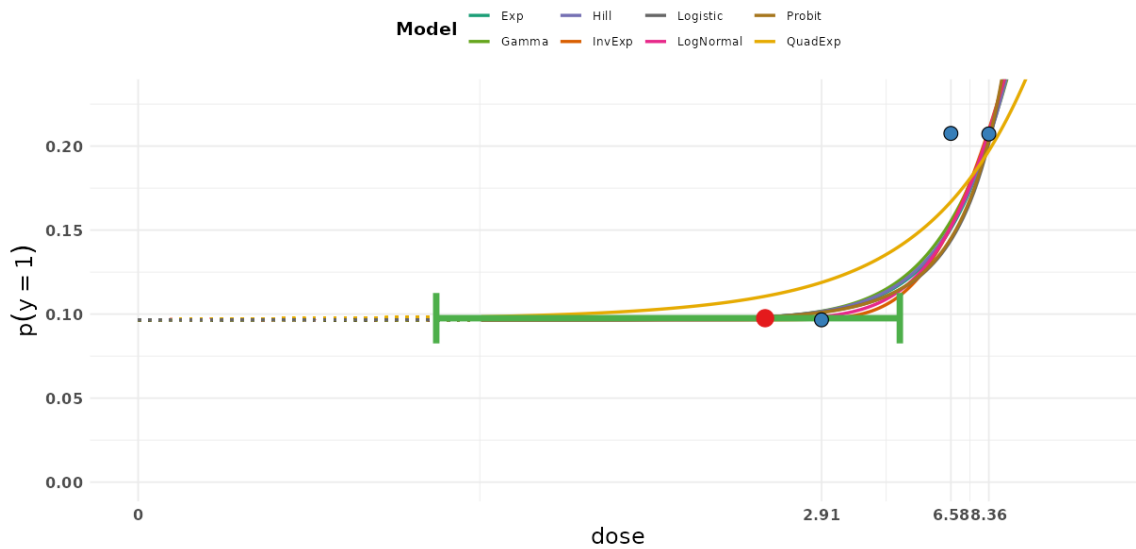
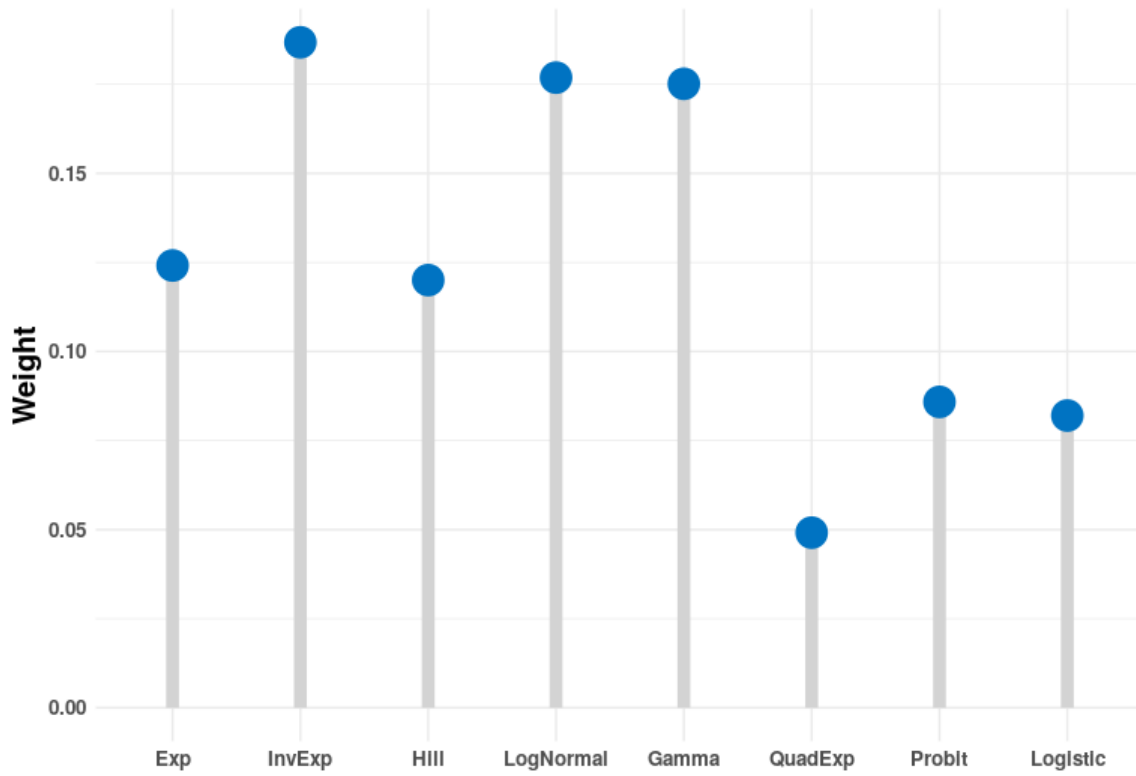
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.251	2.065	4.874

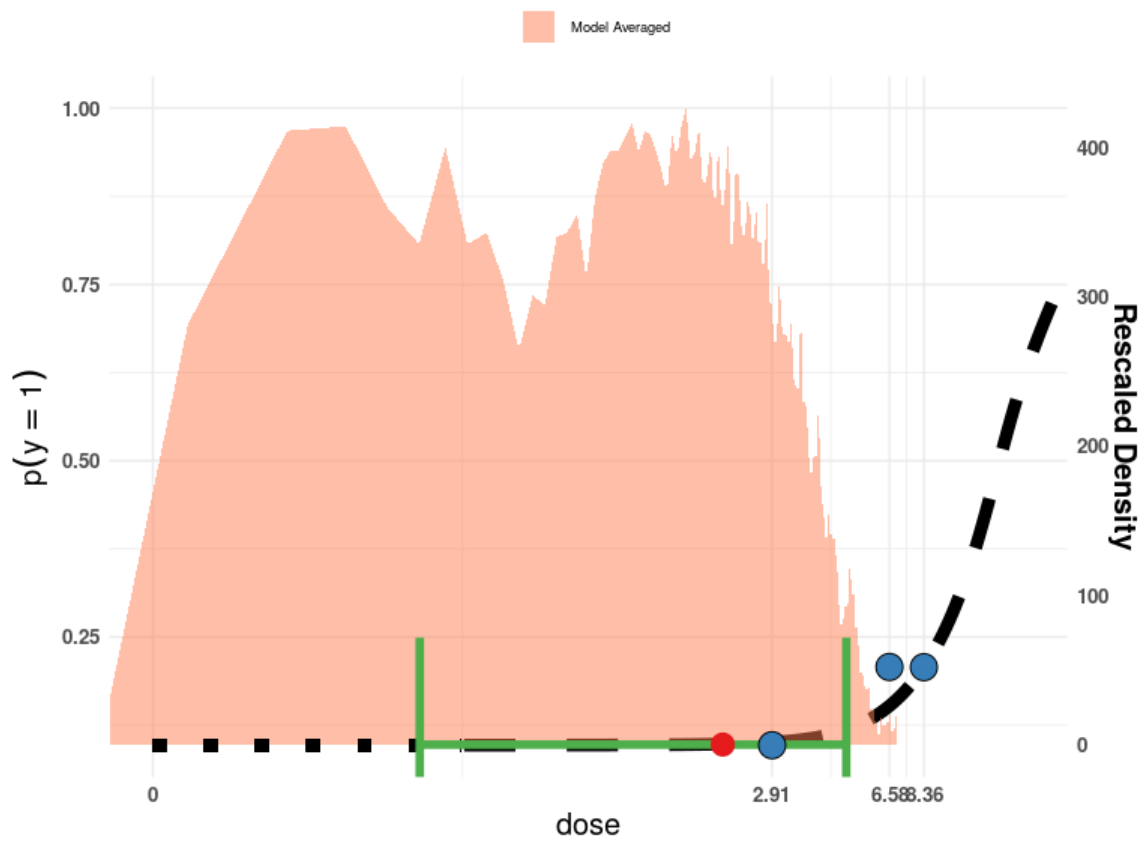
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.355	1.790	4.822	0.124	1
IE4_Q	1.164	3.205	5.794	0.187	1
H4_Q	0.346	1.741	4.357	0.120	1
LN4_Q	0.720	2.526	4.888	0.177	1
G4_Q	0.392	1.788	3.739	0.175	1
QE4_Q	0.079	0.190	0.485	0.049	1
P4_Q	0.321	1.685	4.264	0.086	1
L4_Q	0.276	1.576	4.201	0.082	1

Plots of Fitted Models







Milton et al. (2005) stillbirth, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for stillbirth

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
2.91	11	176
6.58	4	53
8.36	48	304

The 'Value for CES' is set to 0.00066667.

Extended dose range is not applied.

Informative background prior: min: 0.06187500; the most likely; 0.06250000; max: 0.06312500. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.02e+00).

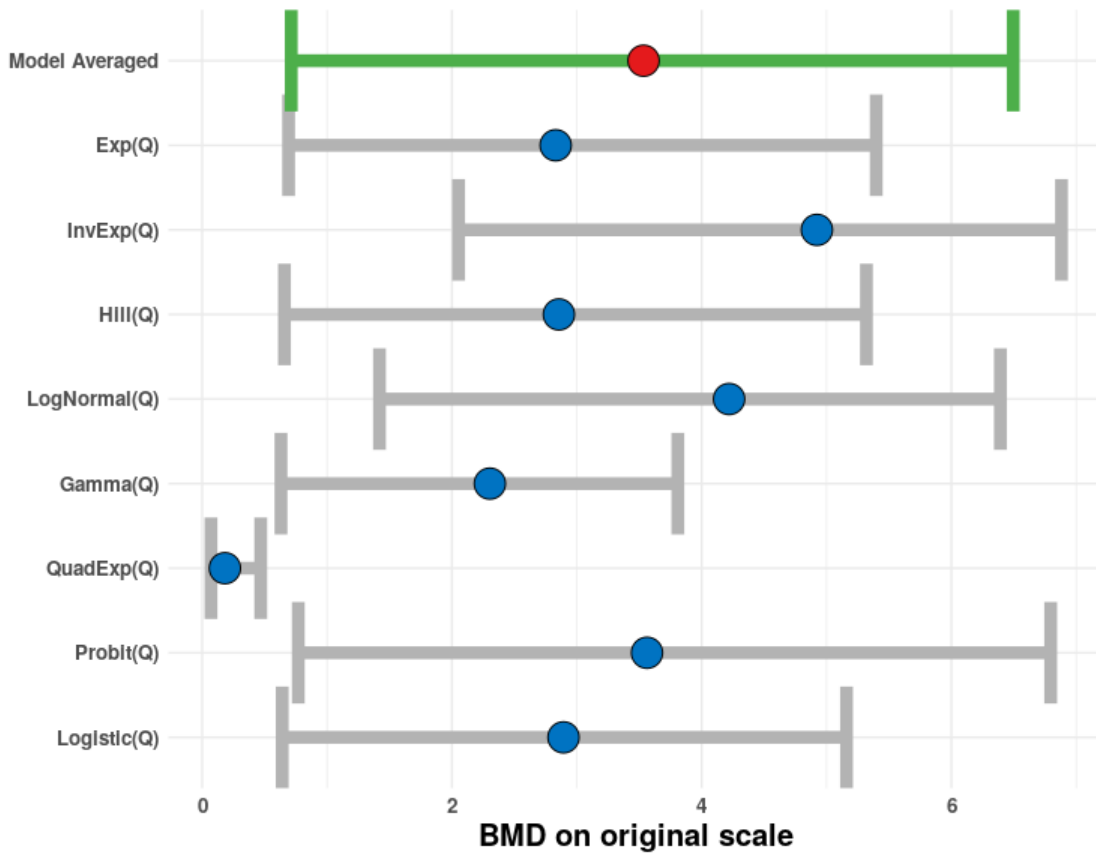
Model Averaged BMD

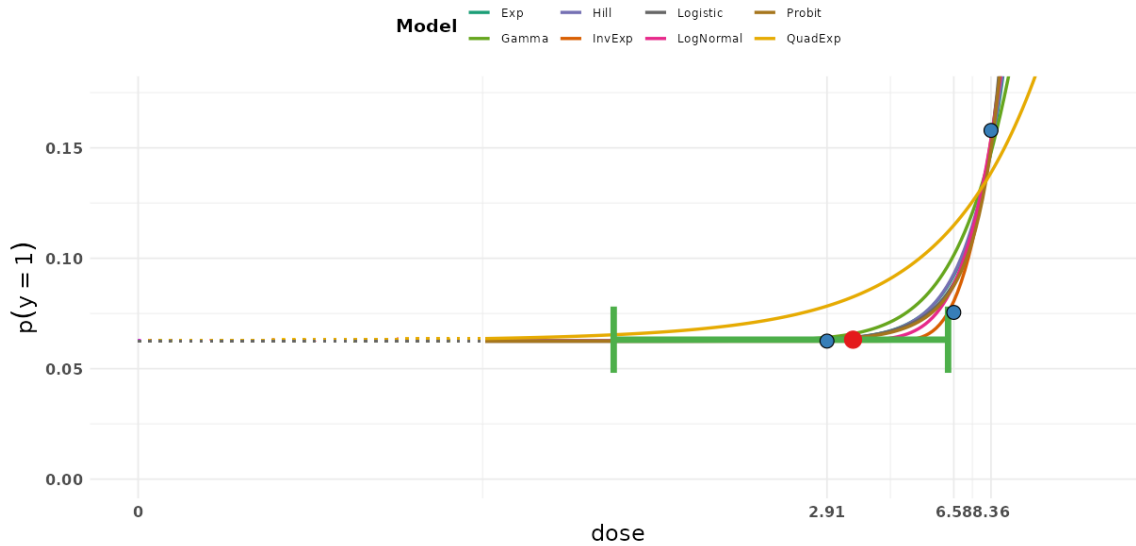
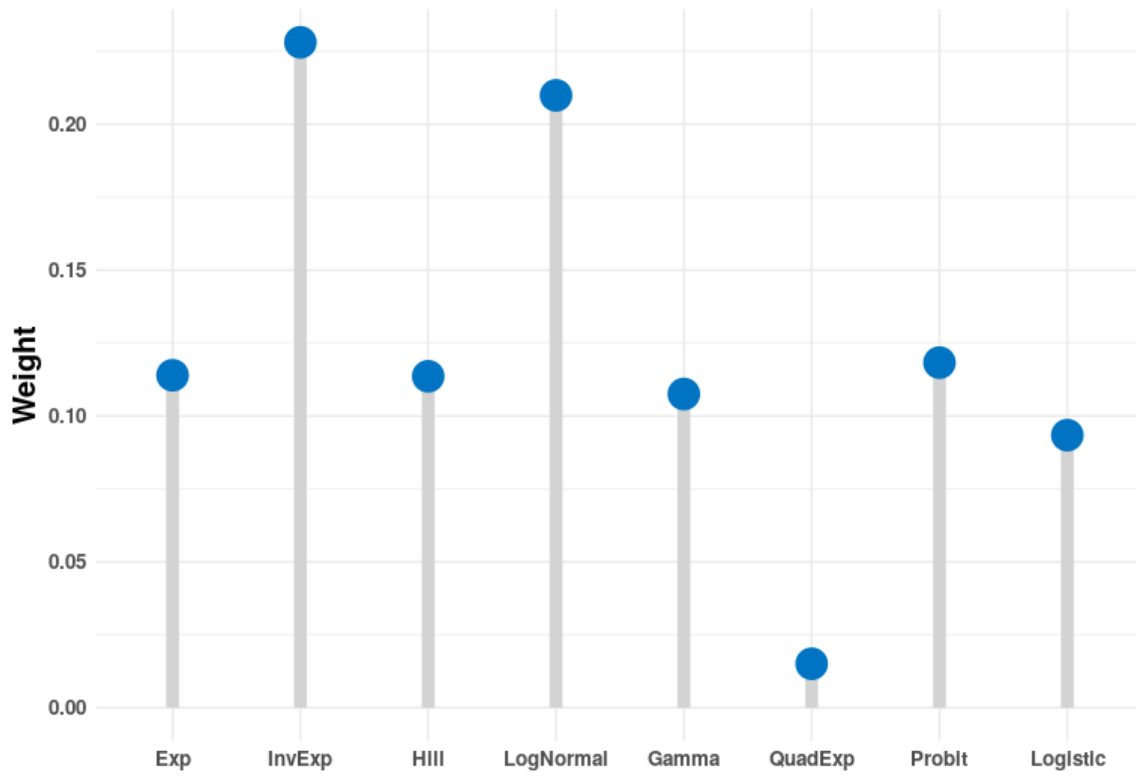
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.713	3.535	6.495

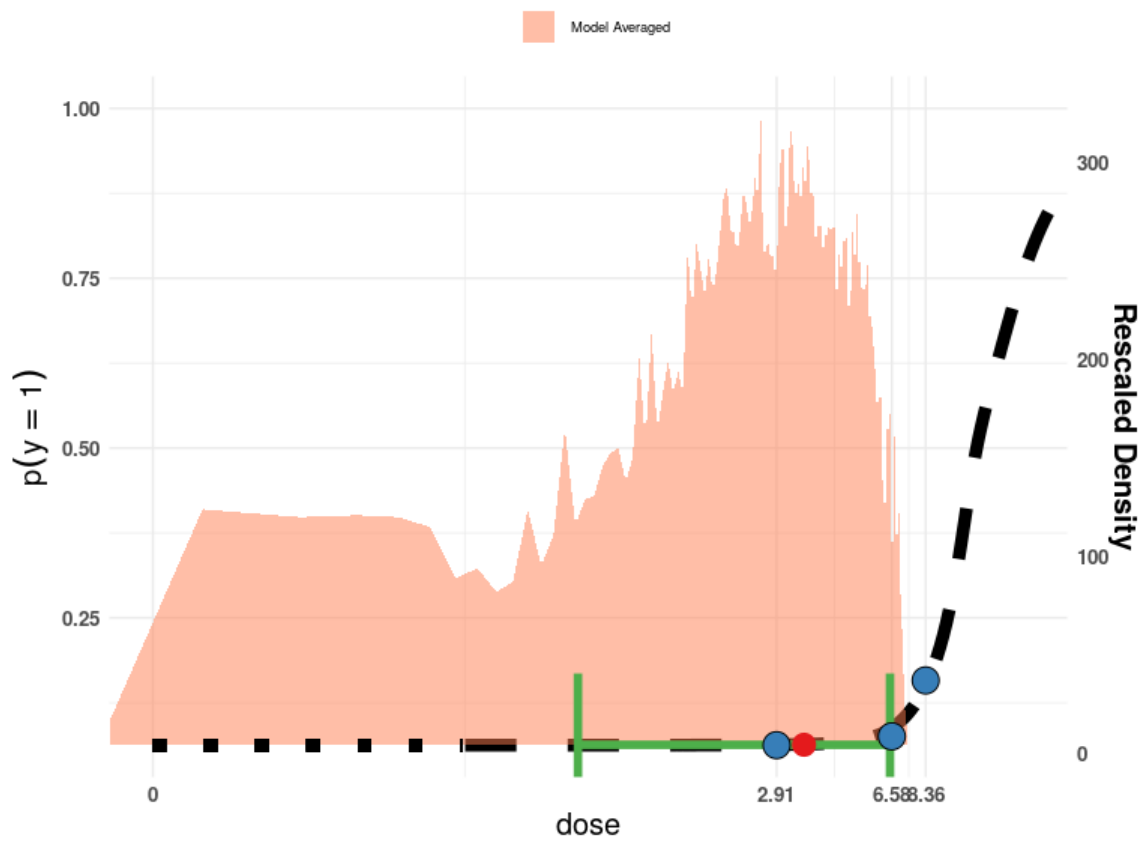
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.692	2.831	5.398	0.114	1
IE4_Q	2.053	4.923	6.882	0.228	1
H4_Q	0.659	2.857	5.320	0.114	1
LN4_Q	1.420	4.220	6.392	0.210	1
G4_Q	0.631	2.304	3.809	0.108	1
QE4_Q	0.070	0.182	0.469	0.015	1
P4_Q	0.770	3.562	6.795	0.118	0
L4_Q	0.641	2.893	5.160	0.093	1

Plots of Fitted Models







Moon et al. (2013) ischemic heart disease, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for ischemic heart disease

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	Person.years
0.089	207	12447
0.150	212	12136
0.250	187	11805
0.440	240	11075

The 'Value for CES' is set to 0.00016912.

Extended dose range is not applied.

Informative background prior: min: 0.01646421; the most likely; 0.01663051; max: 0.01679682. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 8.56e-03).

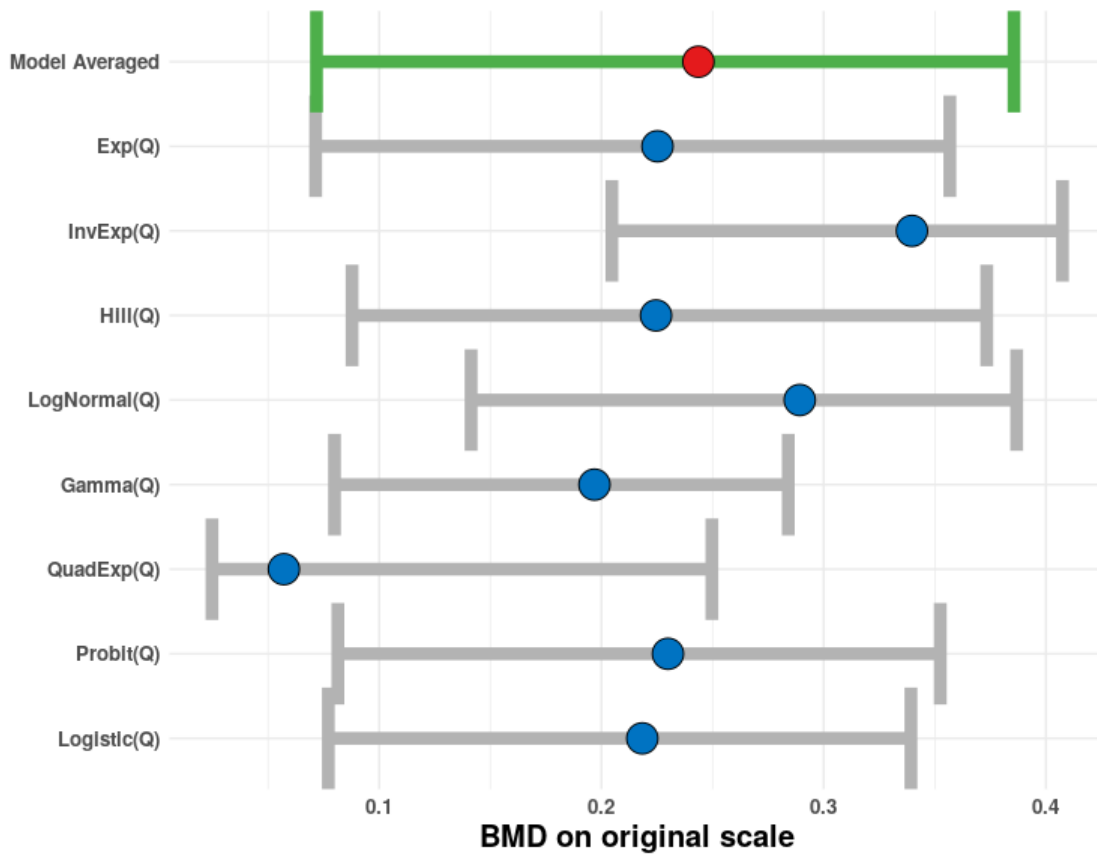
Model Averaged BMD

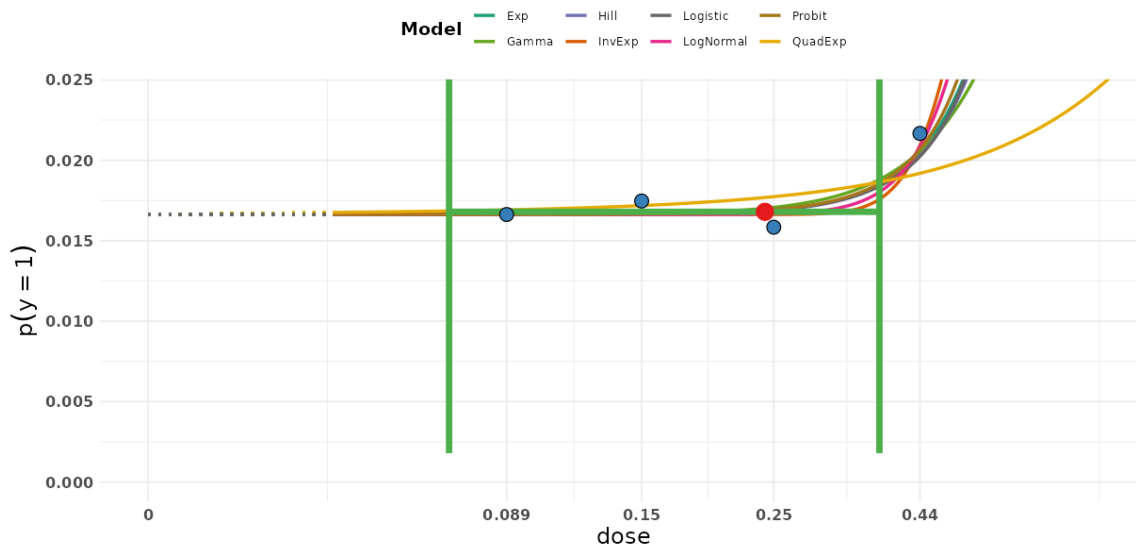
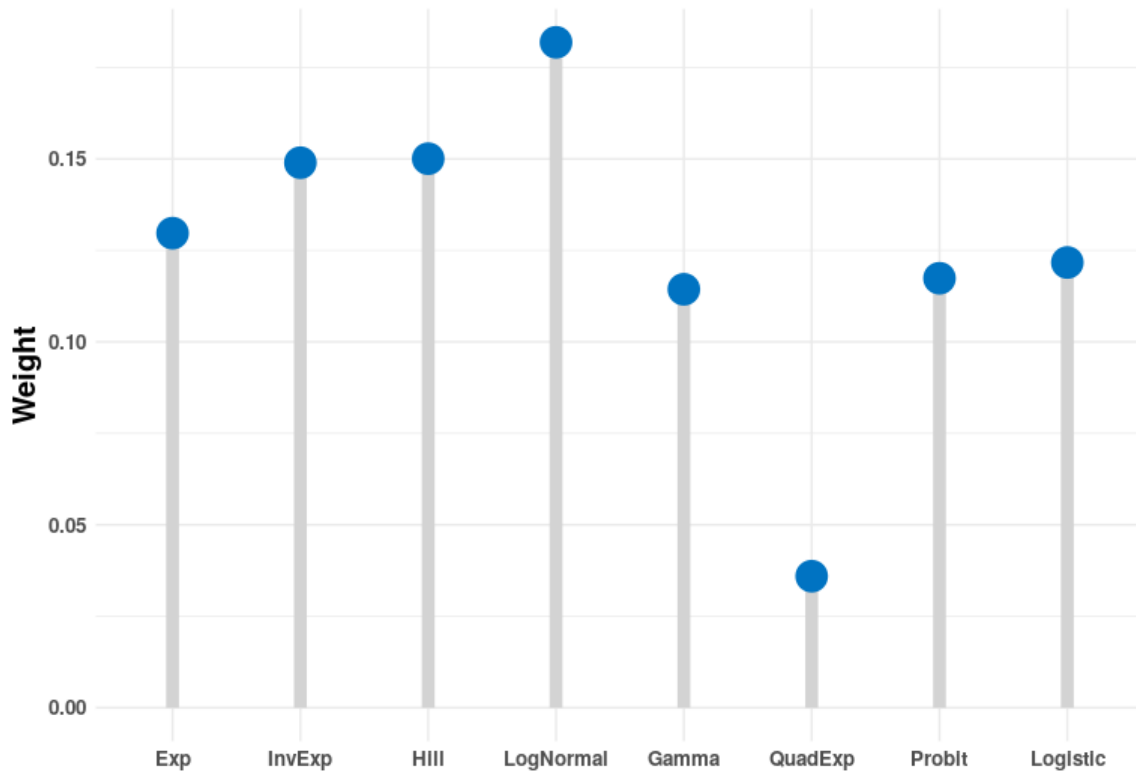
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.072	0.244	0.386

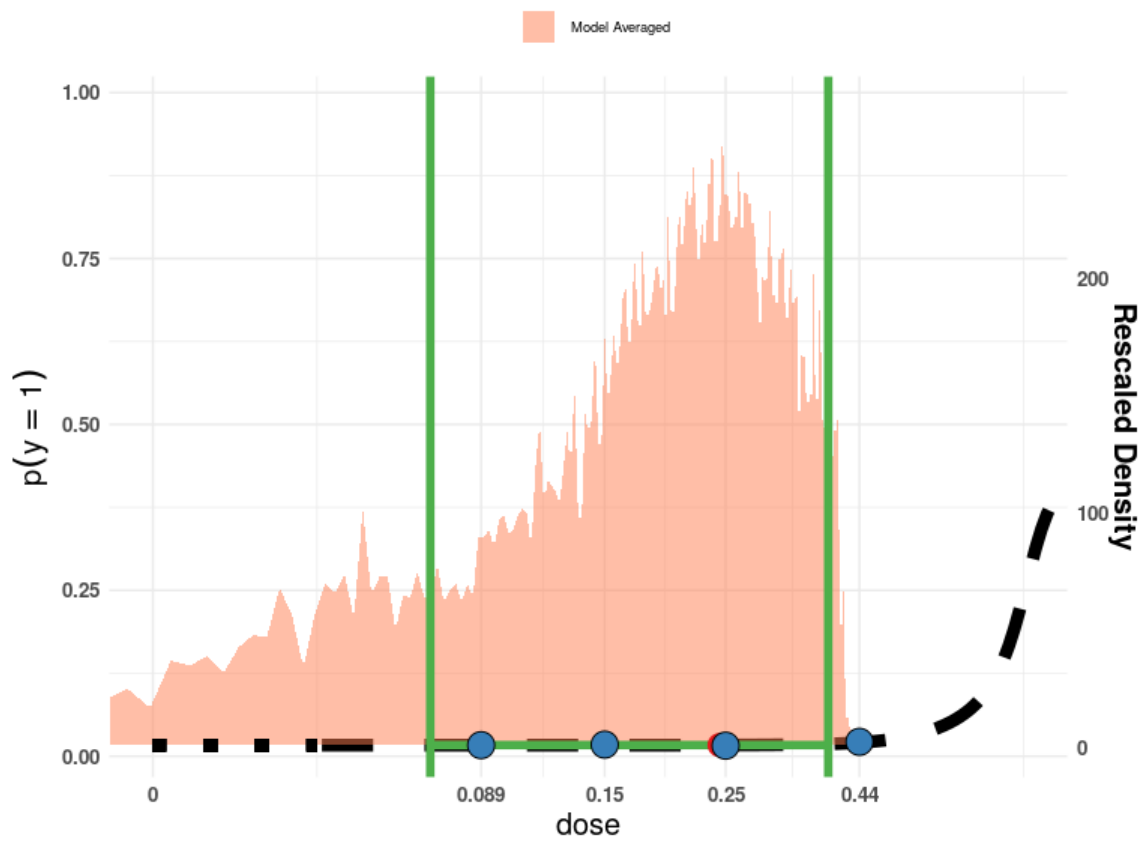
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.071	0.225	0.357	0.130	1
IE4_Q	0.205	0.340	0.407	0.149	1
H4_Q	0.088	0.225	0.373	0.150	1
LN4_Q	0.141	0.289	0.387	0.182	1
G4_Q	0.080	0.197	0.284	0.114	1
QE4_Q	0.025	0.057	0.250	0.036	1
P4_Q	0.081	0.230	0.352	0.117	1
L4_Q	0.077	0.218	0.339	0.122	1

Plots of Fitted Models







Parvez et al. (2013) FEV1 (lung function), BMR 1%

Data Description

The endpoint to be analyzed is: FEV1 response

Data used for analysis:

Dose	Response	SD	N
1.78	1574	522	312
5.31	1541	522	315
8.15	1494	525	315

The 'Value for CES' is set to 0.01.

Extended dose range is not applied.

Informative background prior: min: 1417; the most likely: 1574; max: 1731. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since none of the candidate models fit the data sufficiently well.

Check for constant variance coefficient of variation

Distributional assumption of constant variance is met, Bartlett test p-value is 0.9932

Distributional assumption of constant variance (on log-scale) is met, Bartlett test p-value is 0.6173

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 5.38e+01).

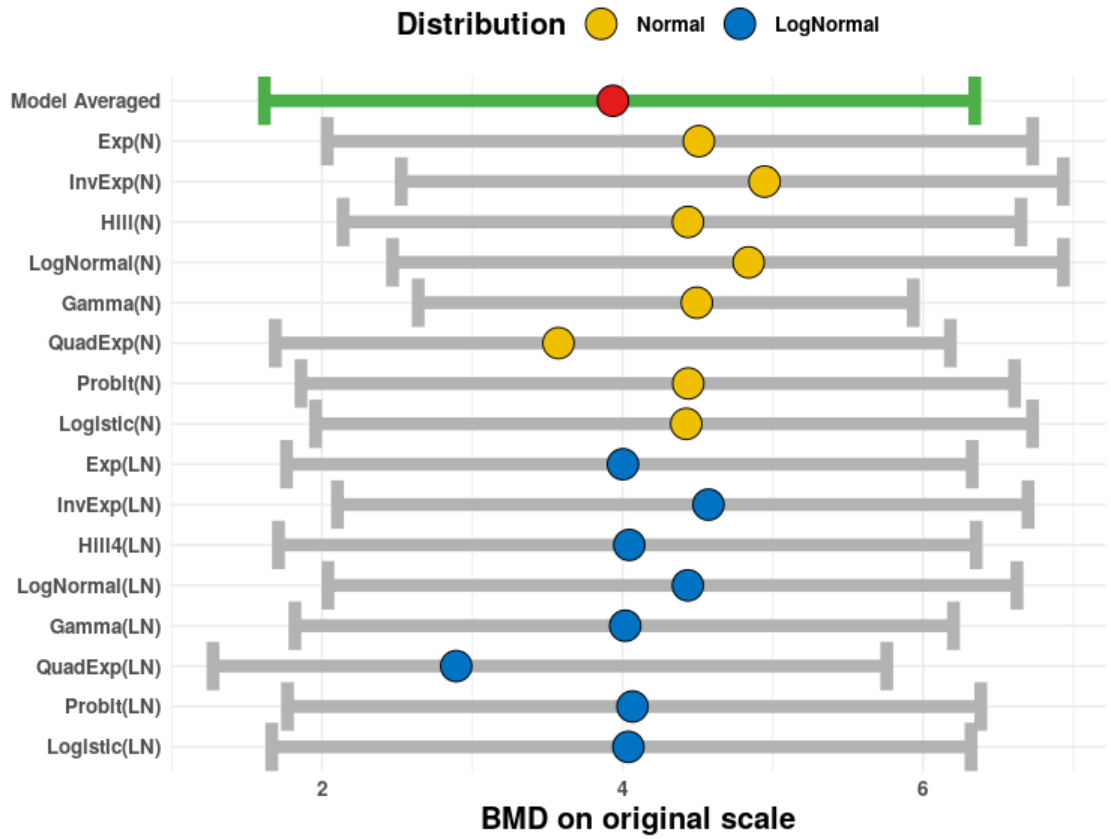
Model Averaged BMD

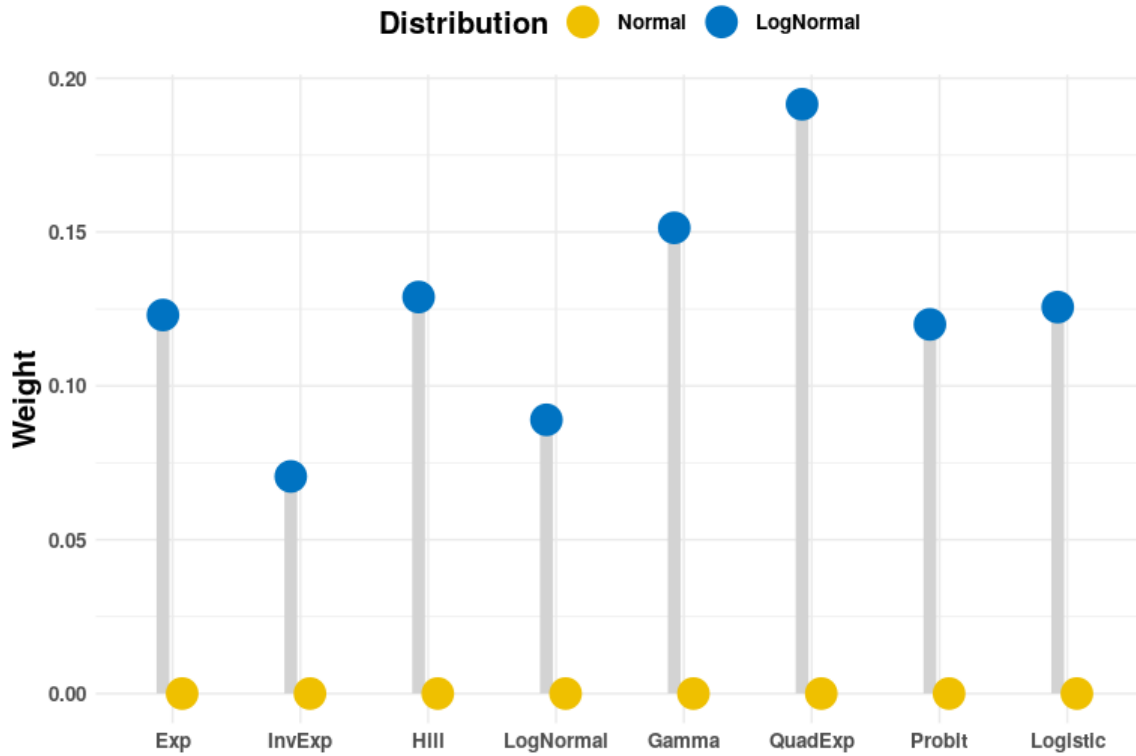
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	1.617	3.936	6.344

Estimated BMDs per model

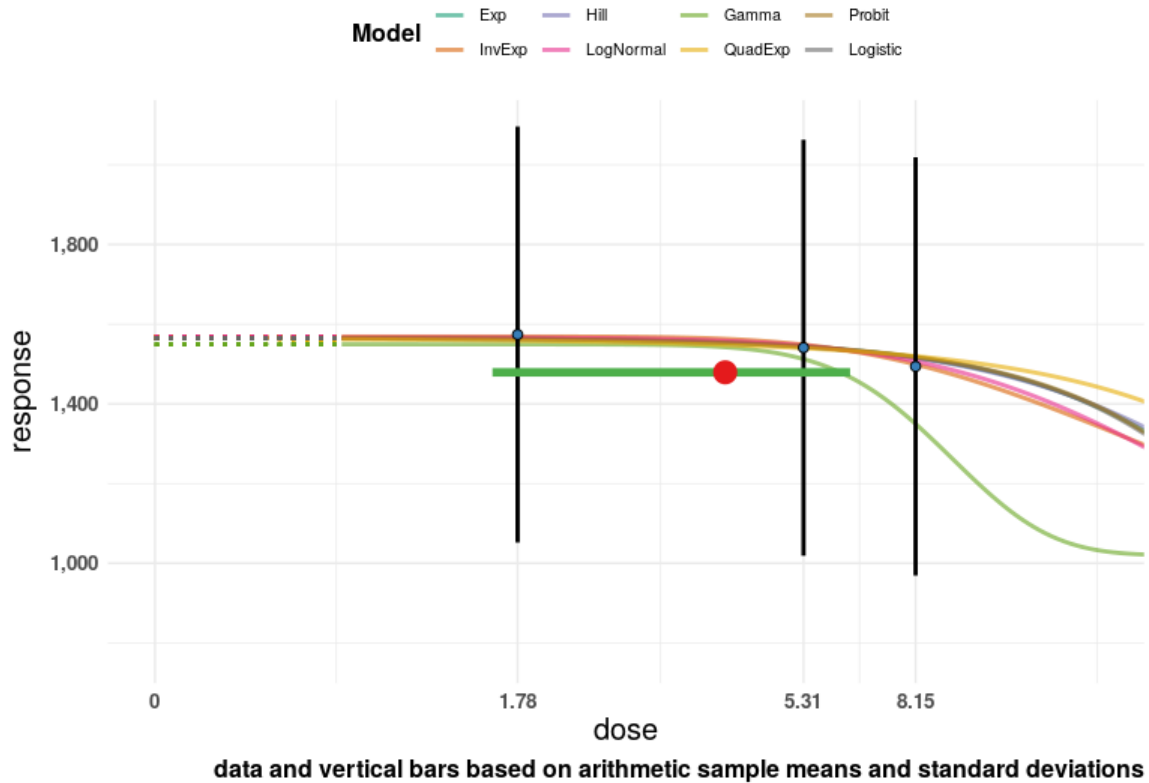
Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_N	2.035	4.508	6.729	0.000	1
IE4_N	2.528	4.945	6.933	0.000	1
H4_N	2.141	4.435	6.651	0.000	1
LN4_N	2.470	4.839	6.934	0.000	1
G4_N	2.641	4.494	5.934	0.000	0
QE4_N	1.690	3.574	6.181	0.000	1
P4_N	1.860	4.437	6.608	0.000	1
L4_N	1.957	4.424	6.728	0.000	1
E4_LN	1.765	4.002	6.327	0.123	1
IE4_LN	2.103	4.571	6.698	0.071	1
H4_LN	1.711	4.045	6.353	0.129	1
LN4_LN	2.040	4.435	6.624	0.089	1
G4_LN	1.820	4.017	6.202	0.151	1
QE4_LN	1.275	2.893	5.758	0.192	1
P4_LN	1.771	4.066	6.384	0.120	1
L4_LN	1.666	4.039	6.319	0.126	1

Plots of Fitted Models

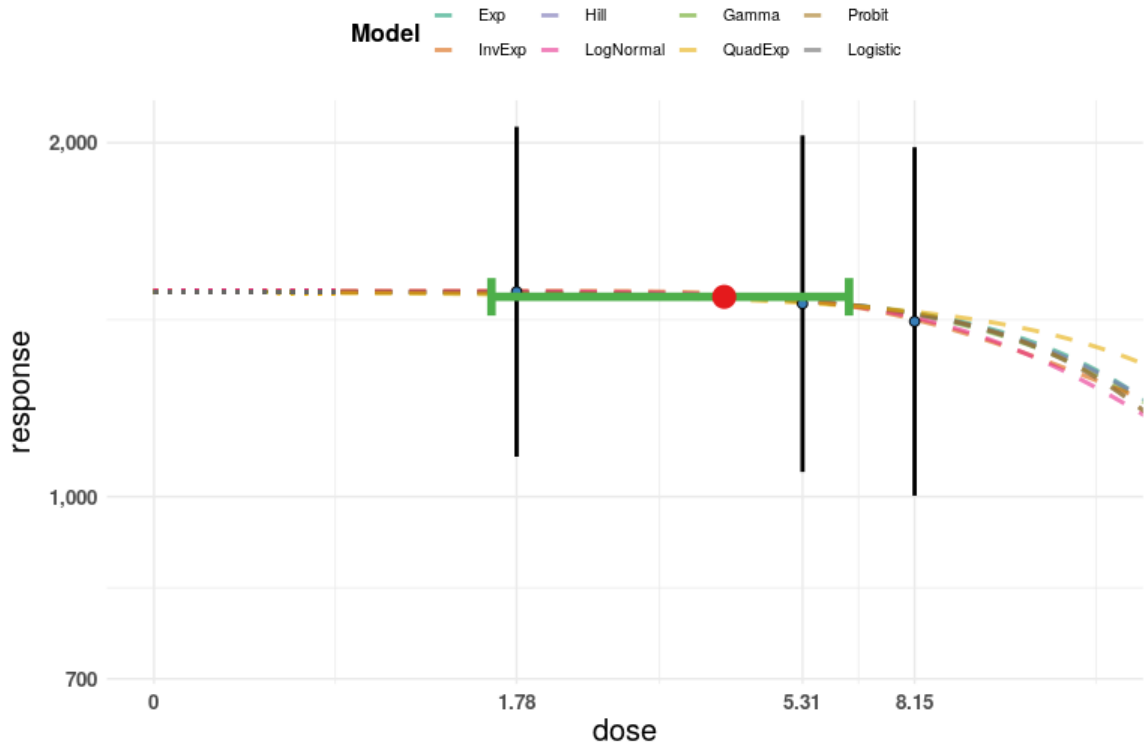




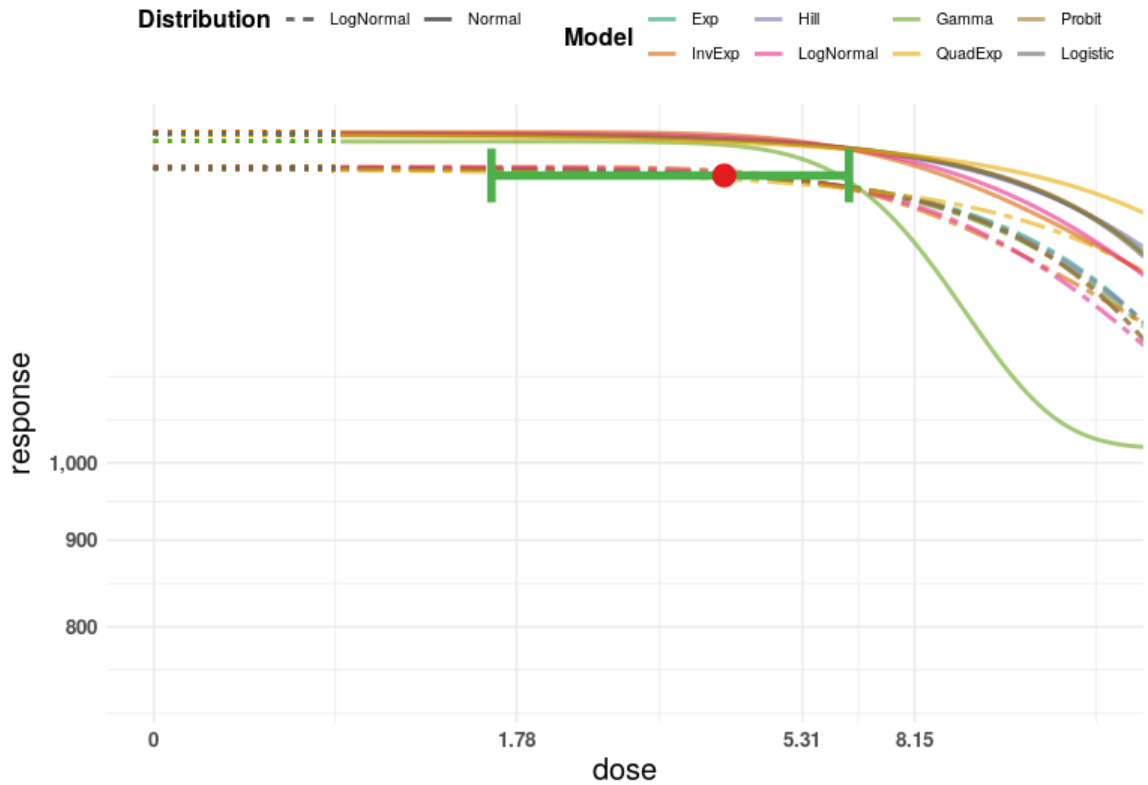
Normal distribution

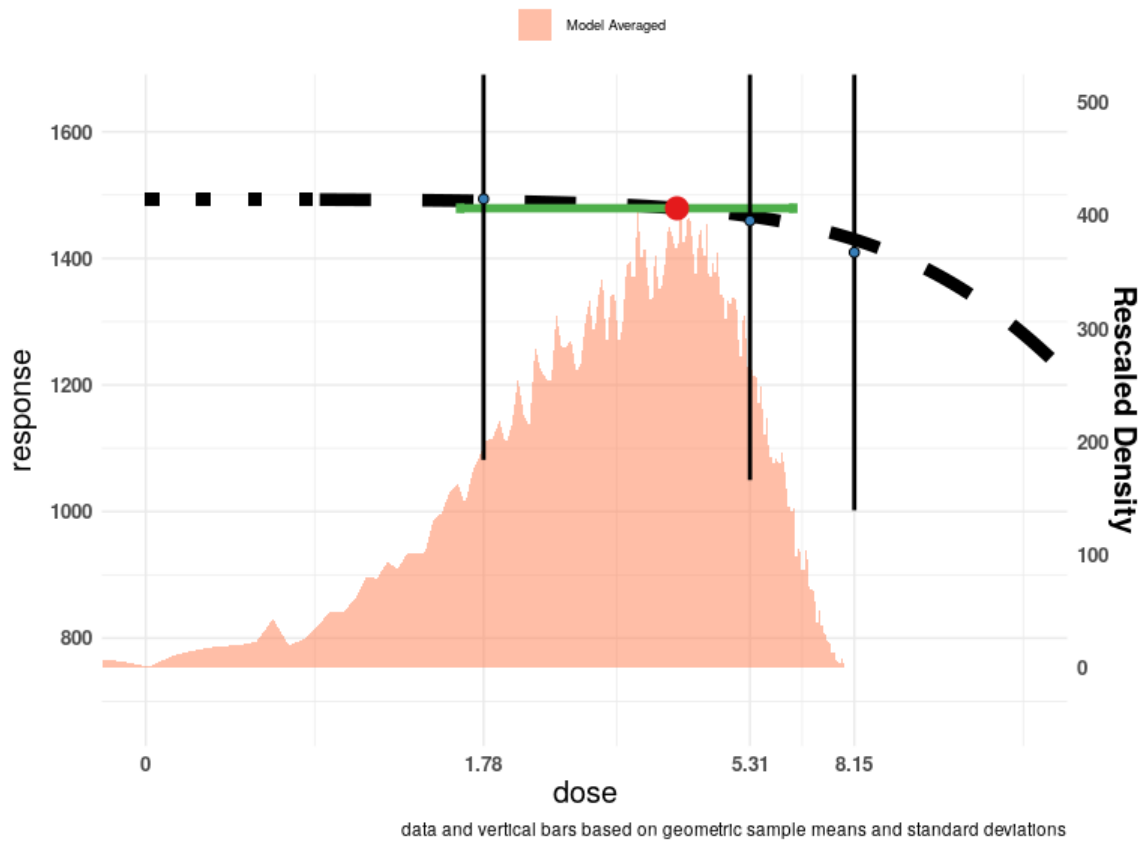


LogNormal distribution



data and vertical bars based on geometric sample means and standard deviations





Parvez et al. (2013) FVC (lung function), BMR 1%

Data Description

The endpoint to be analyzed is: FVC response

Data used for analysis:

Dose	Response	SD	N
1.78	2268	538	312
5.31	2254	539	315
8.15	2170	541	315

The 'Value for CES' is set to 0.01.

Extended dose range is not applied.

Informative background prior: min: 2041; the most likely: 2268; max: 2495. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since none of the candidate models fit the data sufficiently well.

Check for constant variance coefficient of variation

Distributional assumption of constant variance is met, Bartlett test p-value is 0.995

Distributional assumption of constant variance (on log-scale) is met, Bartlett test p-value is 0.6541

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 7.57e+01).

Model Averaged BMD

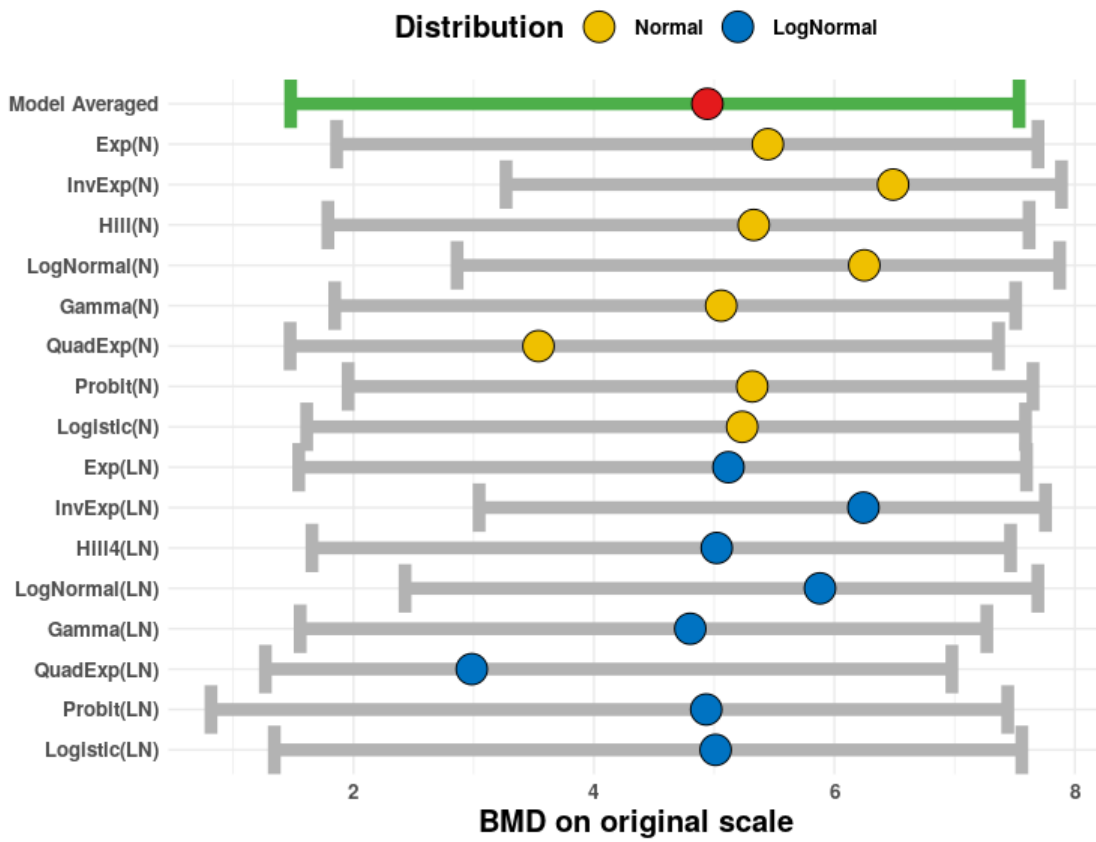
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	1.478	4.943	7.536

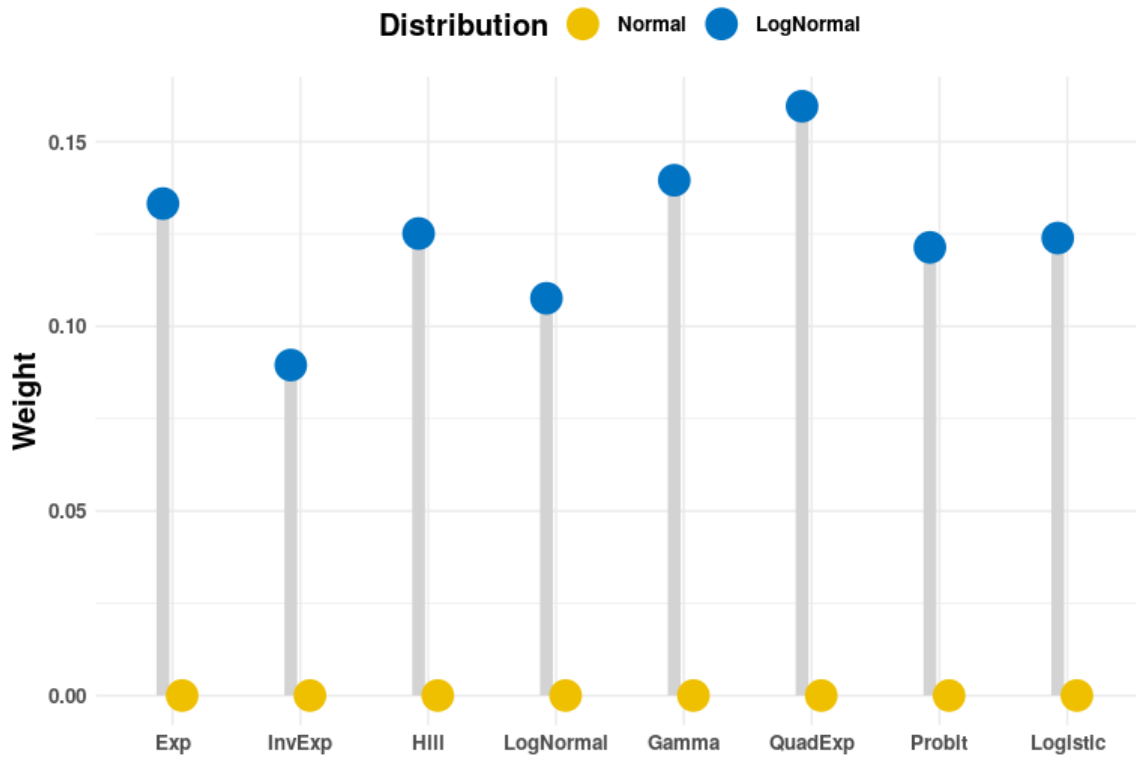
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_N	1.860	5.446	7.693	0.000	1
IE4_N	3.269	6.488	7.889	0.000	1
H4_N	1.788	5.329	7.620	0.000	1
LN4_N	2.862	6.249	7.873	0.000	1
G4_N	1.844	5.058	7.508	0.000	1
QE4_N	1.473	3.539	7.365	0.000	1
P4_N	1.956	5.316	7.652	0.000	1

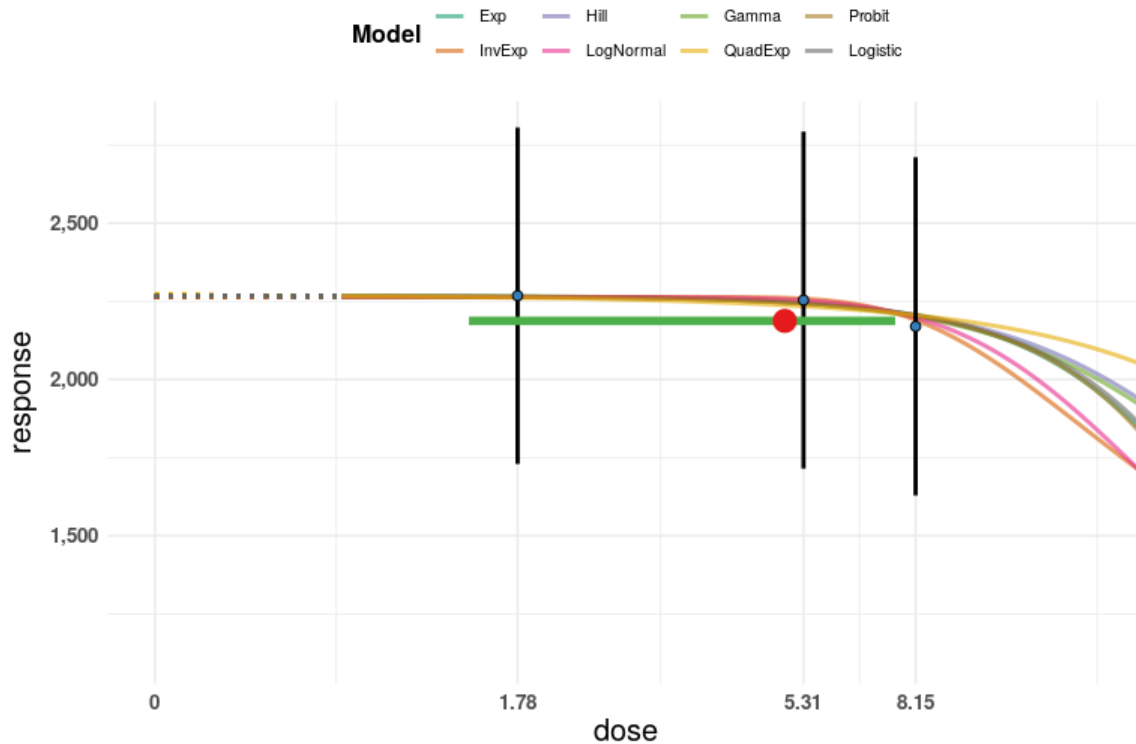
L4_N	1.611	5.233	7.589	0.000	1
E4_LN	1.545	5.119	7.598	0.133	0
IE4_LN	3.045	6.241	7.756	0.090	1
H4_LN	1.655	5.021	7.465	0.125	1
LN4_LN	2.429	5.880	7.692	0.108	1
G4_LN	1.557	4.801	7.268	0.140	1
QE4_LN	1.267	2.984	6.977	0.160	1
P4_LN	0.815	4.934	7.442	0.121	0
L4_LN	1.341	5.012	7.559	0.124	1

Plots of Fitted Models

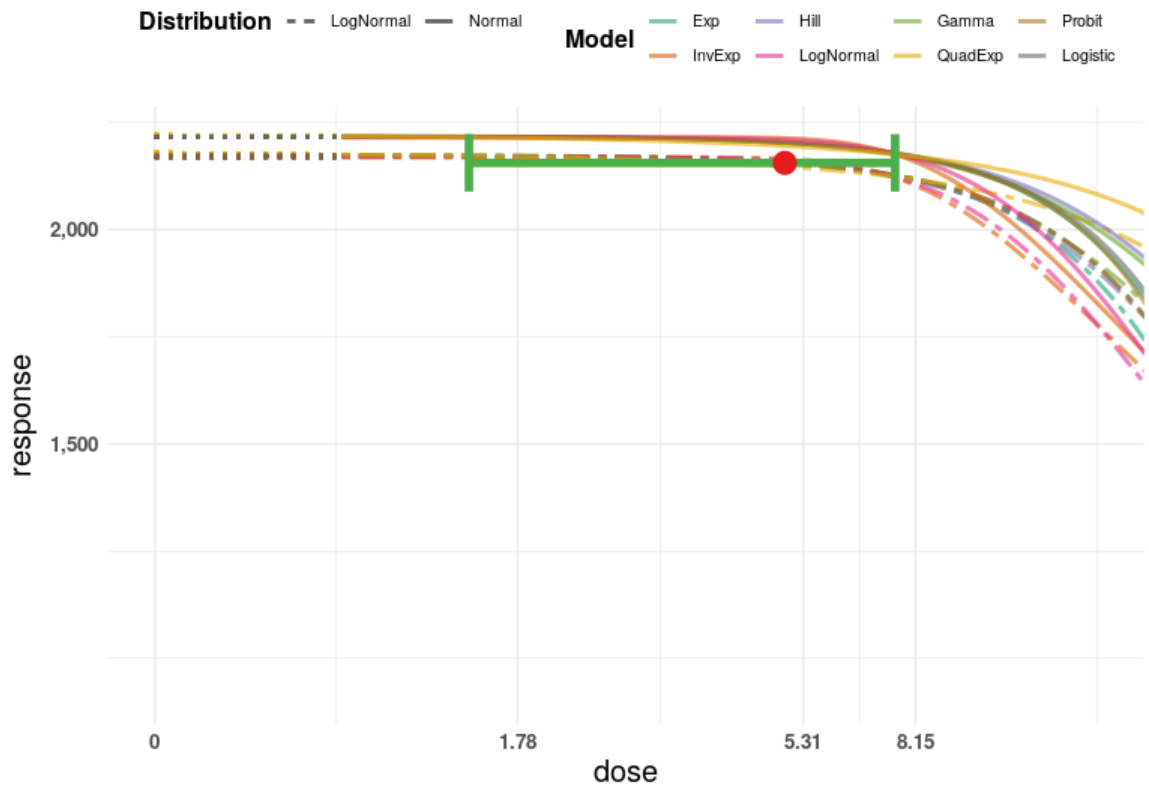
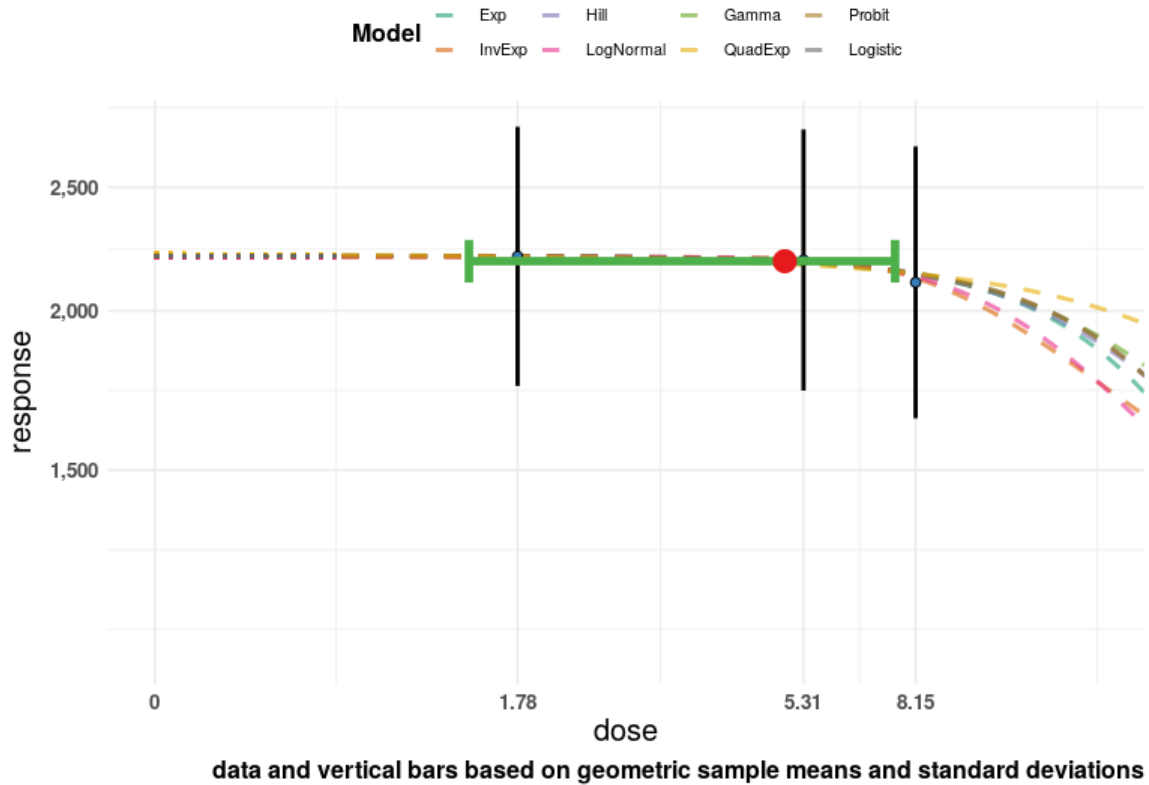


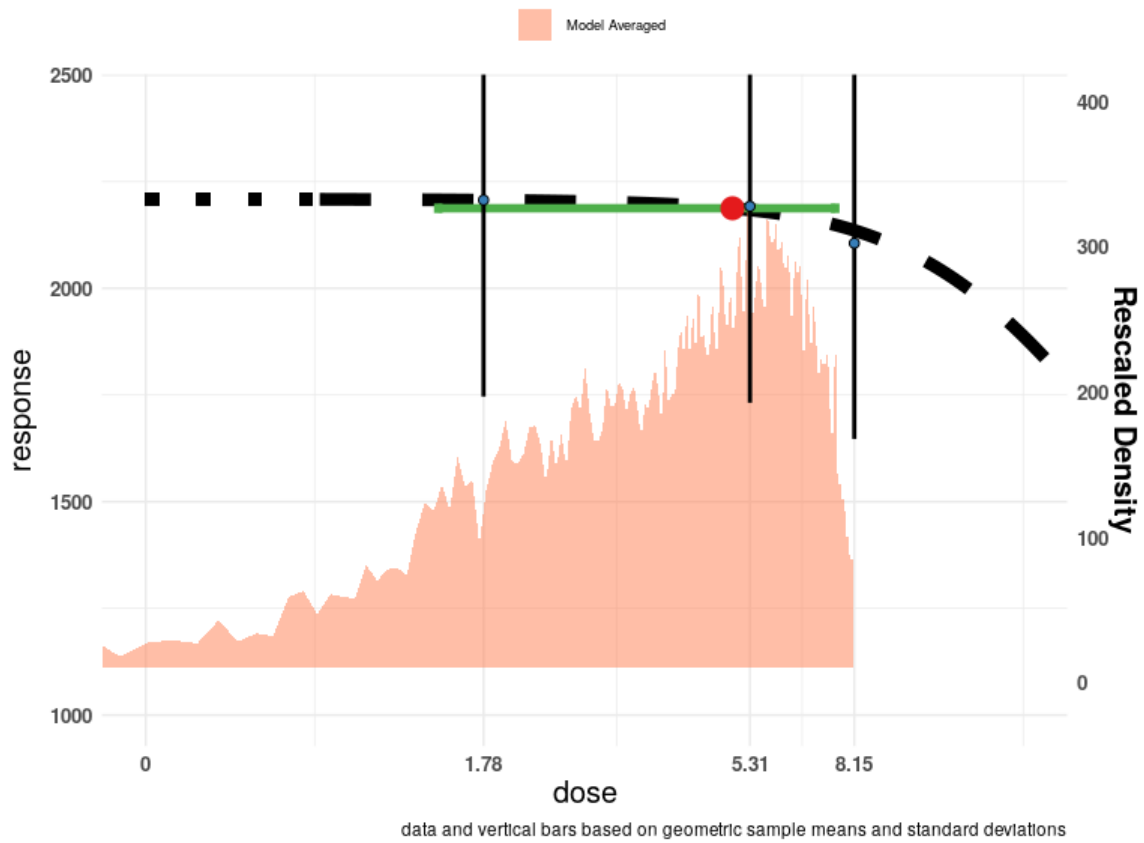


Normal distribution



LogNormal distribution





Pierce et al. (2011) skin lesions, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for skin lesions

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.46	117	2358
3.28	123	2118
6.55	145	1726
12.00	314	2855
15.64	115	617

The 'Value for CES' is set to 0.00052209.

Extended dose range is not applied.

Informative background prior: min: 0.04912214; the most likely; 0.04961832; max: 0.05011450. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 6.21e-03).

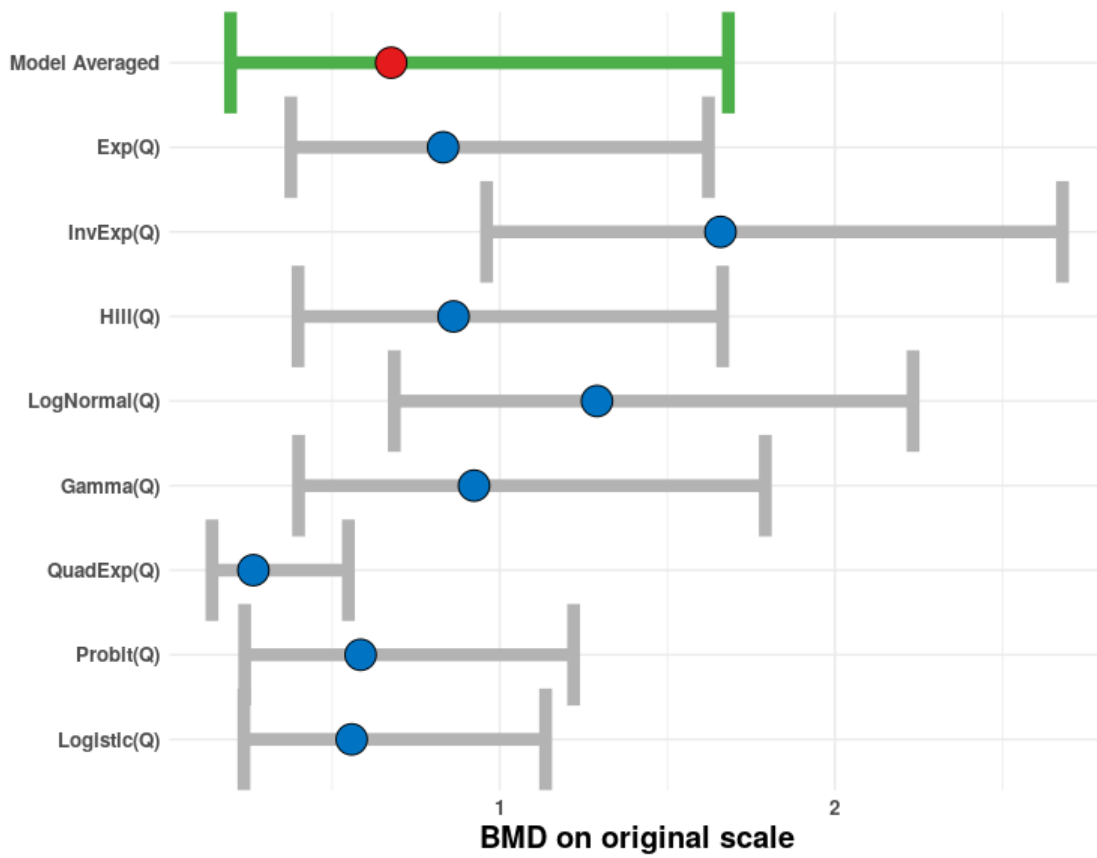
Model Averaged BMD

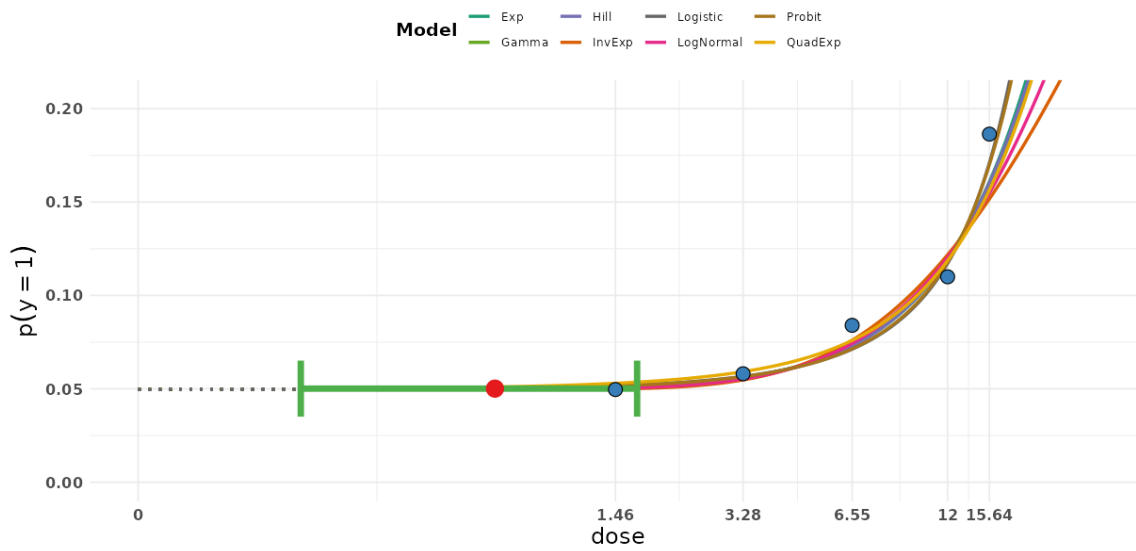
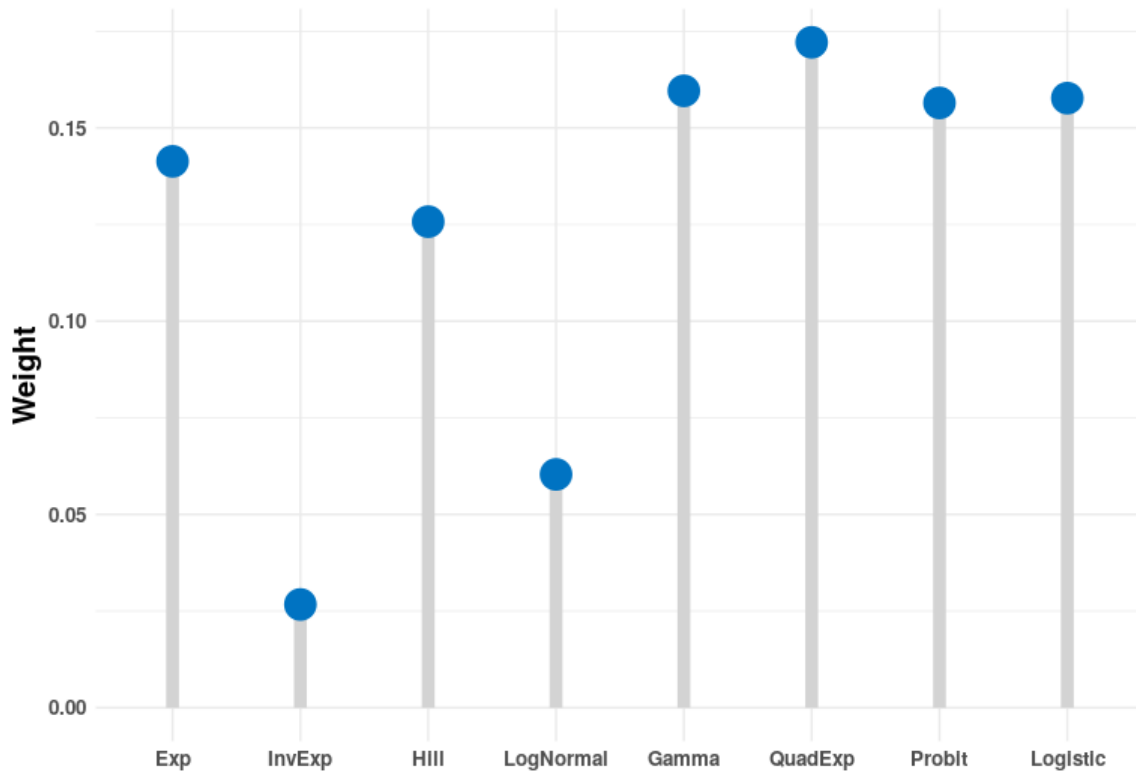
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.196	0.676	1.682

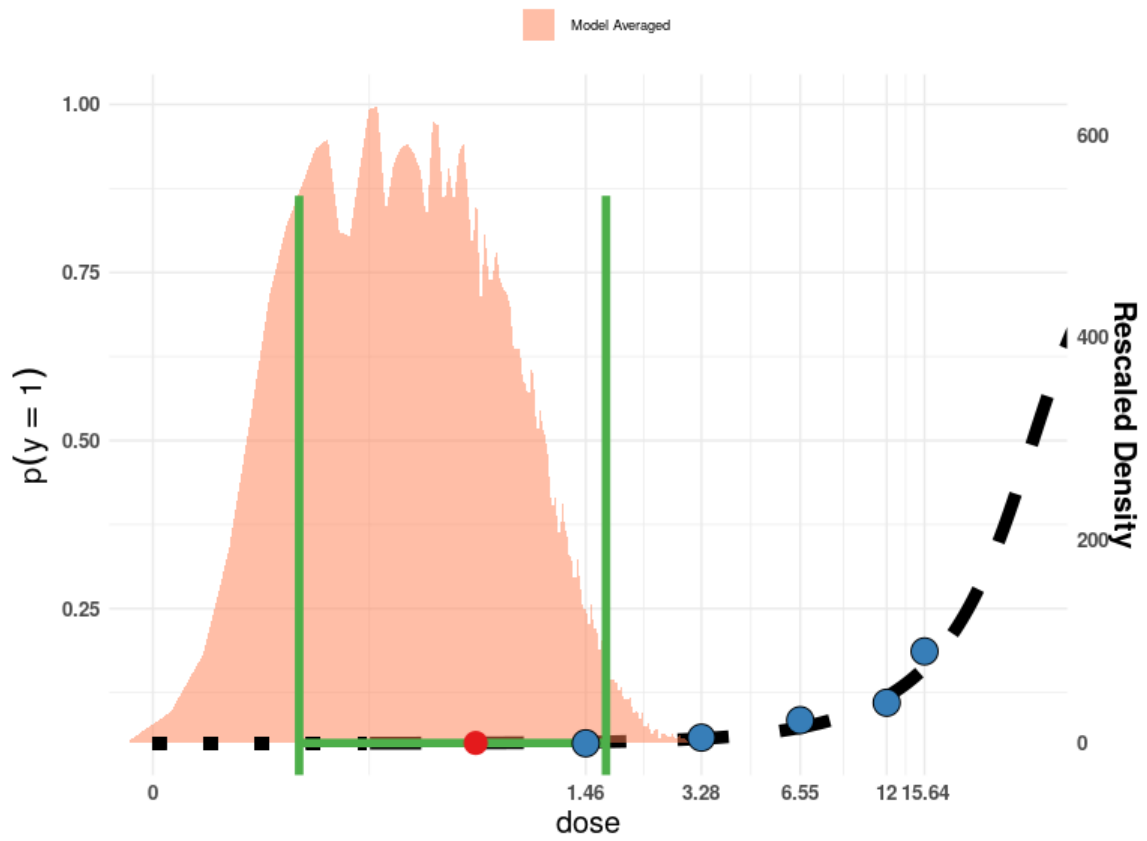
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.376	0.831	1.623	0.141	1
IE4_Q	0.961	1.658	2.679	0.027	1
H4_Q	0.398	0.862	1.665	0.126	1
LN4_Q	0.685	1.290	2.233	0.060	1
G4_Q	0.399	0.923	1.792	0.160	1
QE4_Q	0.141	0.265	0.548	0.172	1
P4_Q	0.239	0.585	1.220	0.156	1
L4_Q	0.236	0.558	1.137	0.158	1

Plots of Fitted Models







Powers et al. (2019) airflow obstruction, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for airflow obstruction

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.073	174	757
0.220	160	636
0.280	124	432

The 'Value for CES' is set to 0.00298456.

Extended dose range is not applied.

Informative background prior: min: 0.22755614; the most likely; 0.22985469; max: 0.23215324. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.19e+00).

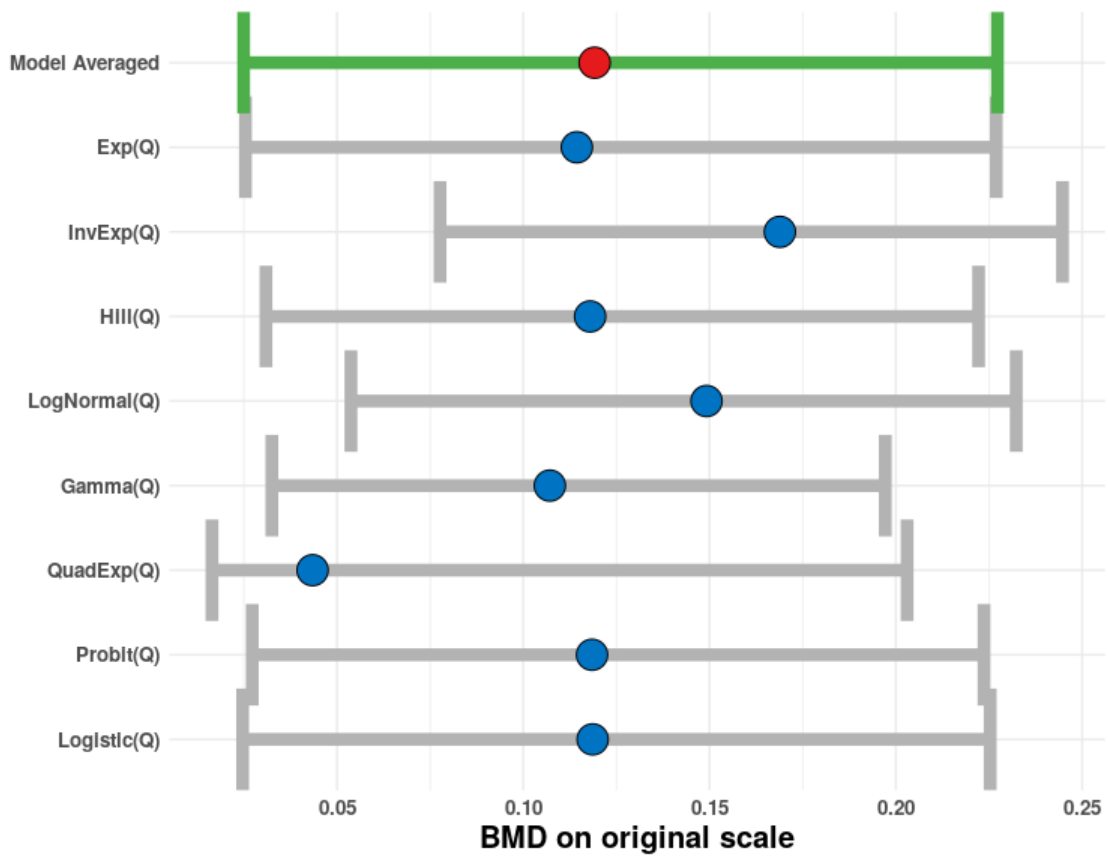
Model Averaged BMD

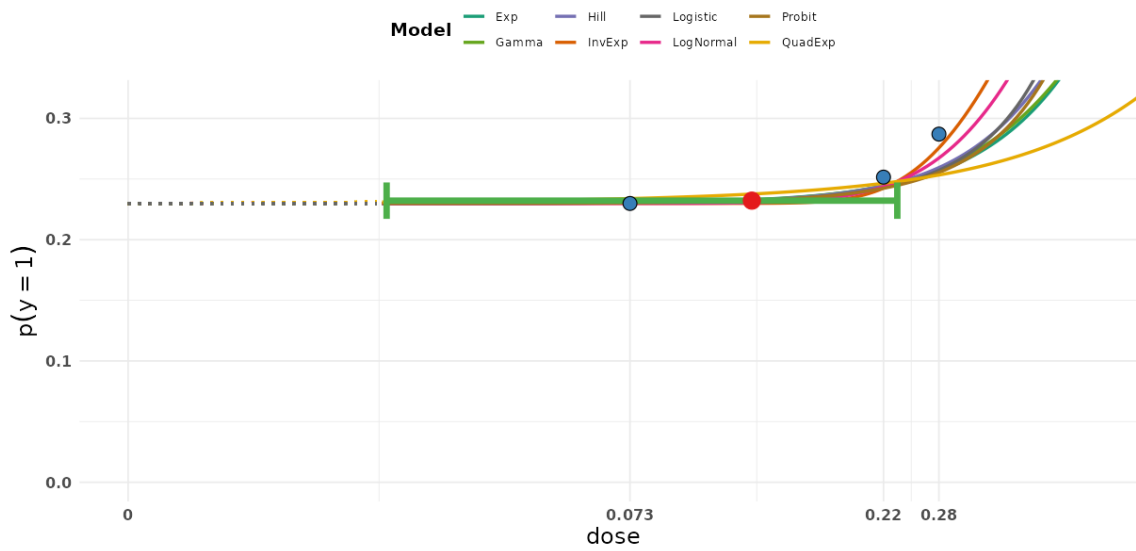
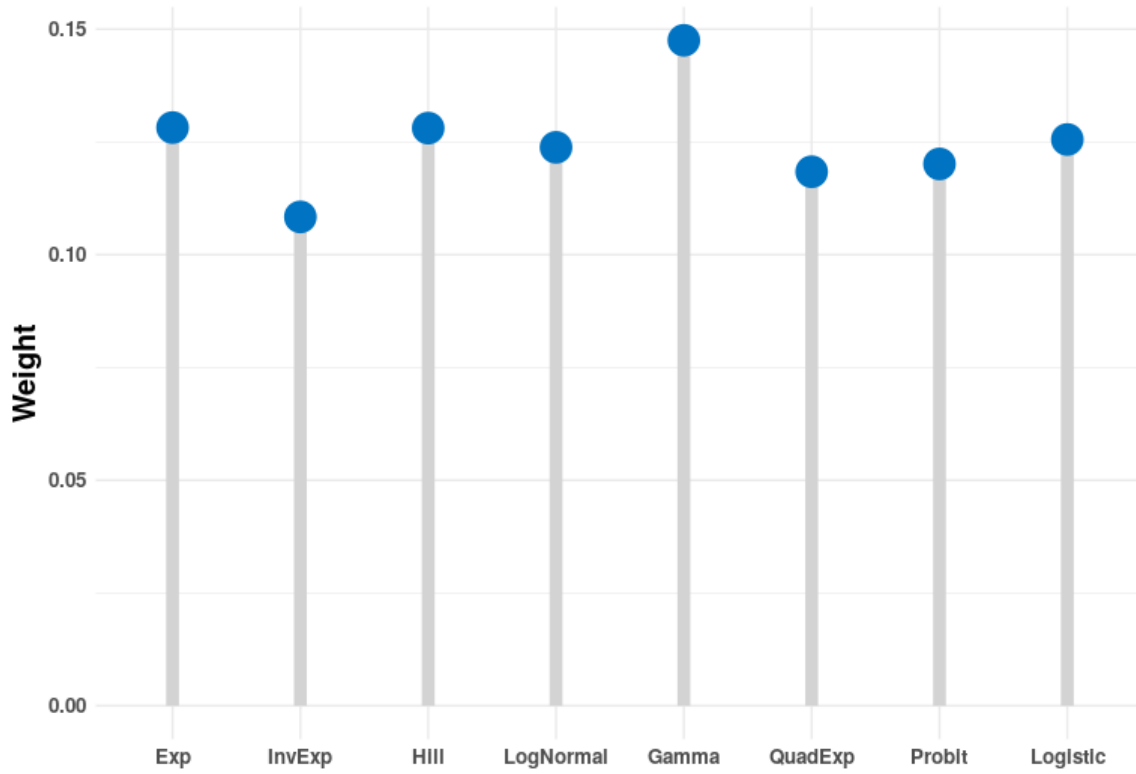
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.025	0.119	0.227

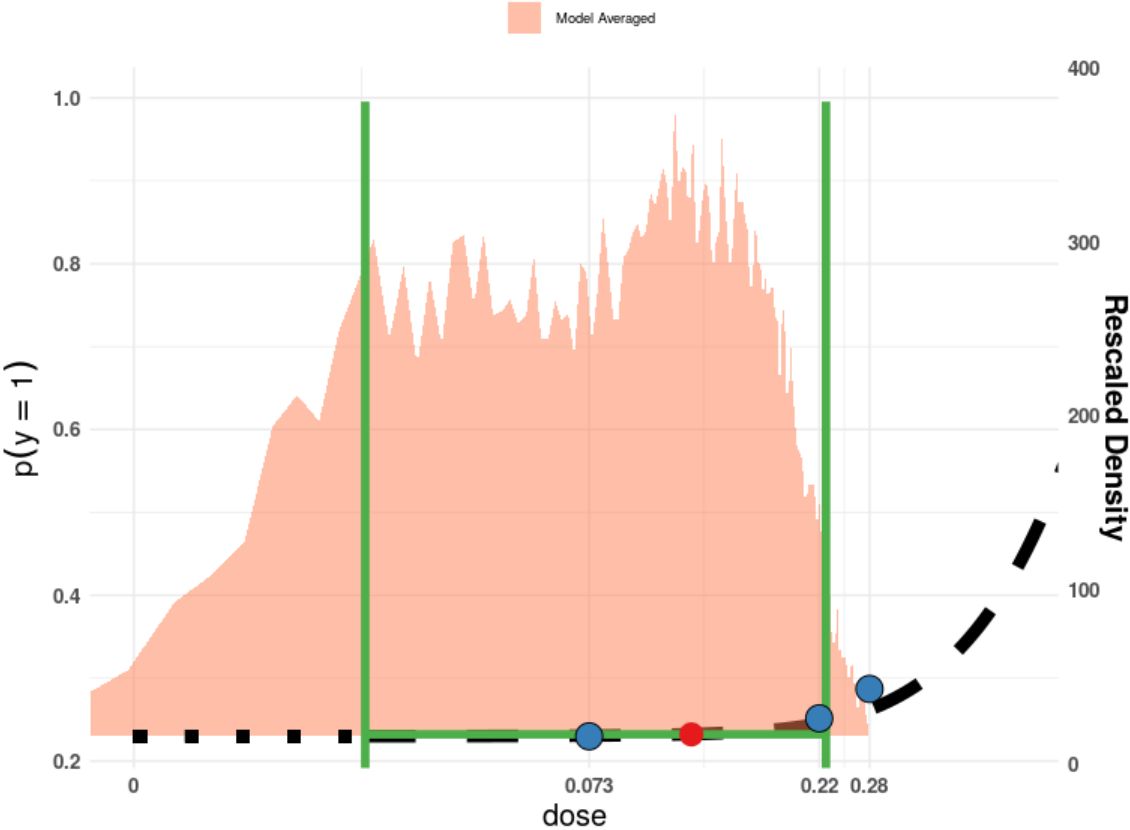
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.025	0.114	0.227	0.128	1
IE4_Q	0.078	0.169	0.245	0.108	1
H4_Q	0.031	0.118	0.222	0.128	1
LN4_Q	0.054	0.149	0.232	0.124	1
G4_Q	0.033	0.107	0.197	0.148	0
QE4_Q	0.016	0.043	0.203	0.118	1
P4_Q	0.027	0.118	0.224	0.120	1
L4_Q	0.025	0.119	0.225	0.126	1

Plots of Fitted Models







Powers et al. (2019) emphysema, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for emphysema

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.073	26	880
0.220	25	718
0.280	27	518

The 'Value for CES' is set to 0.00030445.

Extended dose range is not applied.

Informative background prior: min: 0.02925000; the most likely: 0.02954545; max: 0.02984091. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.04e+00).

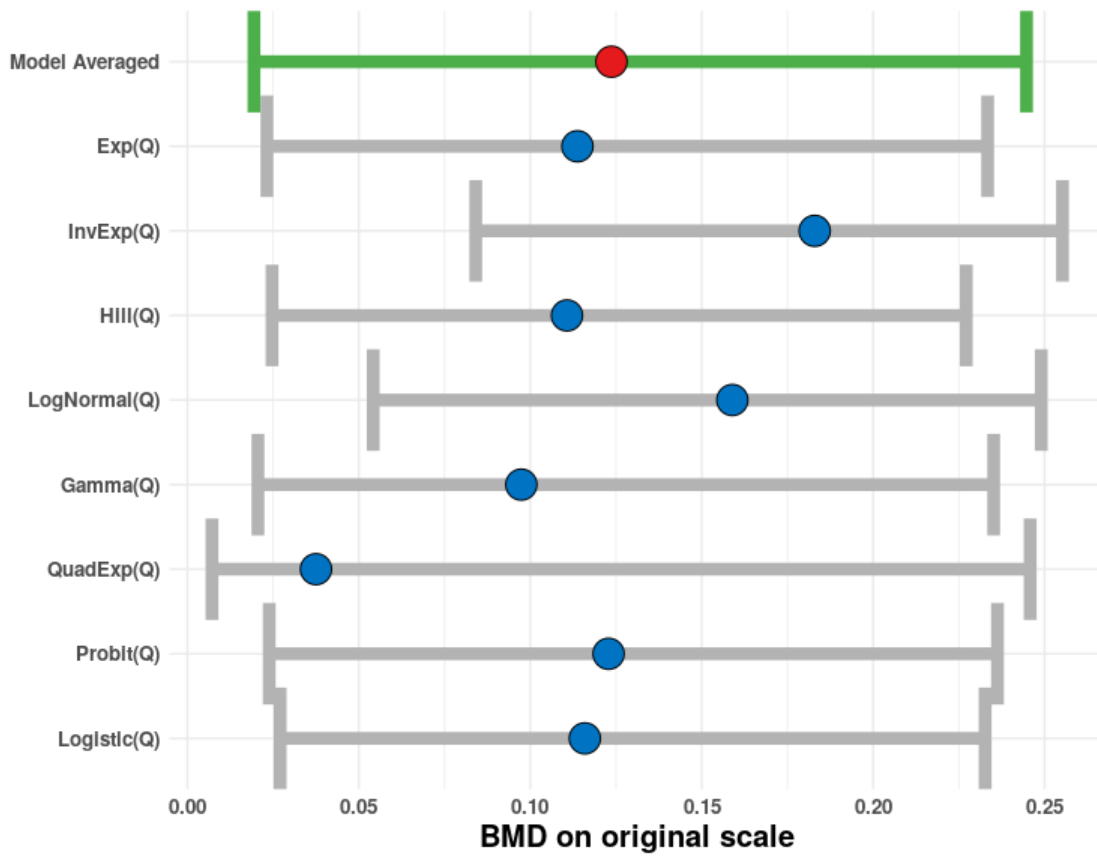
Model Averaged BMD

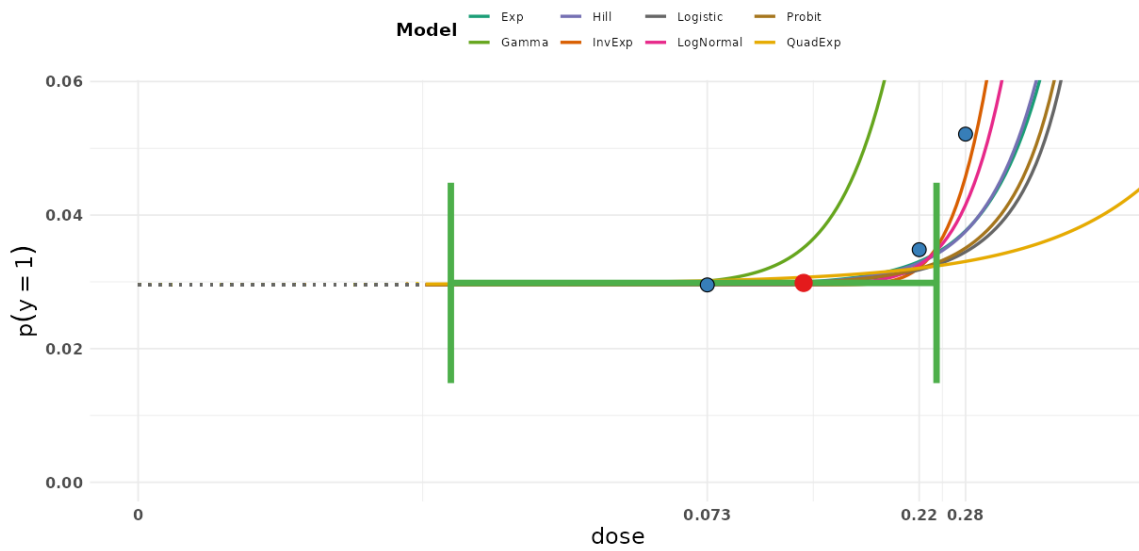
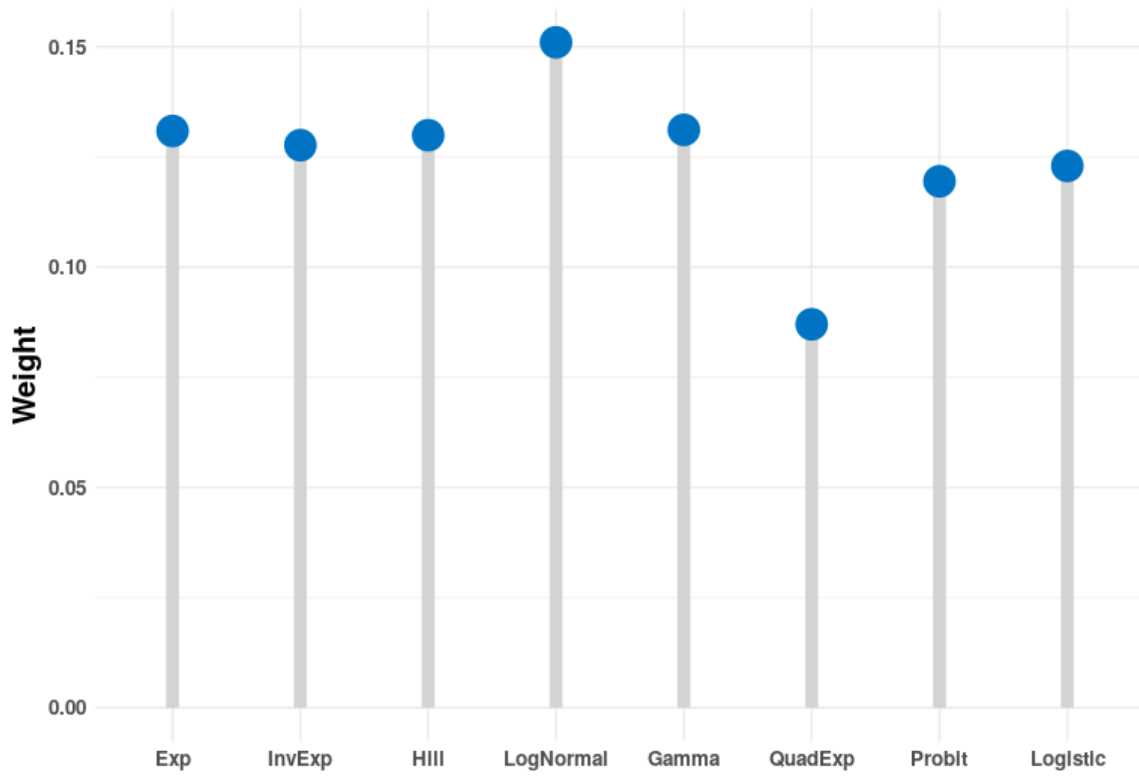
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.019	0.124	0.245

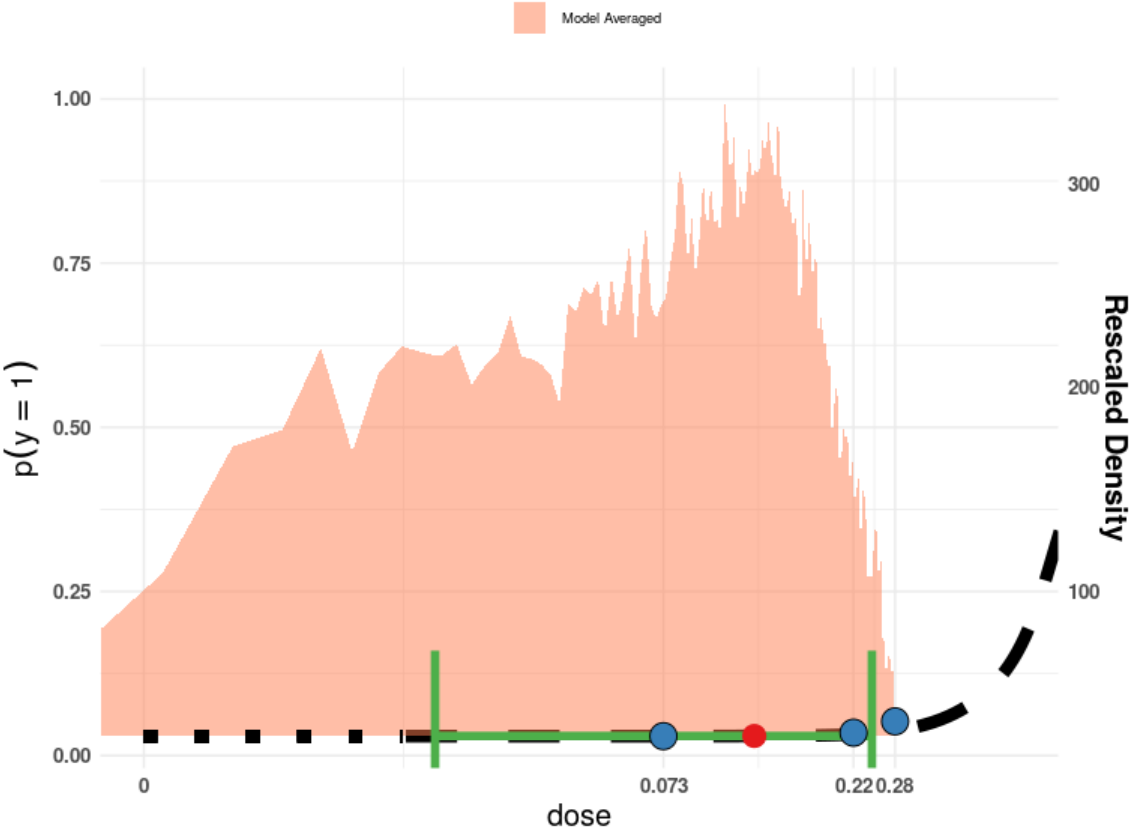
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.023	0.114	0.233	0.131	1
IE4_Q	0.084	0.183	0.255	0.128	1
H4_Q	0.025	0.111	0.227	0.130	1
LN4_Q	0.054	0.159	0.249	0.151	1
G4_Q	0.021	0.097	0.235	0.131	1
QE4_Q	0.007	0.037	0.246	0.087	1
P4_Q	0.024	0.123	0.236	0.119	1
L4_Q	0.027	0.116	0.233	0.123	1

Plots of Fitted Models







Powers et al. (2019) restrictive pattern, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for restrictive pattern

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.073	133	725
0.220	92	558
0.280	81	391

The 'Value for CES' is set to 0.00224662.

Extended dose range is not applied.

Informative background prior: min: 0.18161379; the most likely: 0.18344828; max: 0.18528276. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 3.89e+00).

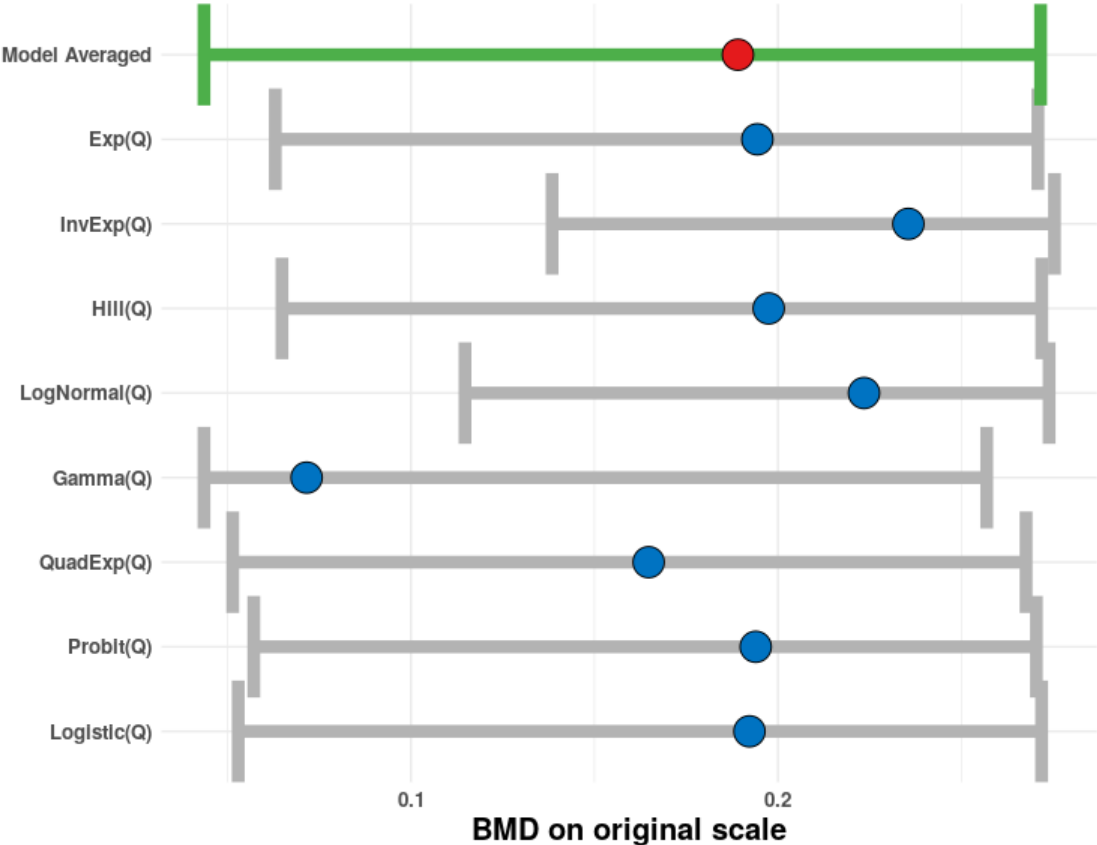
Model Averaged BMD

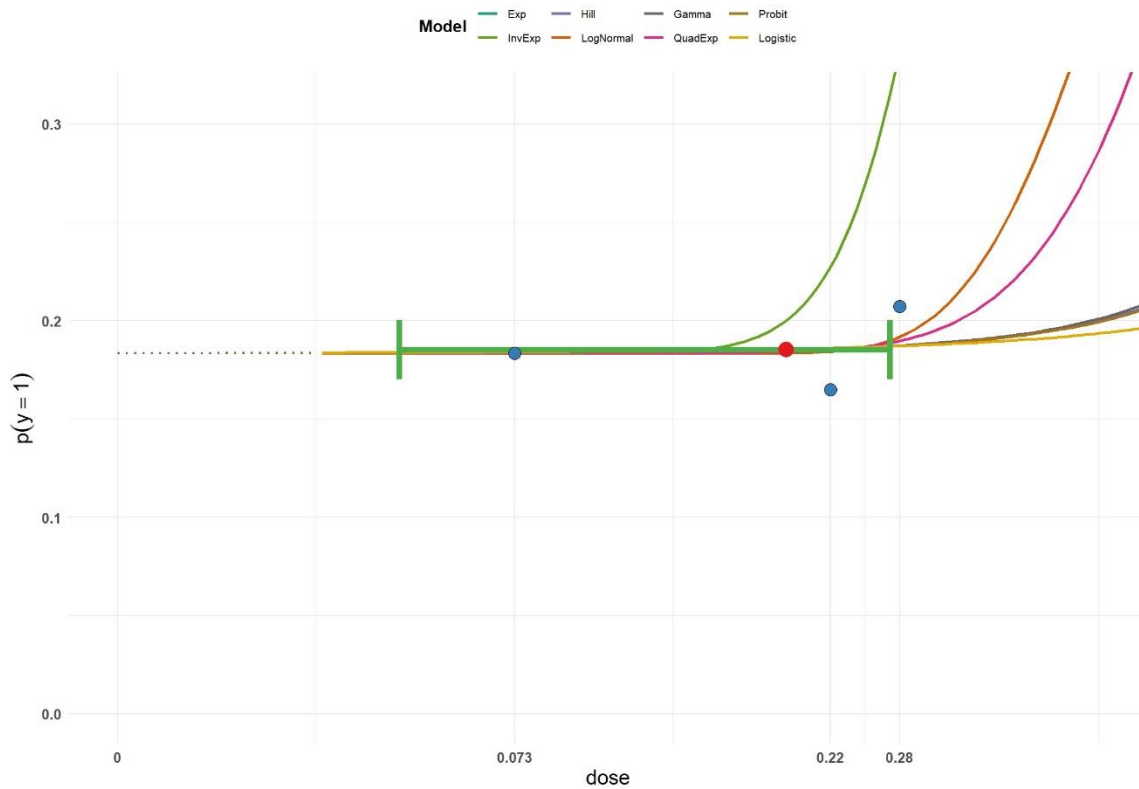
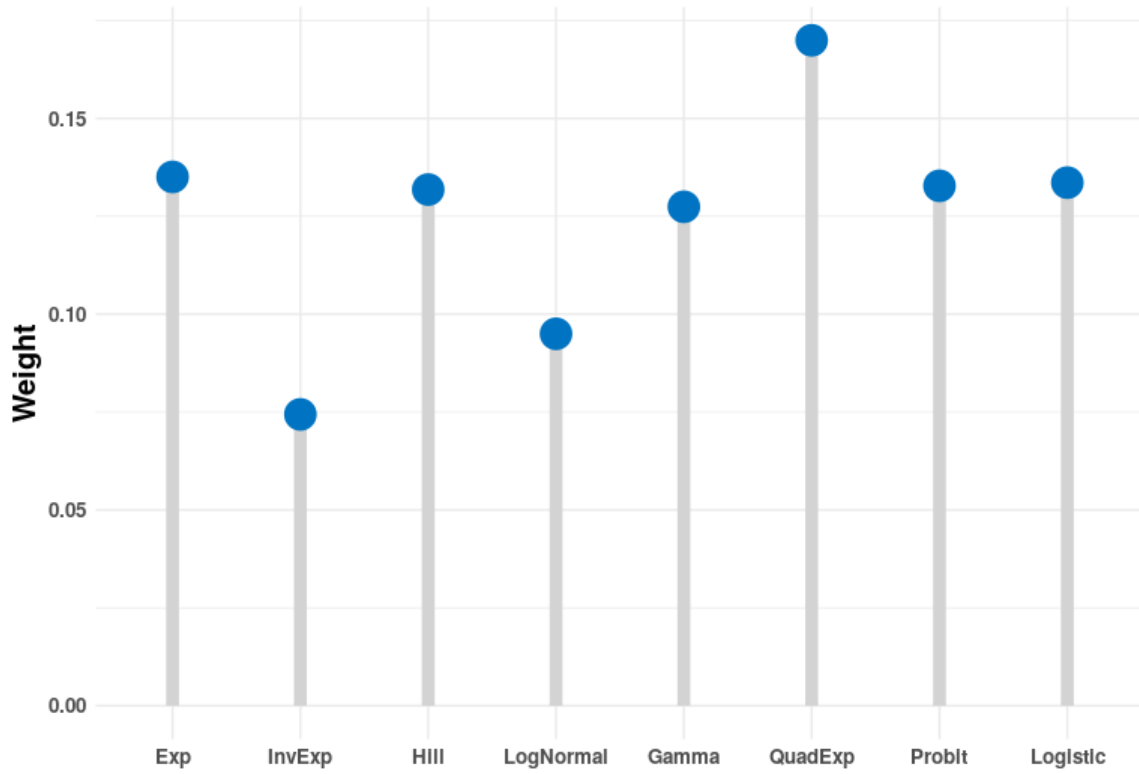
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.044	0.189	0.272

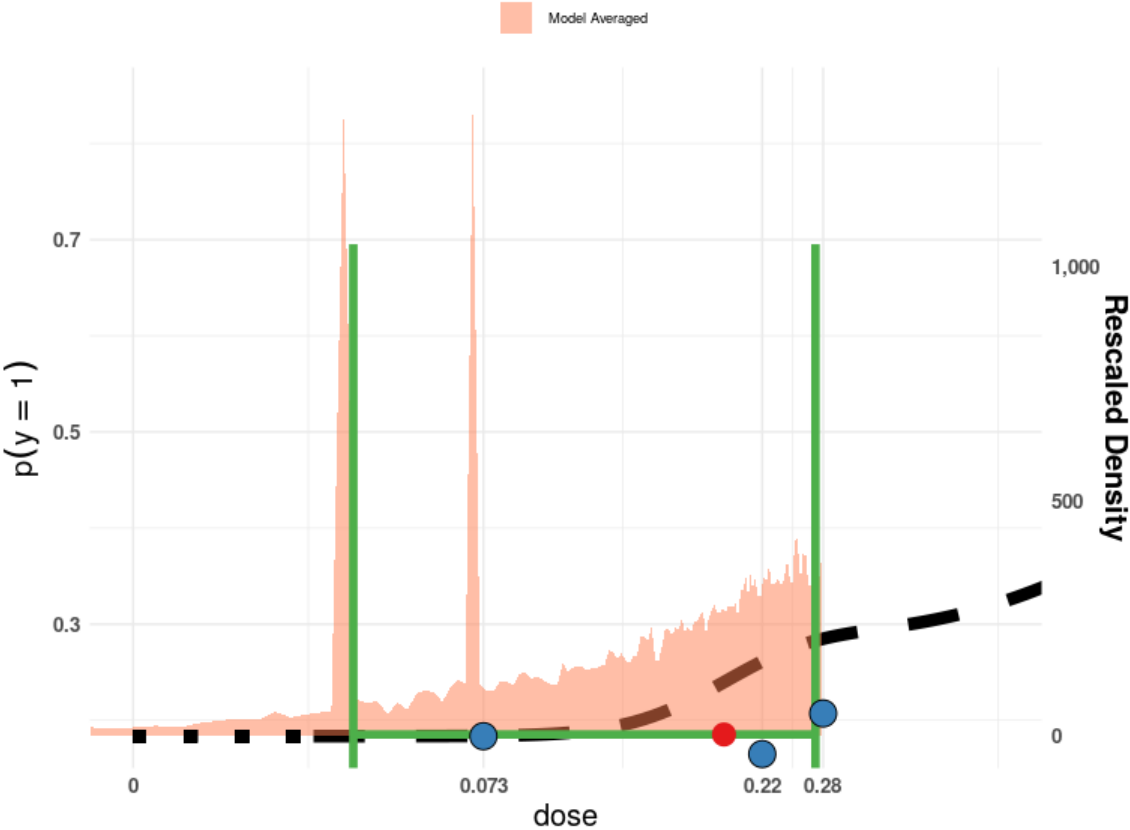
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.063	0.194	0.271	0.135	1
IE4_Q	0.138	0.236	0.275	0.074	1
H4_Q	0.065	0.197	0.272	0.132	1
LN4_Q	0.115	0.223	0.274	0.095	1
G4_Q	0.044	0.072	0.257	0.127	0
QE4_Q	0.051	0.165	0.268	0.170	1
P4_Q	0.057	0.194	0.270	0.133	1
L4_Q	0.053	0.192	0.272	0.134	1

Plots of Fitted Models







Rahman et al. (2007) infant death, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for infant death

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.13	237	5119
6.47	267	5113
17.38	282	5122
25.75	306	5131
38.55	281	5109

The 'Value for CES' is set to 0.00048546.

Extended dose range is not applied.

Informative background prior: min: 0.04583512; the most likely: 0.04629811; max: 0.04676109. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.61e-03).

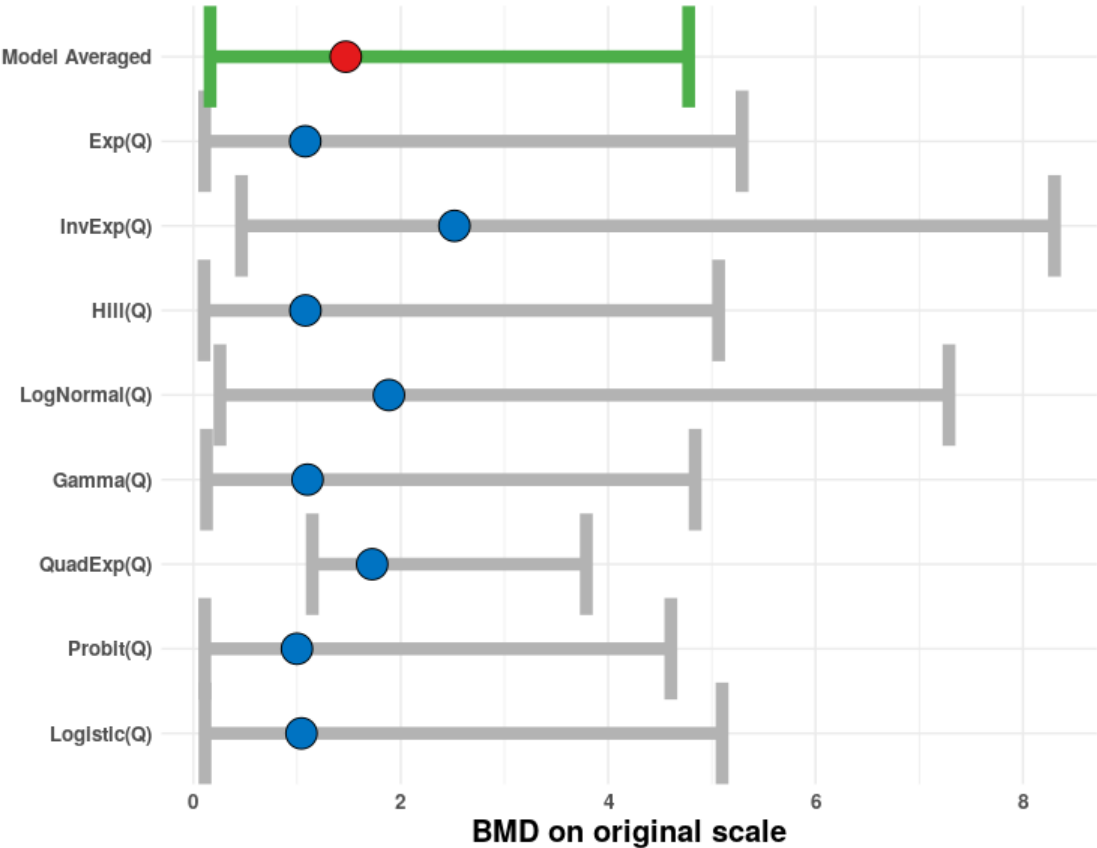
Model Averaged BMD

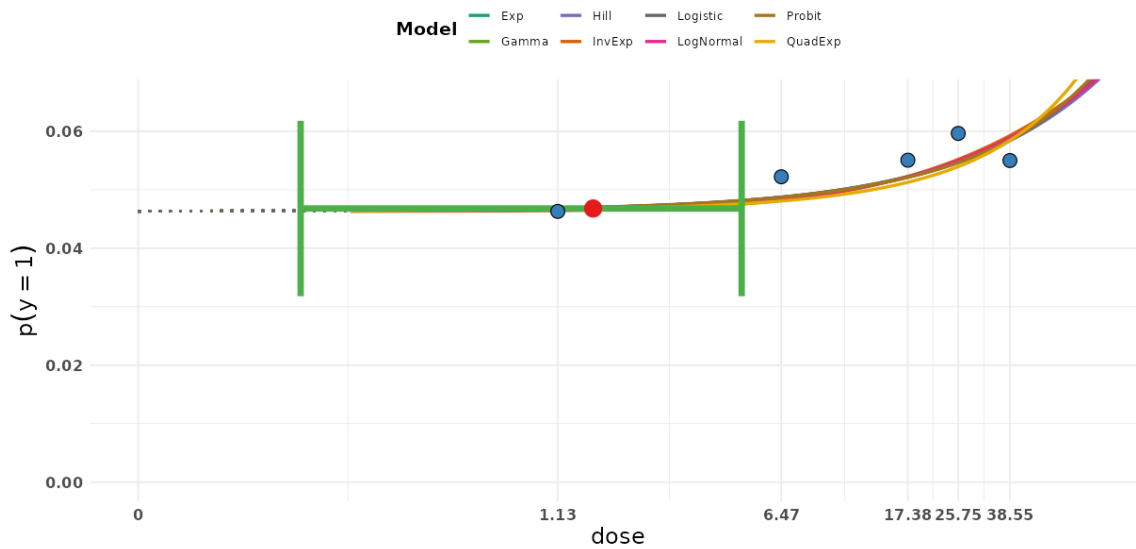
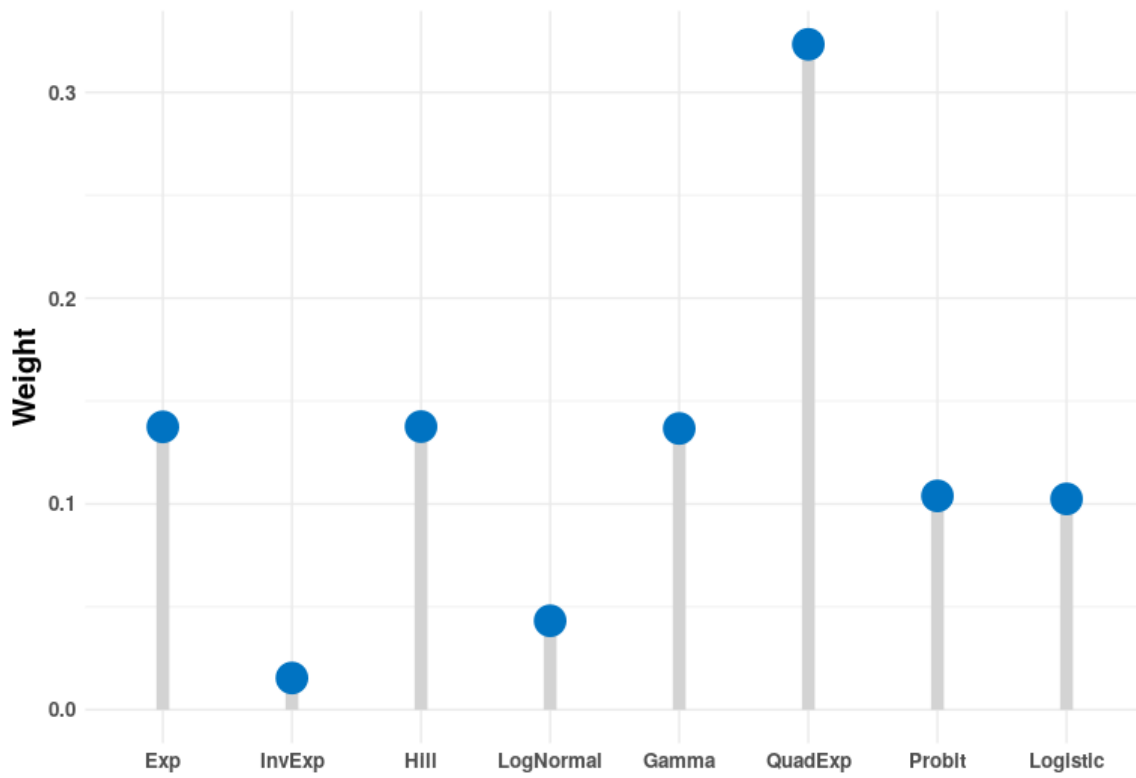
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.161	1.47	4.776

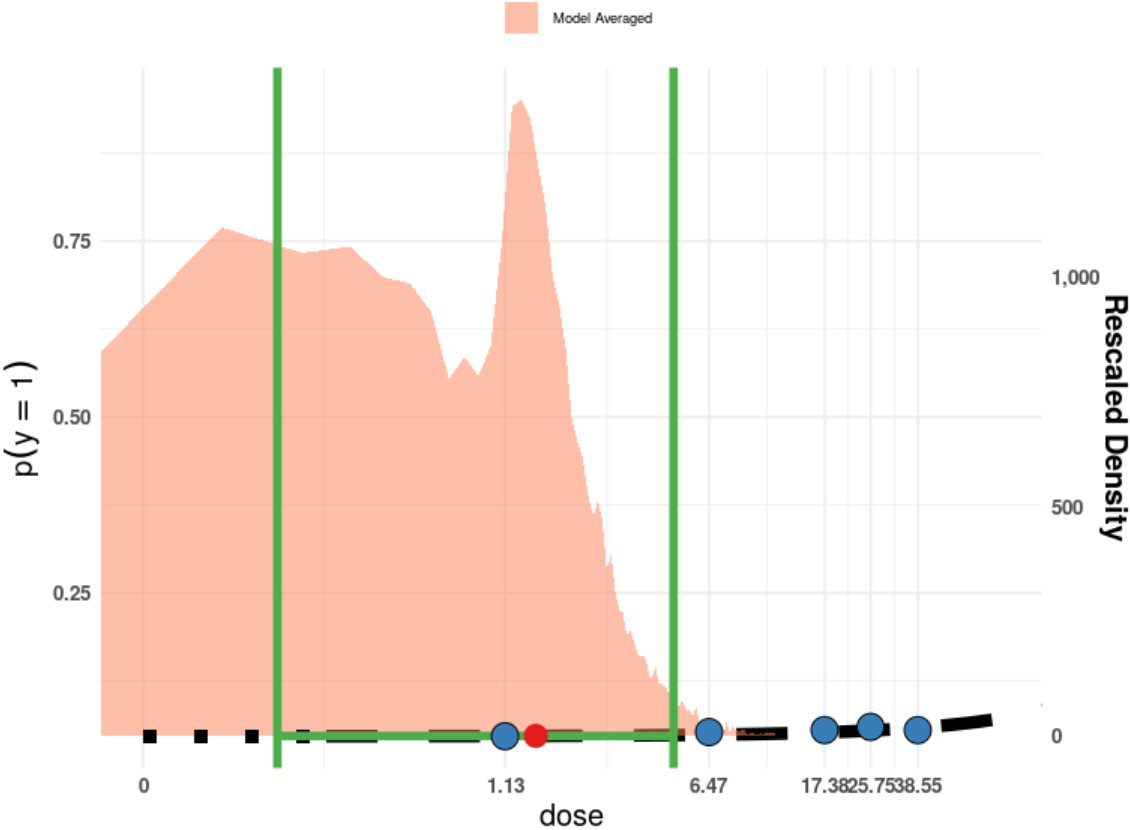
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.109	1.079	5.292	0.137	1
IE4_Q	0.464	2.518	8.304	0.015	1
H4_Q	0.102	1.081	5.065	0.138	1
LN4_Q	0.256	1.886	7.287	0.043	1
G4_Q	0.127	1.101	4.839	0.137	1
QE4_Q	1.147	1.724	3.790	0.323	1
P4_Q	0.110	0.999	4.604	0.104	1
L4_Q	0.112	1.042	5.098	0.102	1

Plots of Fitted Models







Rahman et al. (2010) infant mortality, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for infant mortality

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.09	3	338
1.82	5	342
3.42	6	339
6.87	7	335
14.18	15	339

The 'Value for CES' is set to 8.955e-05.

Extended dose range is not applied.

Informative background prior: min: 0.00878698; the most likely: 0.00887574; max: 0.00896450. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since $BMDU/BMDL > 50$.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.04e-03).

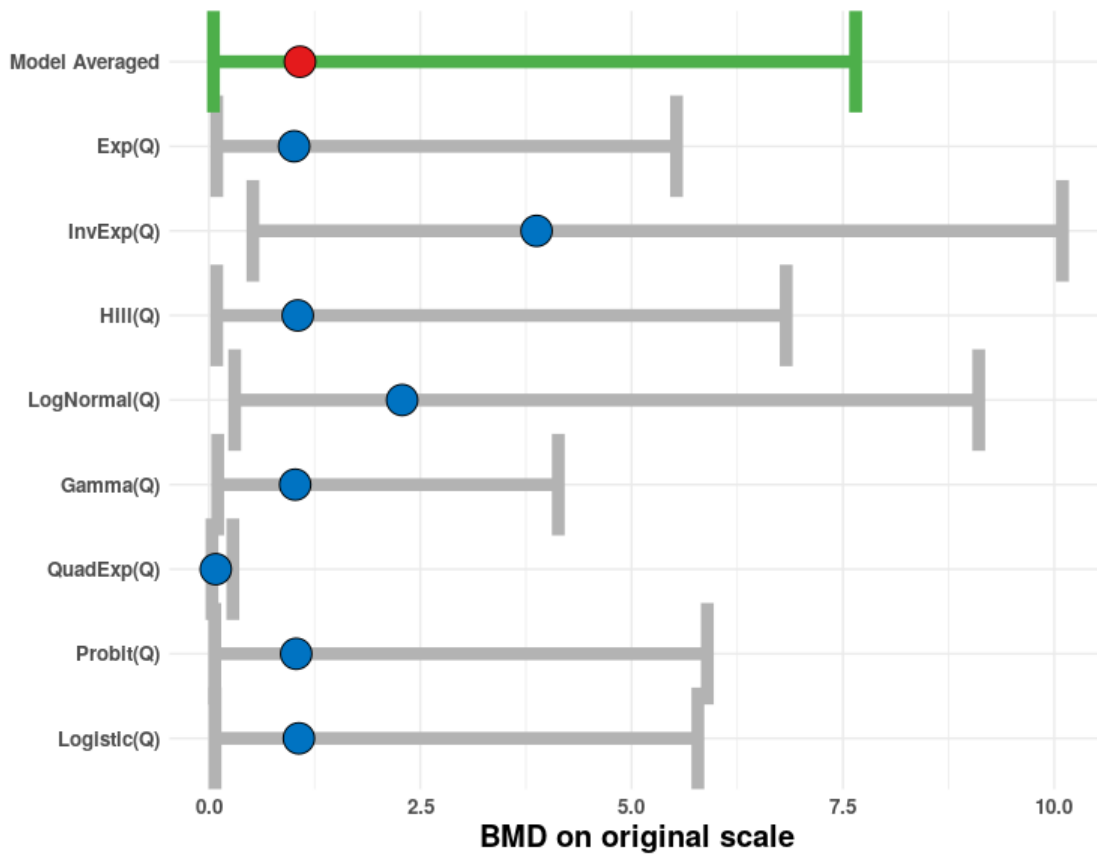
Model Averaged BMD

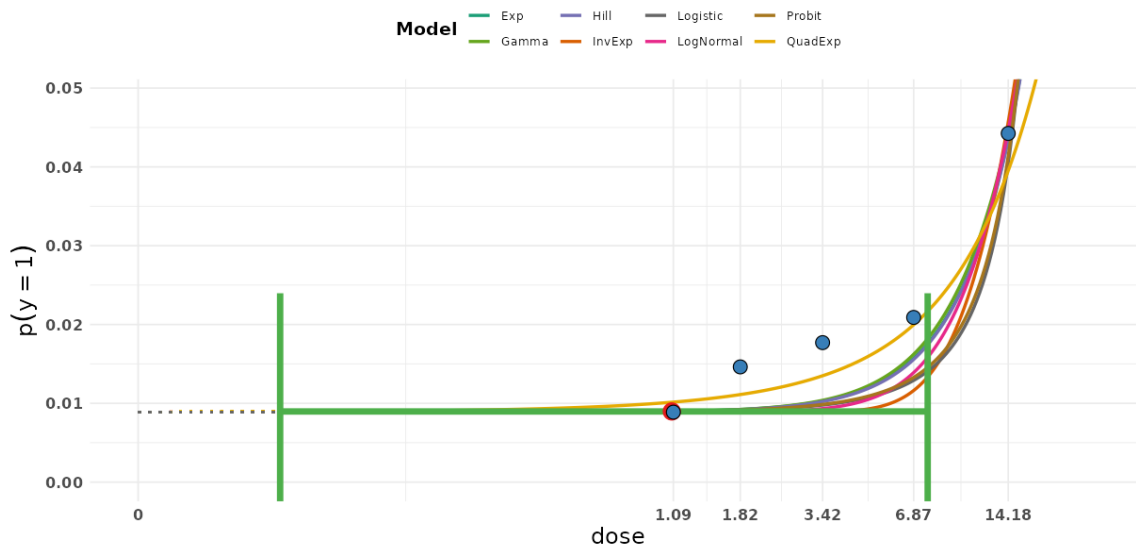
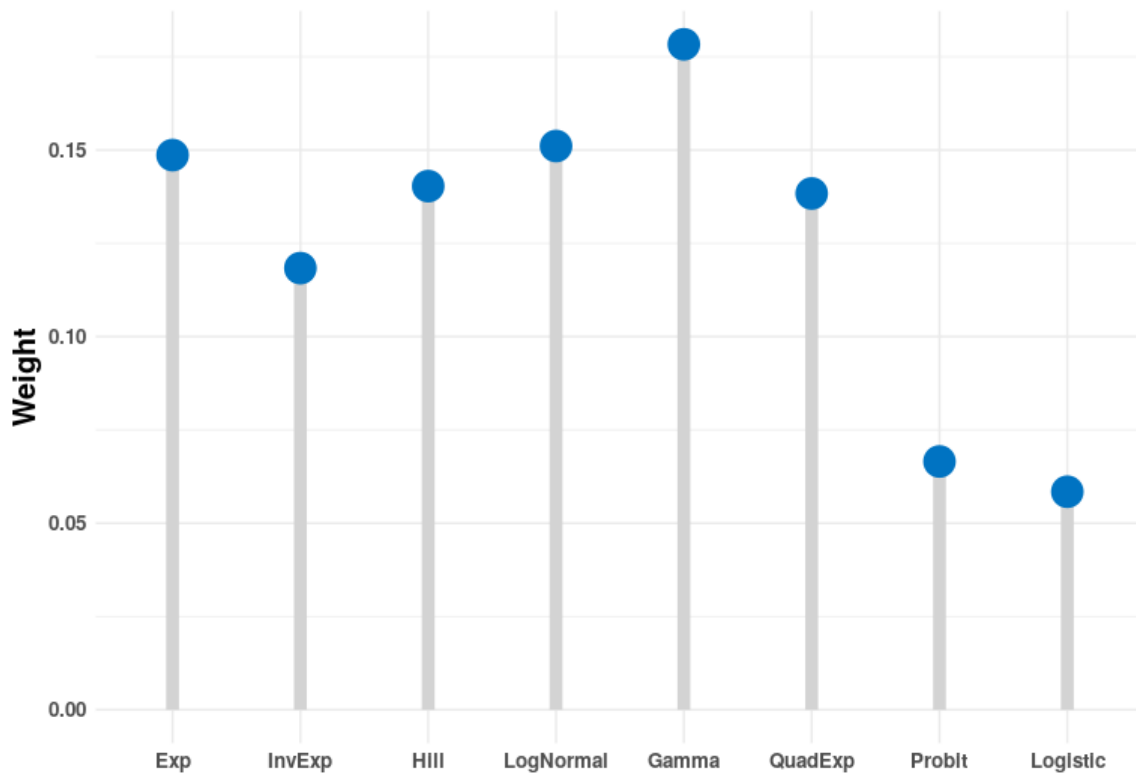
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.054	1.077	7.65

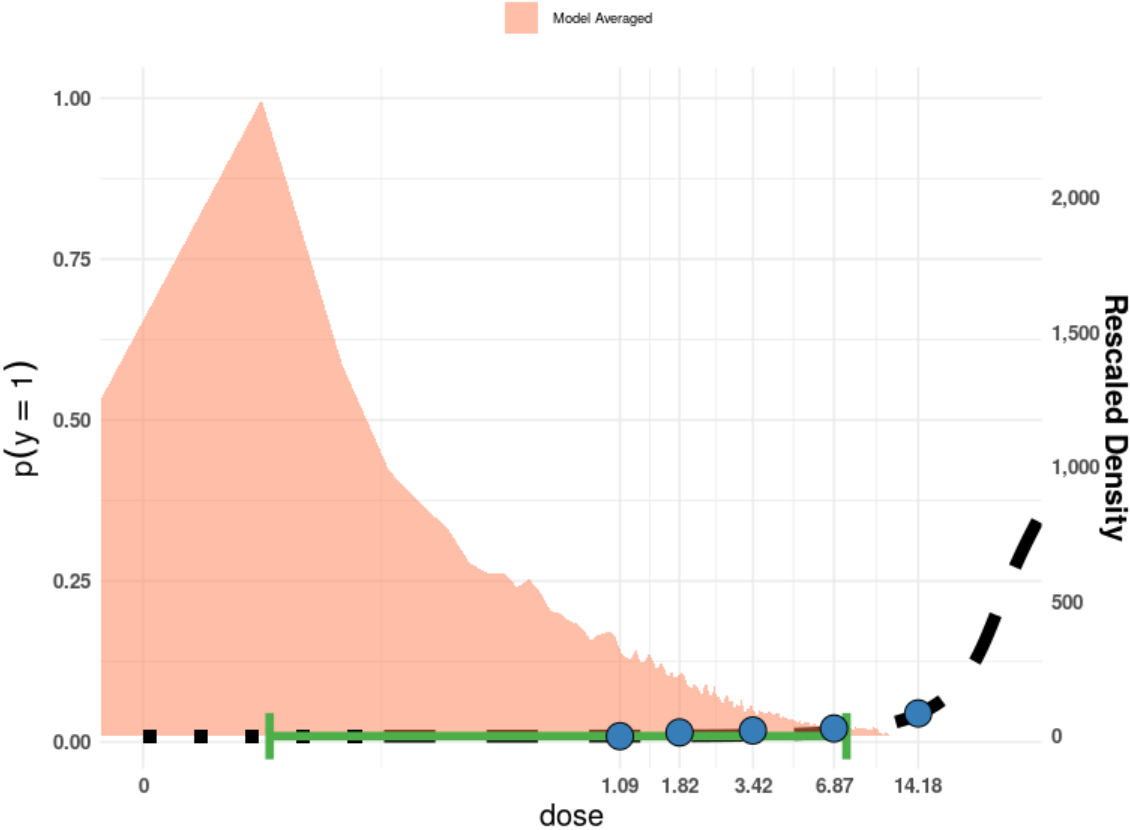
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.093	1.008	5.531	0.149	1
IE4_Q	0.520	3.876	10.097	0.118	1
H4_Q	0.092	1.051	6.829	0.140	1
LN4_Q	0.305	2.285	9.107	0.151	0
G4_Q	0.104	1.020	4.133	0.178	1
QE4_Q	0.036	0.081	0.283	0.138	1
P4_Q	0.069	1.032	5.896	0.067	1
L4_Q	0.072	1.064	5.784	0.058	1

Plots of Fitted Models







Rahman et al. (2010) spontaneous abortion, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for spontaneous abortion

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.84	45	553
1.53	57	558
2.91	63	567
6.44	47	549
13.89	63	557

The 'Value for CES' is set to 0.00088583.

Extended dose range is not applied.

Informative background prior: min: 0.08056058; the most likely: 0.08137432; max: 0.08218807. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The study was rejected following visual screening due to the non-monotonic dose-response seen.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 3.78e-02).

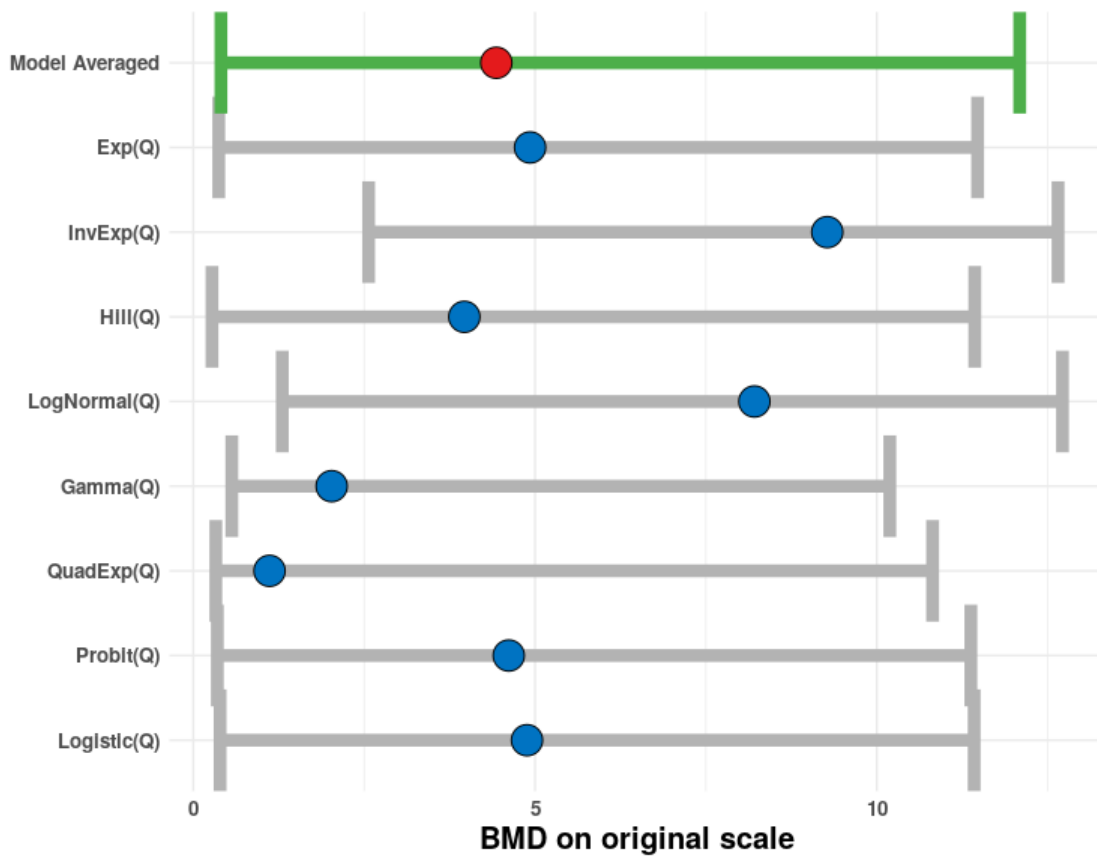
Model Averaged BMD

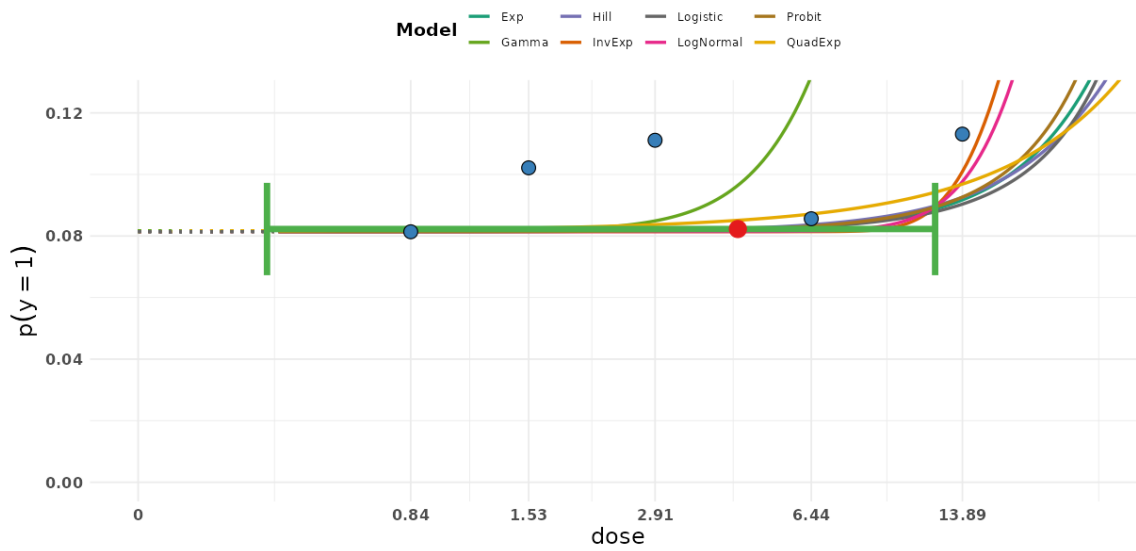
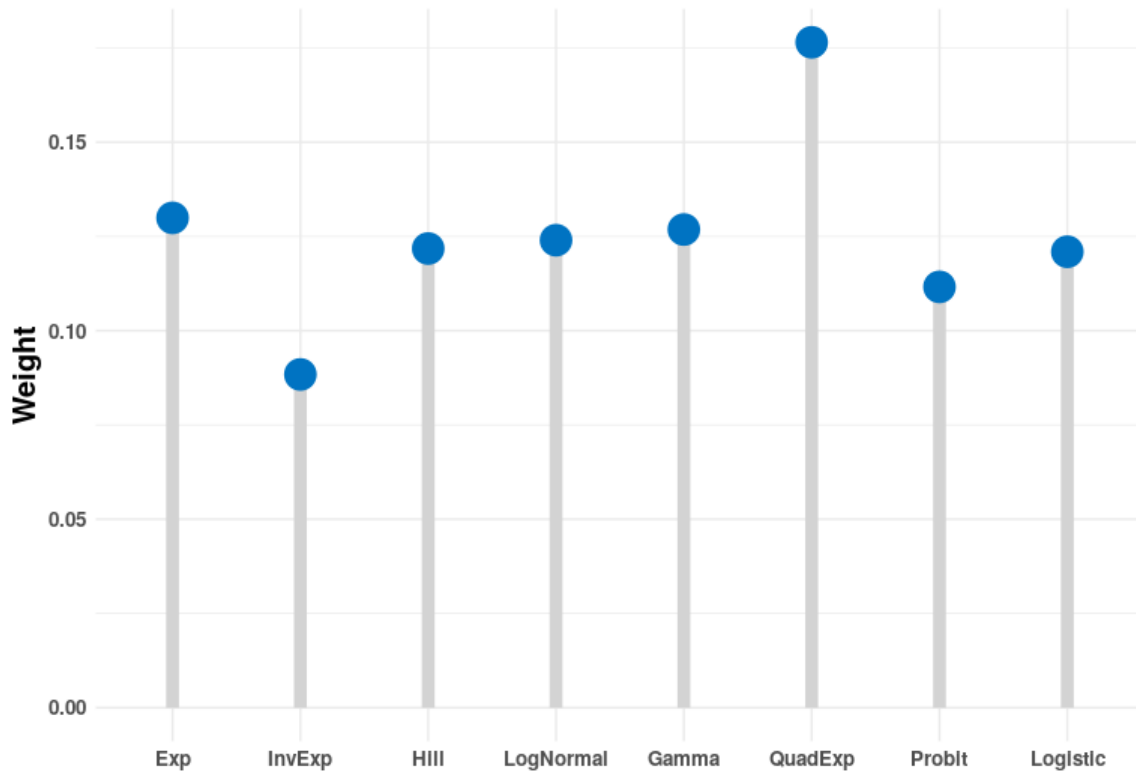
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.404	4.433	12.091

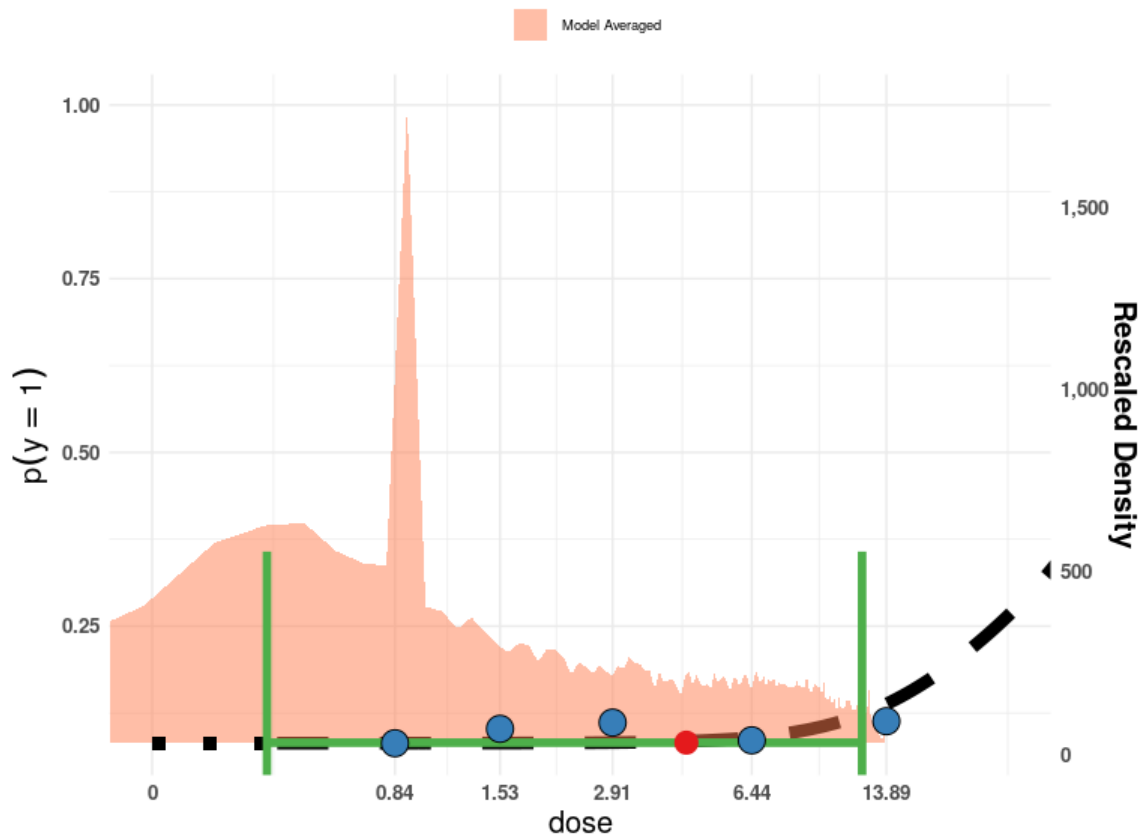
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.373	4.927	11.475	0.130	1
IE4_Q	2.565	9.275	12.652	0.088	1
H4_Q	0.274	3.966	11.433	0.122	1
LN4_Q	1.302	8.209	12.717	0.124	0
G4_Q	0.564	2.025	10.190	0.127	0
QE4_Q	0.330	1.116	10.816	0.176	1
P4_Q	0.352	4.615	11.376	0.112	1
L4_Q	0.392	4.883	11.425	0.121	0

Plots of Fitted Models







Rahman et al. (2010) stillbirth, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for stillbirth

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.09	3	341
1.82	6	348
3.42	7	346
6.87	10	345
14.18	6	345

The 'Value for CES' is set to 8.876e-05.

Extended dose range is not applied.

Informative background prior: min: 0.00870968; the most likely: 0.00879765; max: 0.00888563. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since BMD/BMDL > 20 and BMDU/BMDL > 50.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.55e-01).

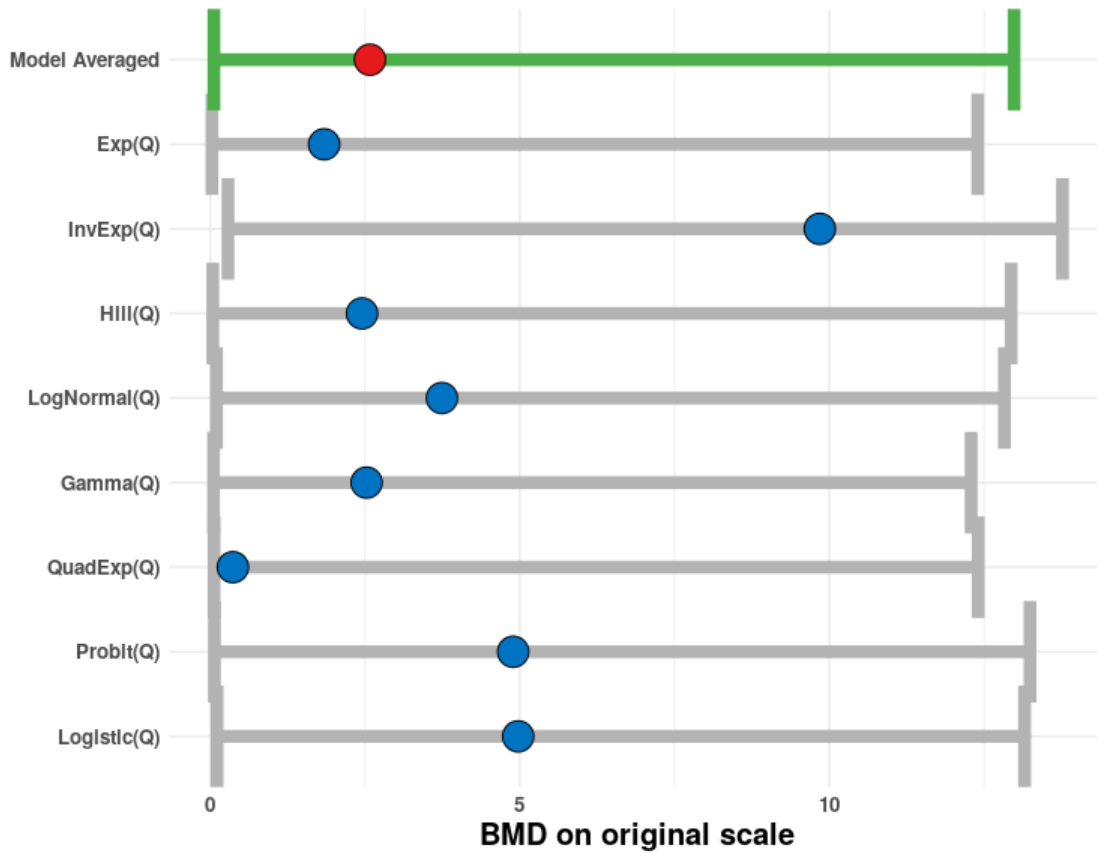
Model Averaged BMD

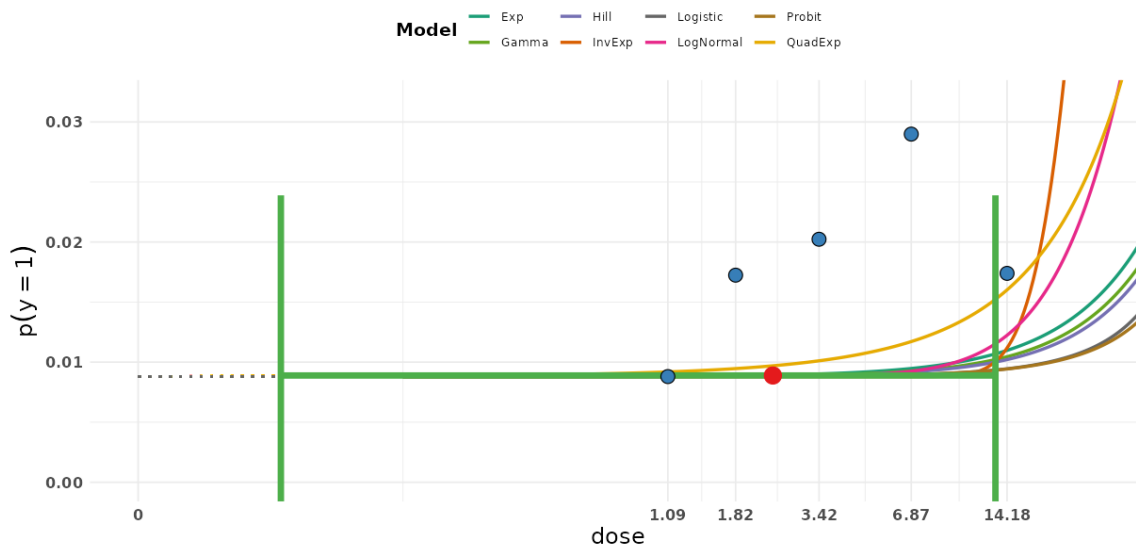
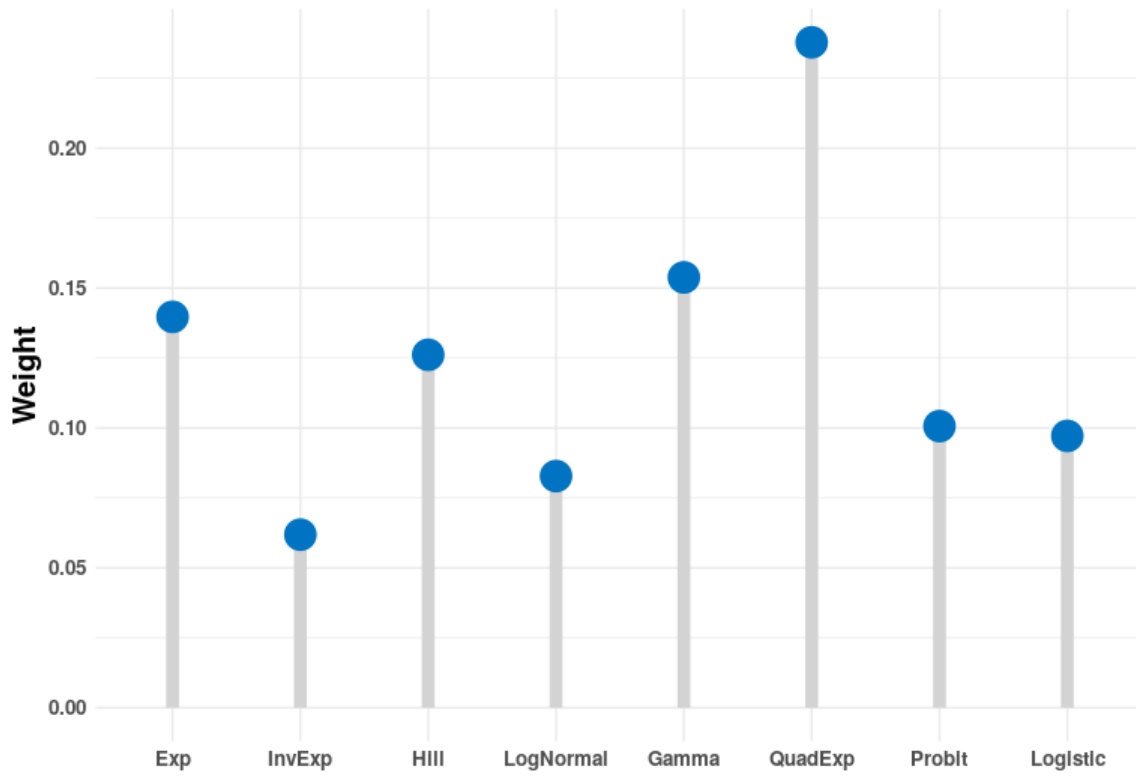
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.059	2.58	12.985

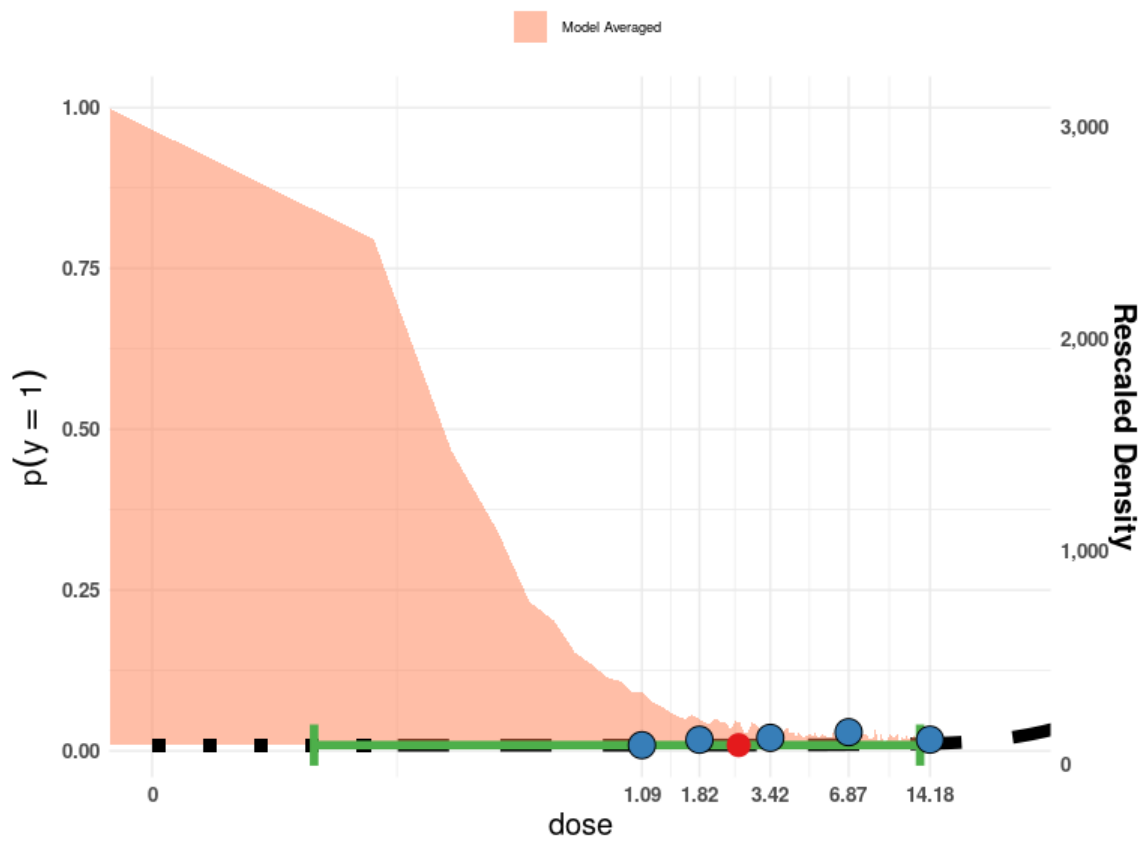
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.028	1.839	12.398	0.140	1
IE4_Q	0.286	9.847	13.767	0.062	0
H4_Q	0.040	2.452	12.937	0.126	1
LN4_Q	0.101	3.742	12.829	0.083	1
G4_Q	0.053	2.525	12.292	0.154	0
QE4_Q	0.061	0.366	12.405	0.238	1
P4_Q	0.067	4.893	13.242	0.101	1
L4_Q	0.110	4.974	13.155	0.097	1

Plots of Fitted Models







Richter et al. (2022) congenital heart disease, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for congenital heart disease

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.12	4453	495970
0.13	2413	235630
0.17	3522	292222
0.22	239	18591

The 'Value for CES' is set to 9.06e-05.

Extended dose range is not applied.

Informative background prior: min: 0.00888858; the most likely: 0.00897837; max: 0.00906815. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (2022) recommendations since none of the candidate models fit the data sufficiently well.

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 7.92e+04).

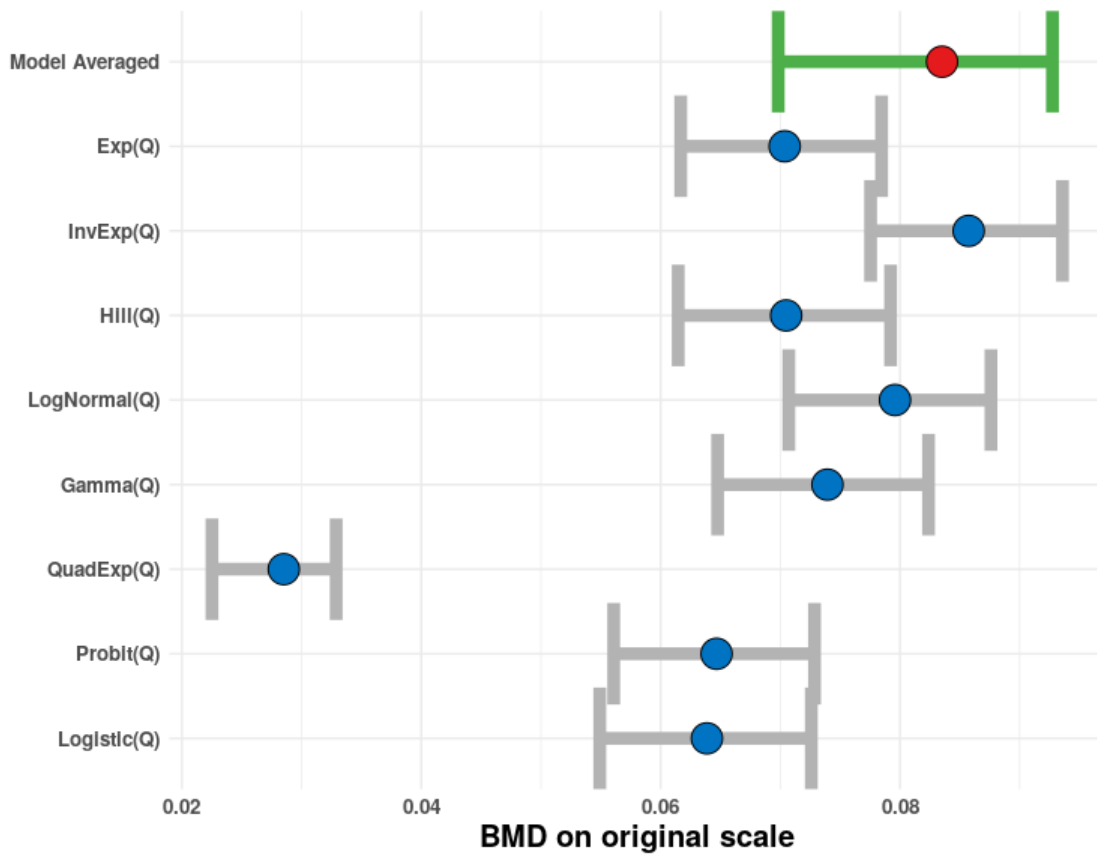
Model Averaged BMD

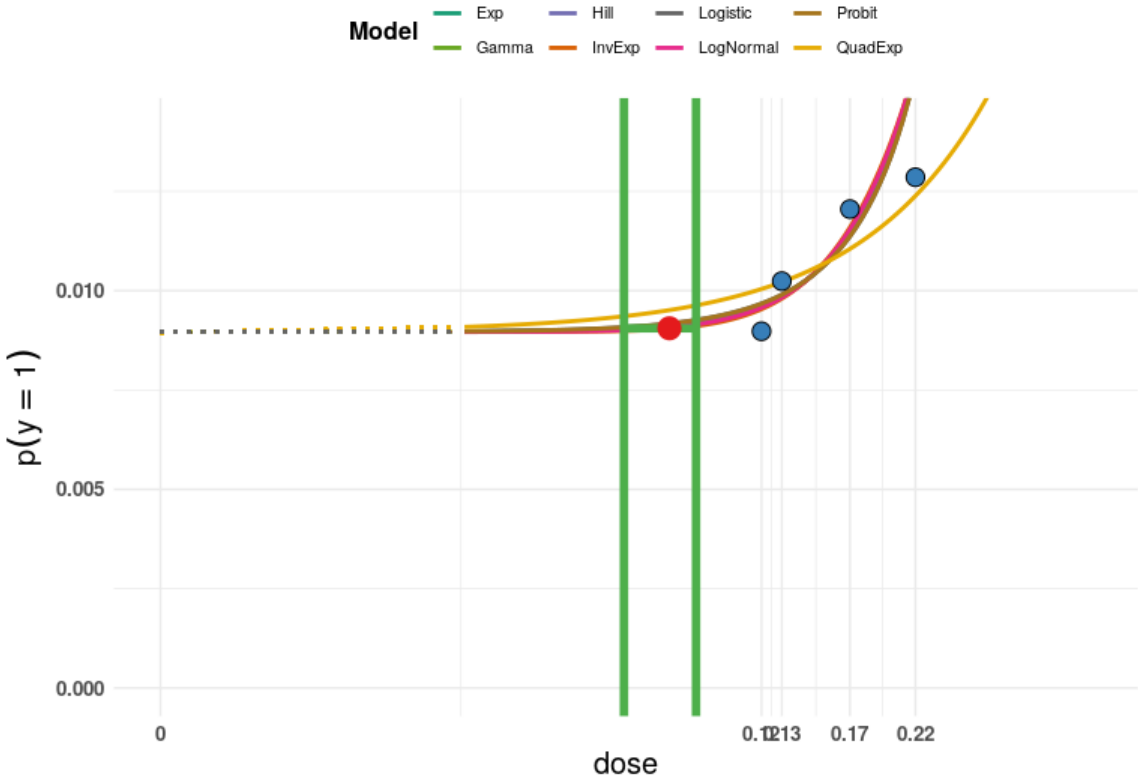
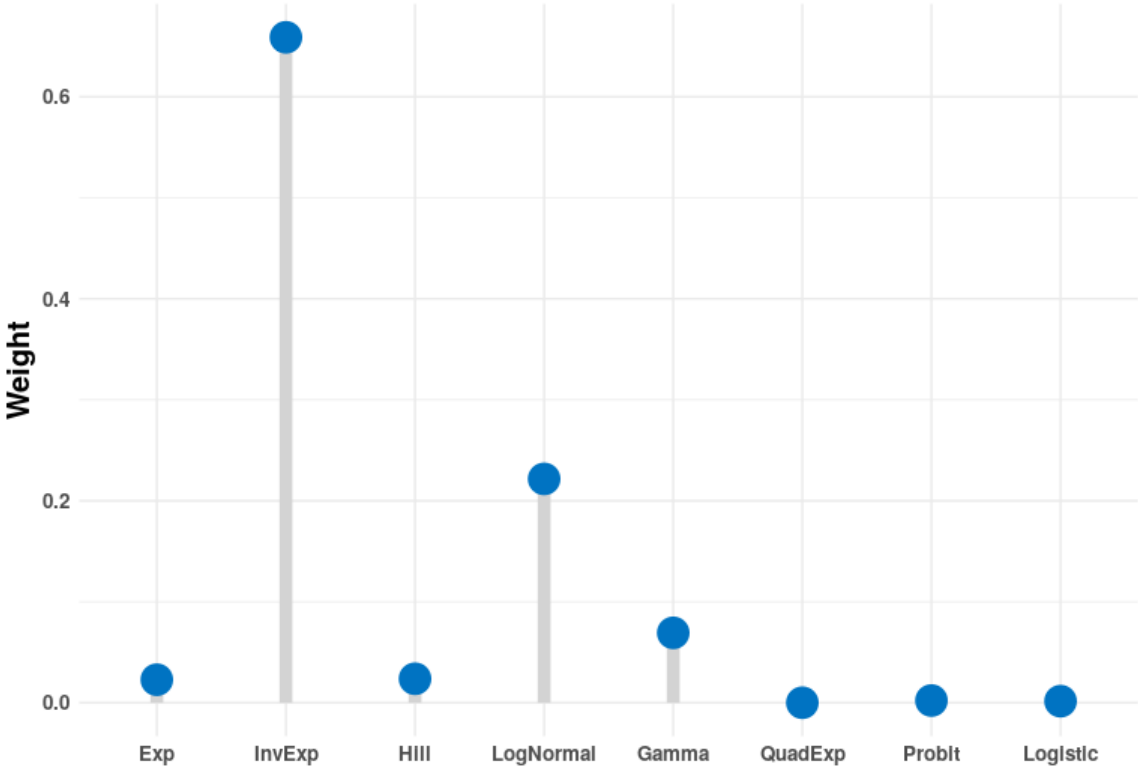
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.07	0.084	0.093

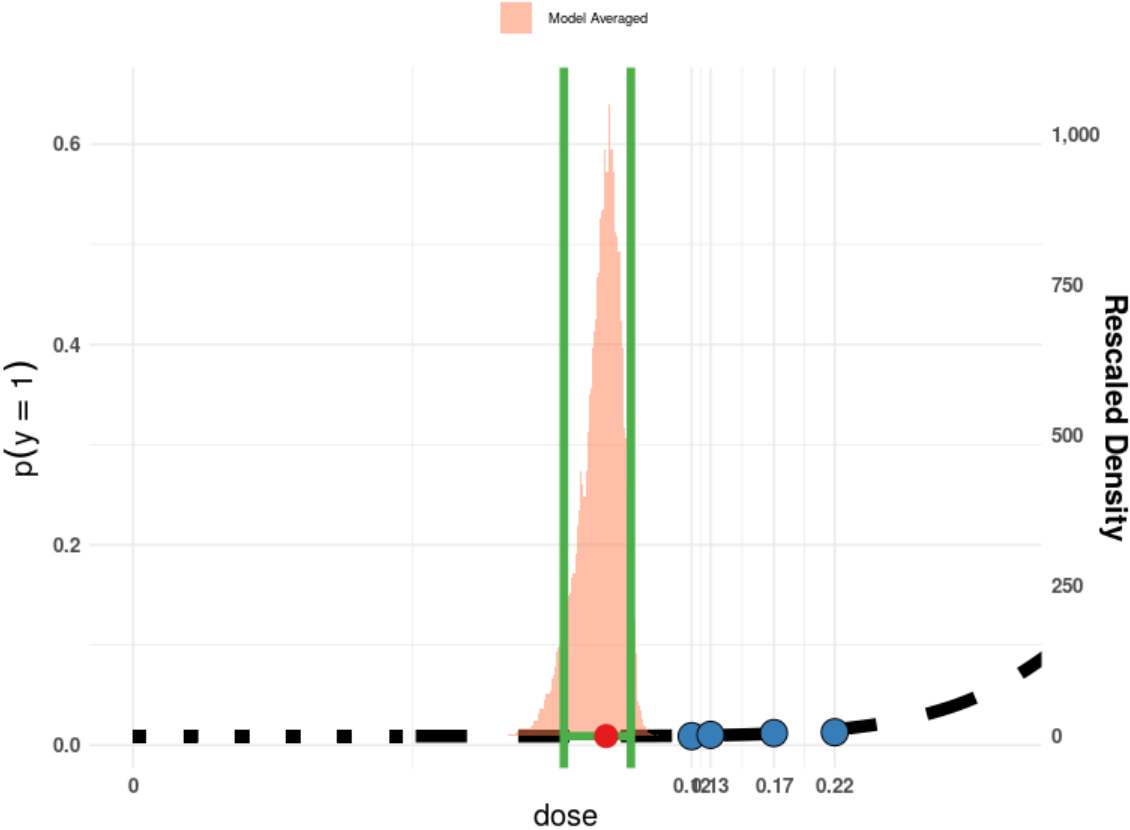
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.062	0.070	0.078	0.023	1
IE4_Q	0.078	0.086	0.094	0.659	1
H4_Q	0.061	0.070	0.079	0.024	1
LN4_Q	0.071	0.080	0.088	0.222	1
G4_Q	0.065	0.074	0.082	0.069	1
QE4_Q	0.023	0.029	0.033	0.000	1
P4_Q	0.056	0.065	0.073	0.002	1
L4_Q	0.055	0.064	0.073	0.002	1

Plots of Fitted Models







Siddique et al. (2020) asthma symptoms, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for asthma symptoms

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.28	14	279
6.16	27	281
71.45	46	282

The 'Value for CES' is set to 0.0005283.

Extended dose range is not applied.

Informative background prior: min: 0.04767025; the most likely: 0.05017921; max: 0.05268817. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since none of the candidate models fit the data sufficiently well, BMD/BMDL > 20 and BMDU/BMDL > 50.

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 1.36e+02).

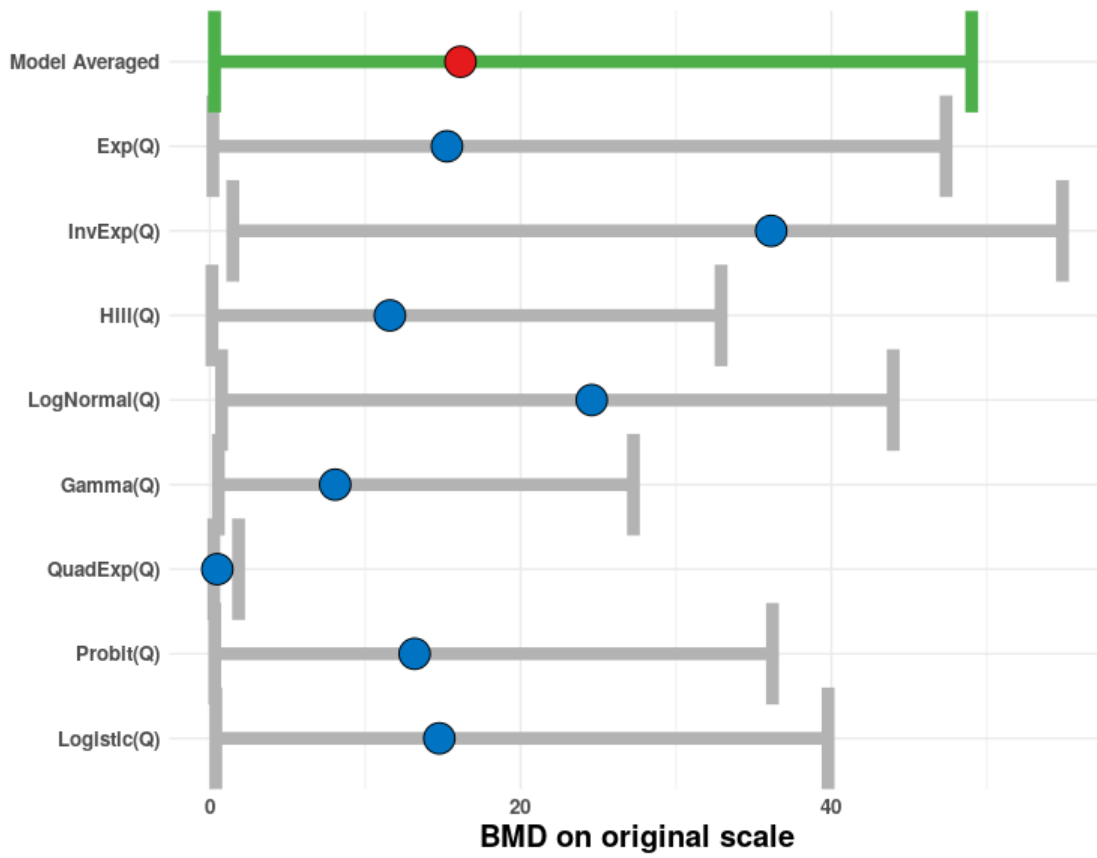
Model Averaged BMD

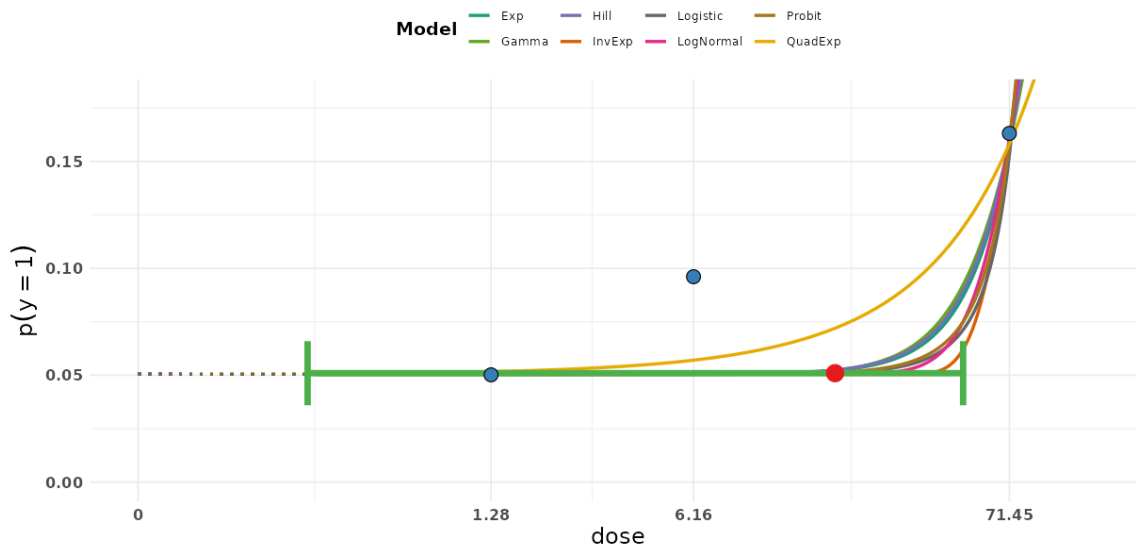
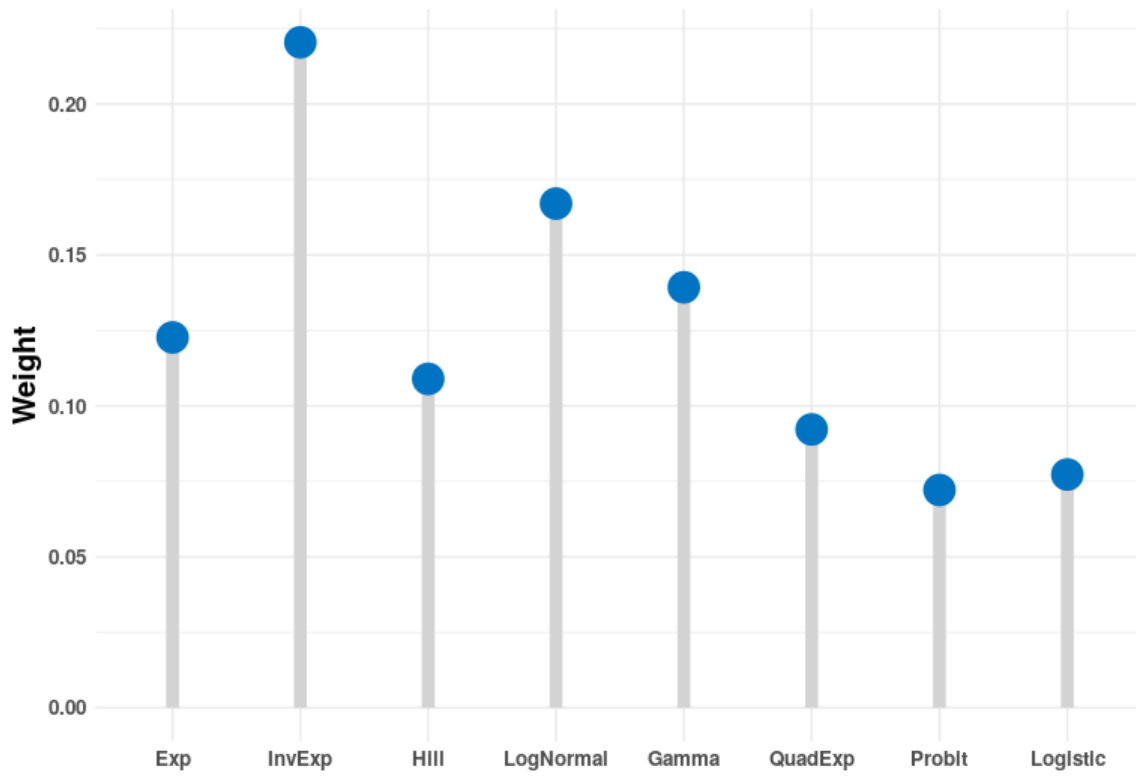
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.303	16.131	49.029

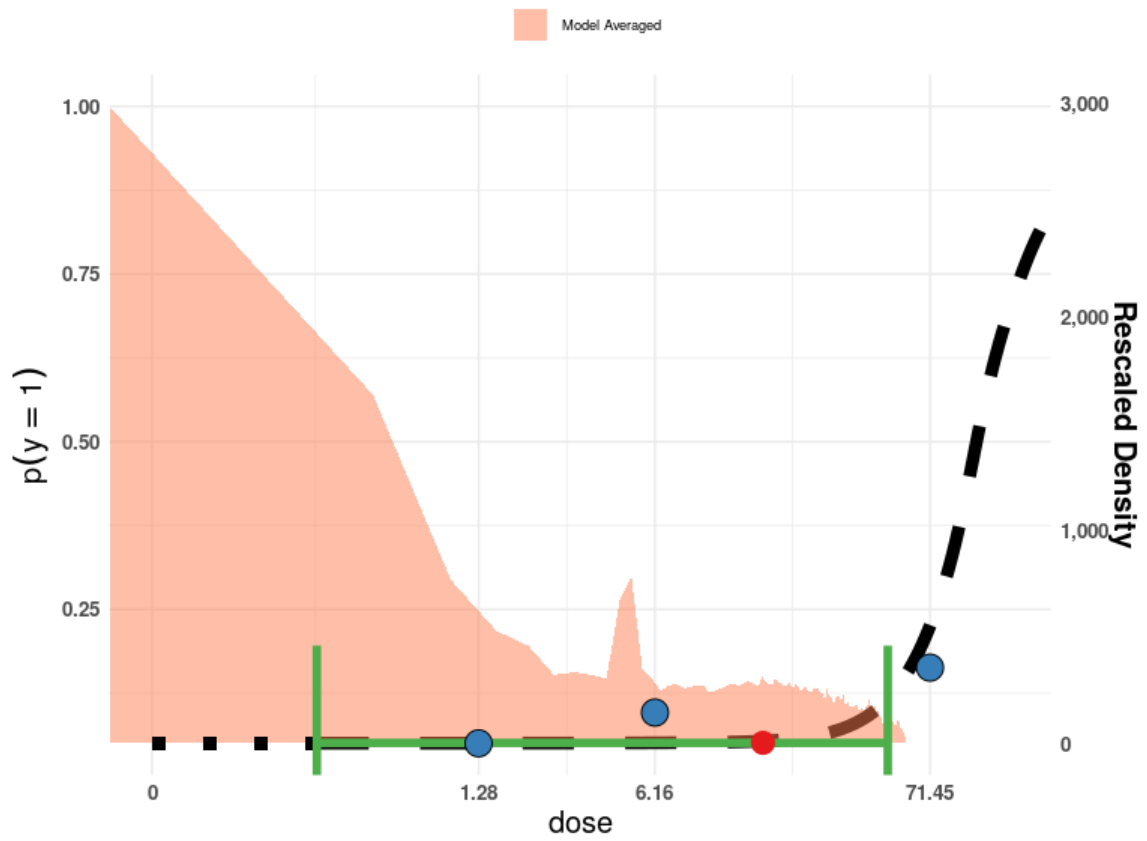
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.198	15.261	47.378	0.123	1
IE4_Q	1.479	36.122	54.869	0.220	1
H4_Q	0.140	11.588	32.899	0.109	1
LN4_Q	0.755	24.575	43.975	0.167	1
G4_Q	0.549	8.068	27.258	0.139	0
QE4_Q	0.256	0.481	1.851	0.092	1
P4_Q	0.319	13.178	36.205	0.072	1
L4_Q	0.390	14.768	39.785	0.077	0

Plots of Fitted Models







Siddique et al. (2020) FEV1 (lung function), BMR 1%

Data Description

The endpoint to be analyzed is: FEV1 response

Data used for analysis:

Exposure.µg.kg.bw.per.day	Response	SD	N
1.28	1.578	0.575	279
6.16	1.455	0.578	281
71.45	1.375	0.797	282

The 'Value for CES' is set to 0.01.

Extended dose range is not applied.

Informative background prior: min: 1.4202; the most likely: 1.578; max: 1.7358. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since none of the candidate models fit the data sufficiently well.

Check for constant variance coefficient of variation

distributional assumption of constant variance for the normal distribution is not met, Bartlett test p-value is 0.0000

distributional assumption of constant variance (on log-scale) is not met, Bartlett test p-value is 0.0000

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 3.29e+01).

Model Averaged BMD

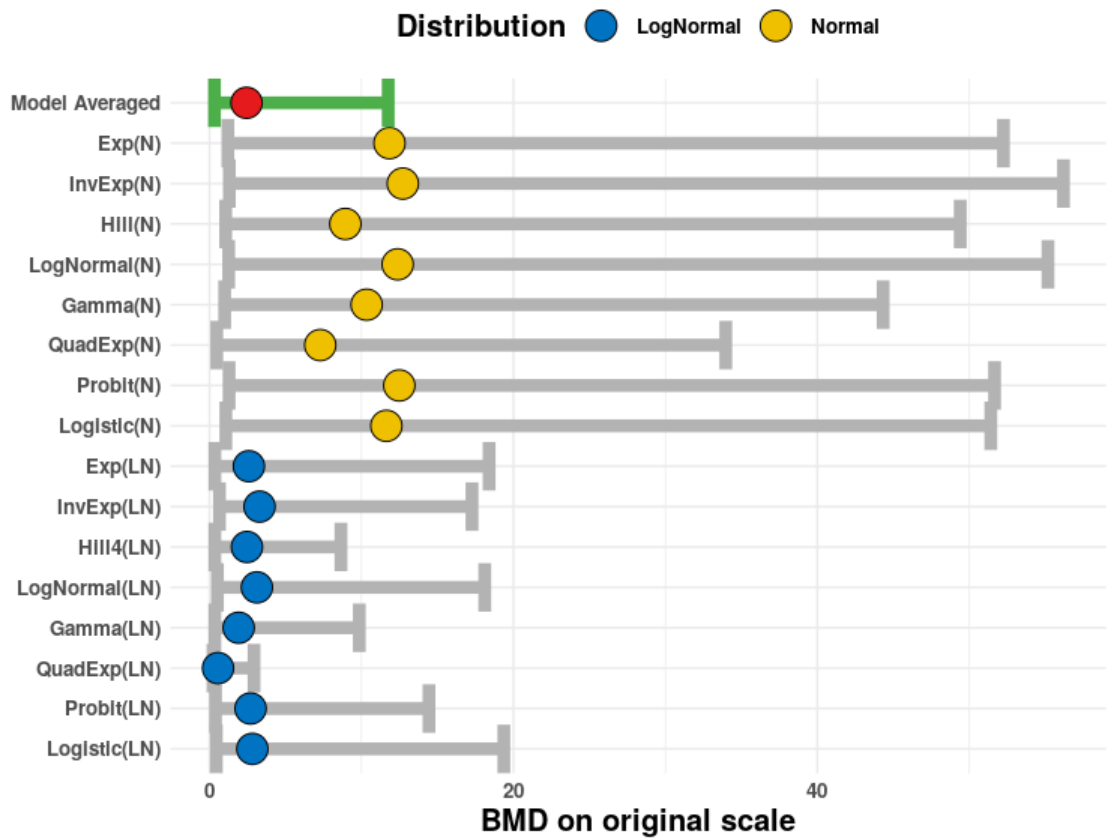
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.330	2.438	11.762
Model Averaged	BS	0.885	5.169	54.132
Model Averaged	BS	1.328	18.280	57.703
Model Averaged	BS	0.311	2.456	5.020

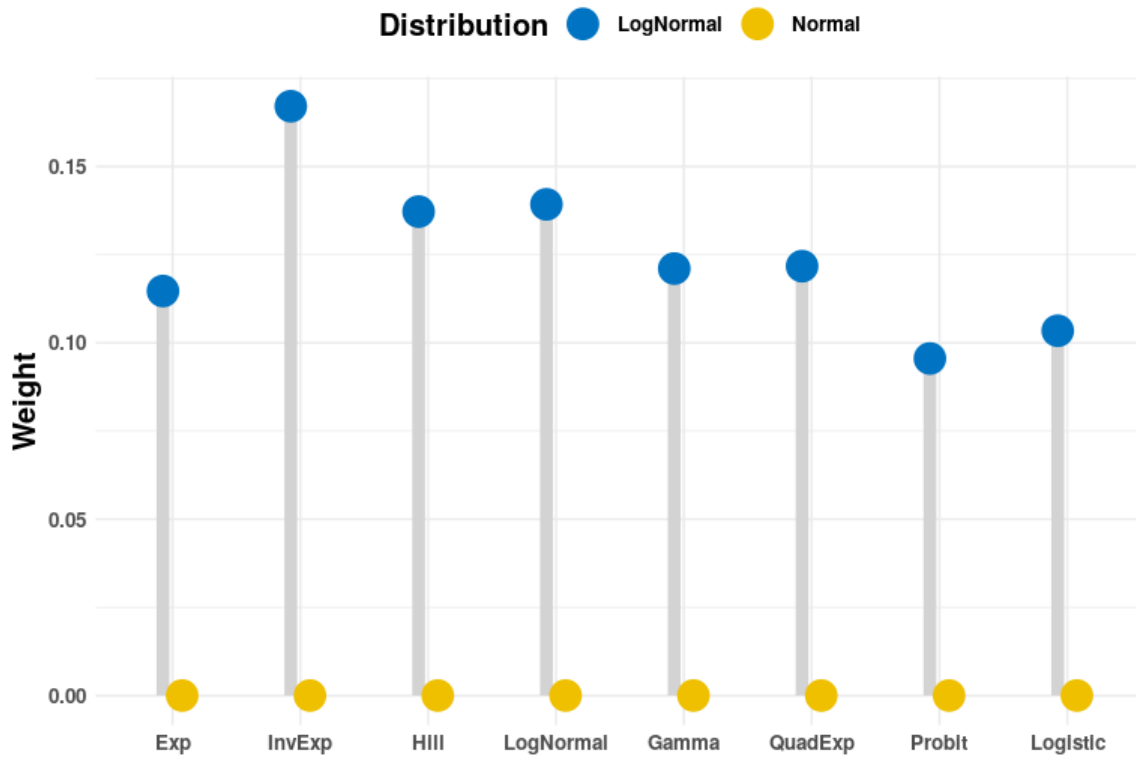
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.392	3.055	33.343

Estimated BMDs per model

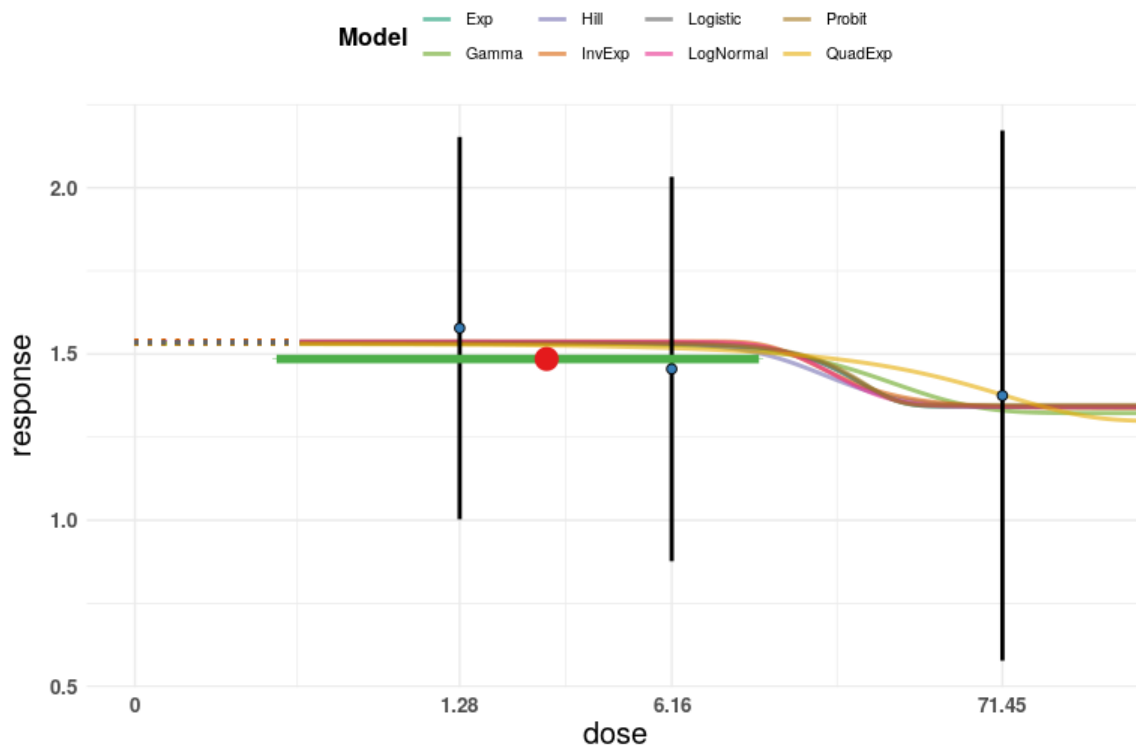
Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_N	1.211	11.847	52.246	0.000	1
IE4_N	1.307	12.722	56.197	0.000	1
H4_N	1.066	8.942	49.402	0.000	1
LN4_N	1.264	12.383	55.175	0.000	1
G4_N	0.998	10.343	44.329	0.000	1
QE4_N	0.478	7.288	33.973	0.000	1
P4_N	1.290	12.490	51.662	0.000	1
L4_N	1.077	11.640	51.413	0.000	1
E4_LN	0.356	2.593	18.400	0.115	1
IE4_LN	0.656	3.293	17.275	0.167	1
H4_LN	0.352	2.465	8.652	0.137	1
LN4_LN	0.521	3.119	18.115	0.139	1
G4_LN	0.352	1.921	9.858	0.121	1
QE4_LN	0.231	0.563	2.929	0.122	1
P4_LN	0.399	2.703	14.444	0.096	1
L4_LN	0.449	2.821	19.371	0.103	1

Plots of Fitted Models

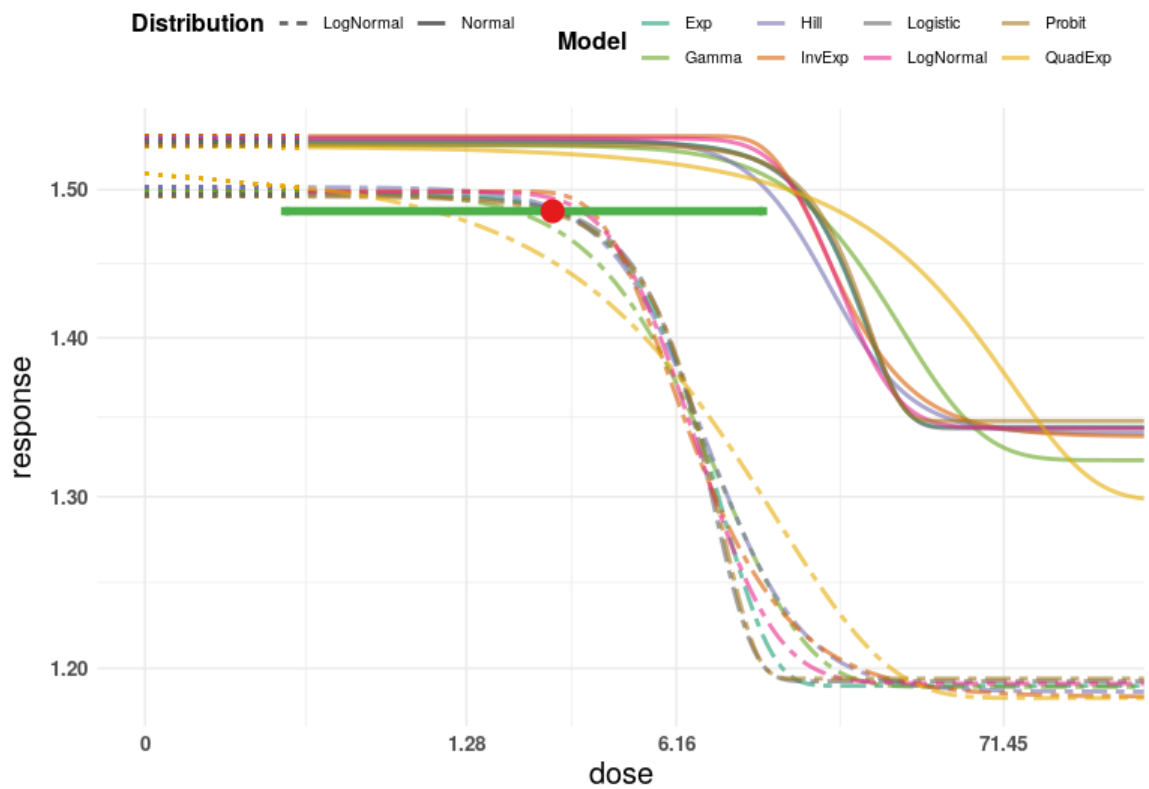
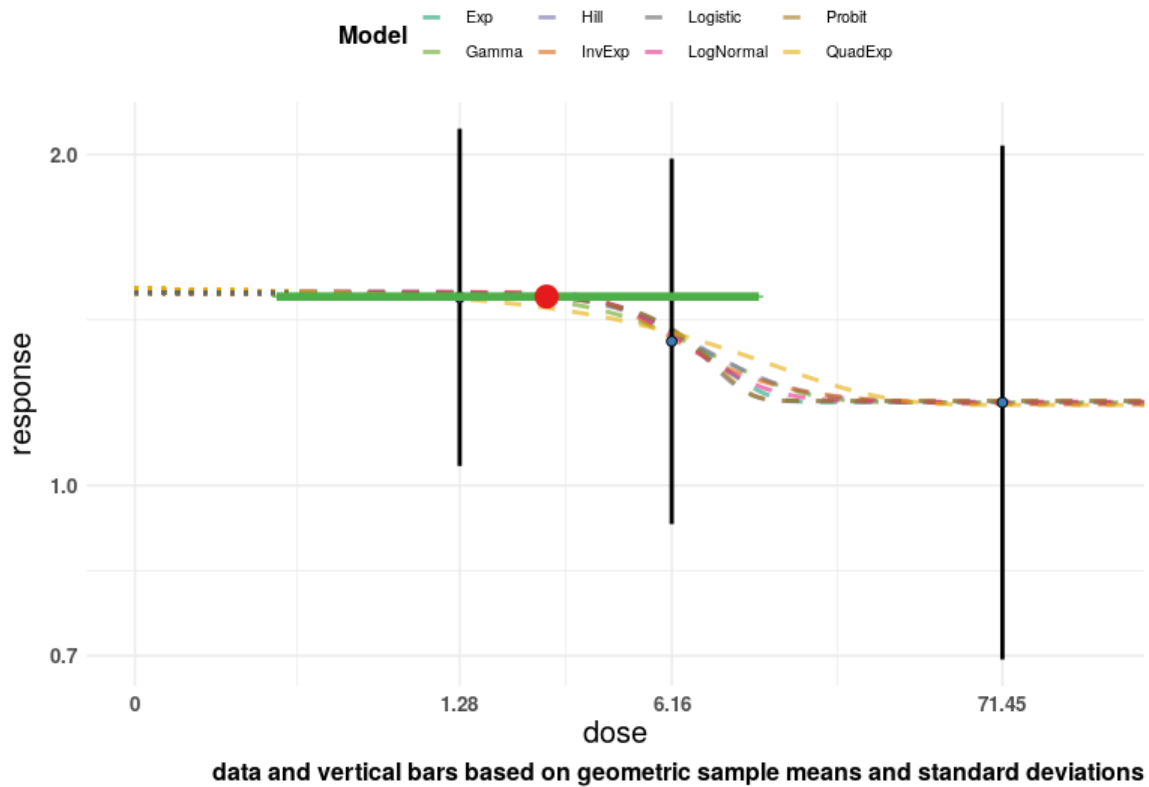


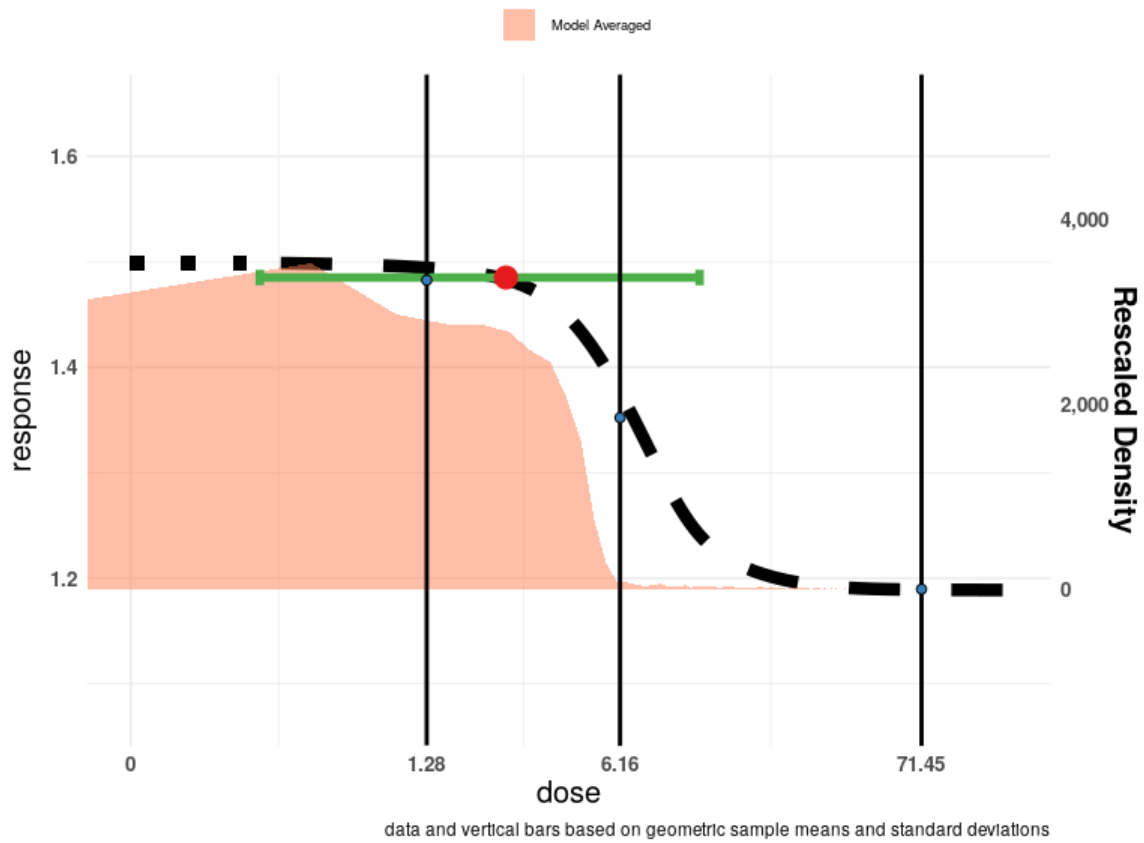


Normal distribution



LogNormal distribution





Siddique et al. (2020) FEV6 (lung function), BMR 1%

Data Description

The endpoint to be analyzed is: FEV6 response

Data used for analysis:

Exposure.µg.kg.bw.per.day	Response	SD	N
1.28	1.669	0.536	279
6.16	1.547	0.538	281
71.45	1.500	0.851	282

The 'Value for CES' is set to 0.01.

Extended dose range is not applied.

Informative background prior: min: 1.5021; the most likely: 1.669; max: 1.8359. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since none of the candidate models fit the data sufficiently well.

Check for constant variance coefficient of variation

distributional assumption of constant variance for the normal distribution is not met, Bartlett test p-value is 0.0000

distributional assumption of constant variance (on log-scale) is not met, Bartlett test p-value is 0.0000

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 3.72e+01).

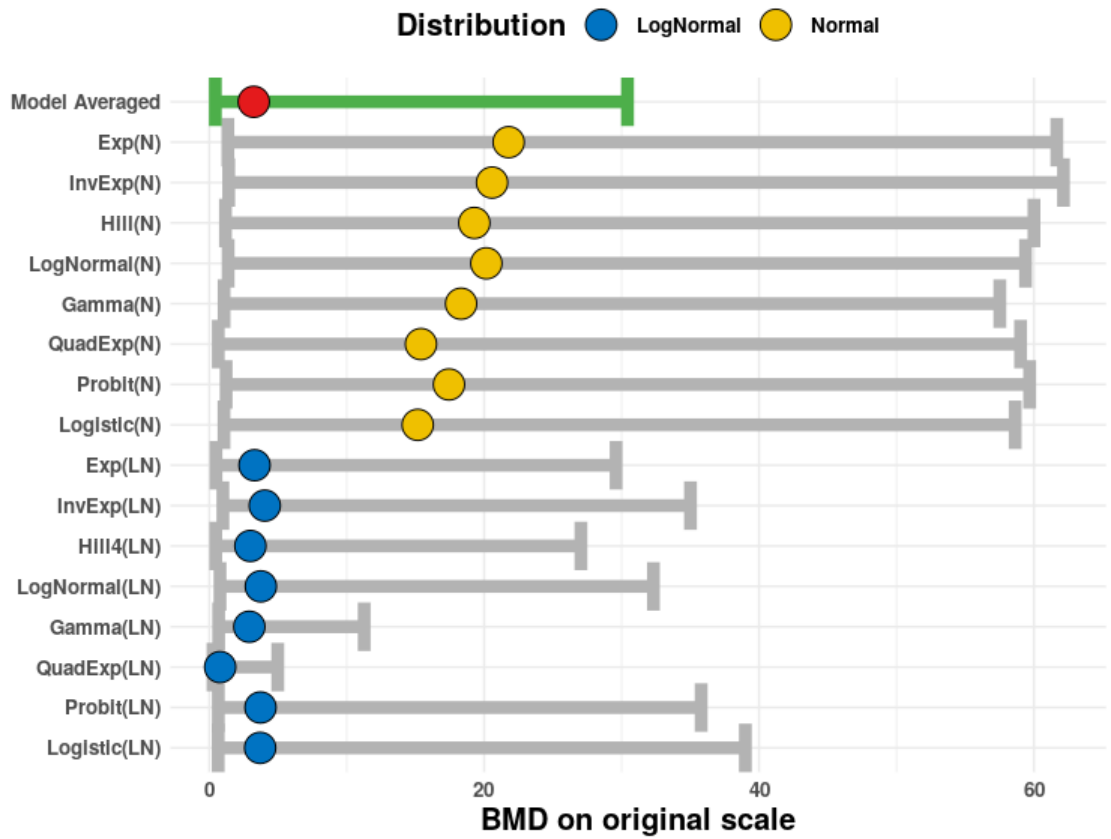
Model Averaged BMD

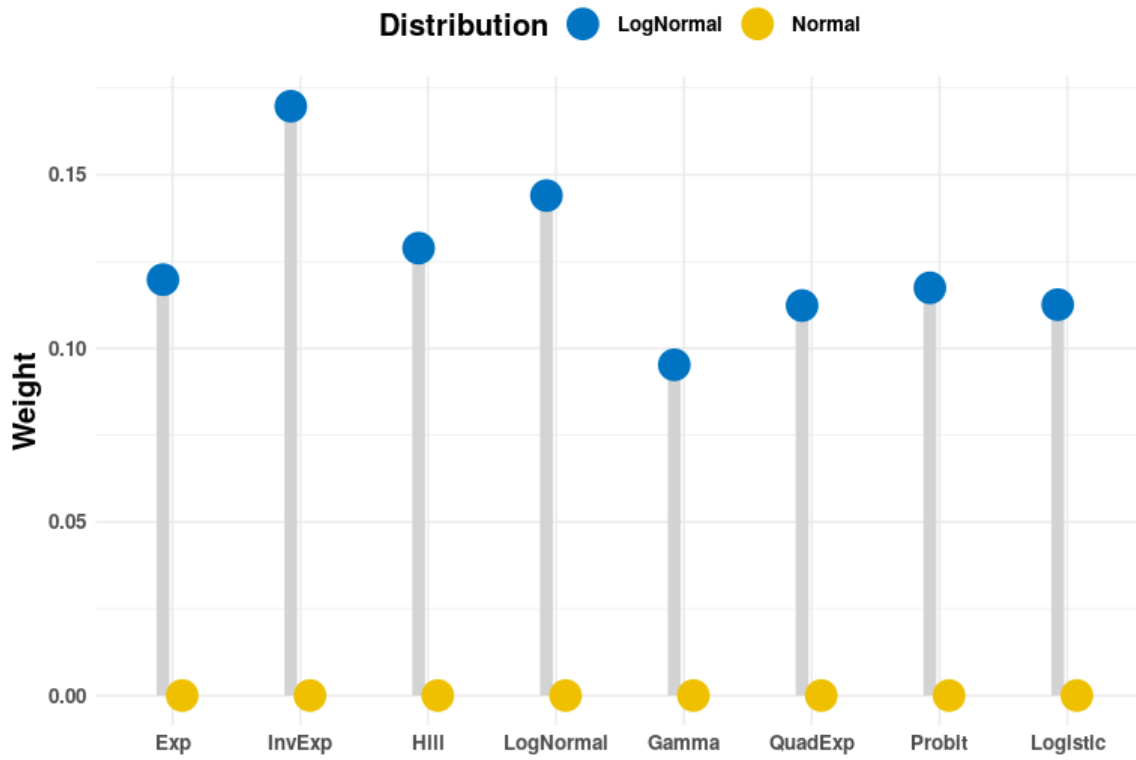
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.443	3.236	30.431

Estimated BMDs per model

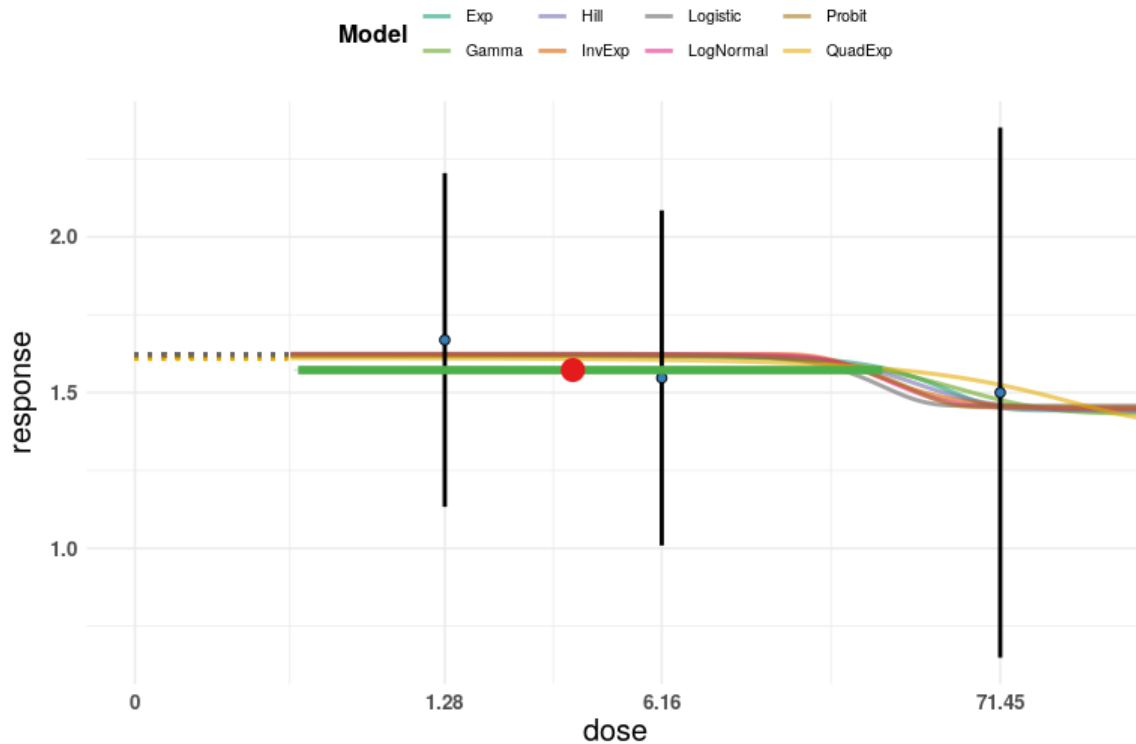
Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_N	1.355	21.783	61.667	0.000	1
IE4_N	1.415	20.576	62.152	0.000	1
H4_N	1.179	19.285	60.004	0.000	1
LN4_N	1.375	20.161	59.392	0.000	1
G4_N	1.077	18.323	57.519	0.000	1
QE4_N	0.656	15.402	59.028	0.000	1
P4_N	1.228	17.442	59.688	0.000	1
L4_N	1.070	15.167	58.636	0.000	1
E4_LN	0.490	3.296	29.600	0.120	1
IE4_LN	0.992	4.041	35.013	0.170	1
H4_LN	0.473	2.991	27.042	0.129	1
LN4_LN	0.782	3.753	32.317	0.144	1
G4_LN	0.683	2.916	11.274	0.095	0
QE4_LN	0.271	0.791	4.984	0.112	1
P4_LN	0.660	3.727	35.788	0.117	0
L4_LN	0.650	3.702	39.006	0.113	1

Plots of Fitted Models

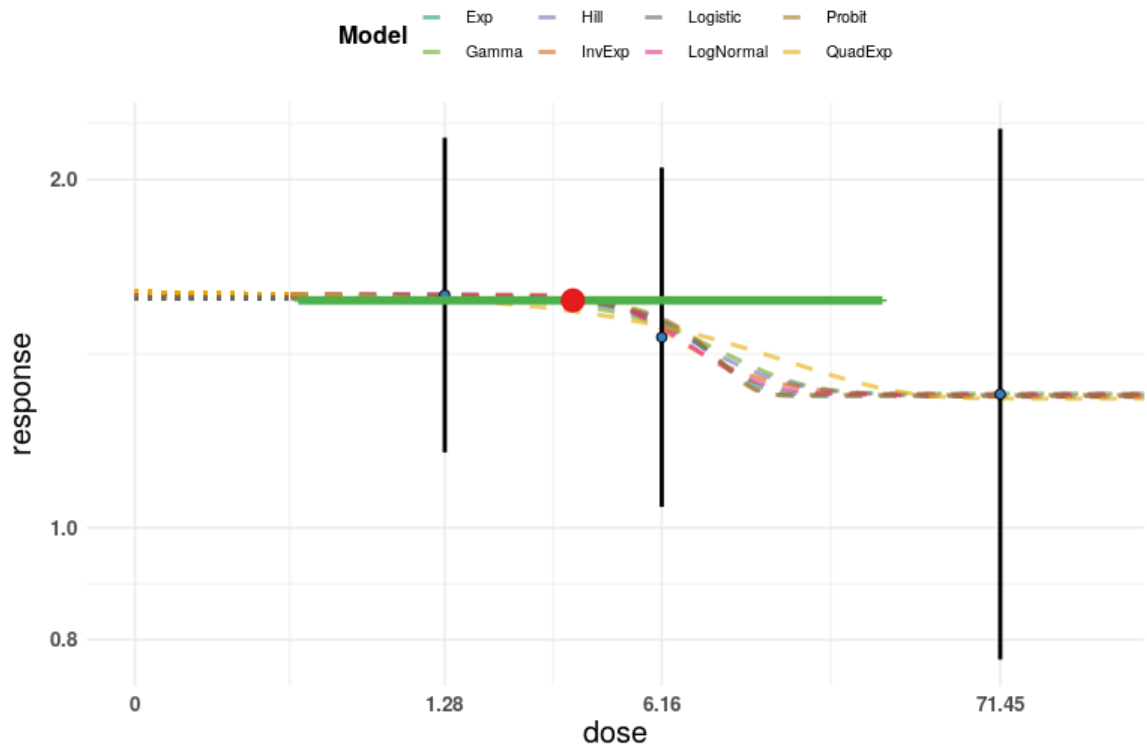




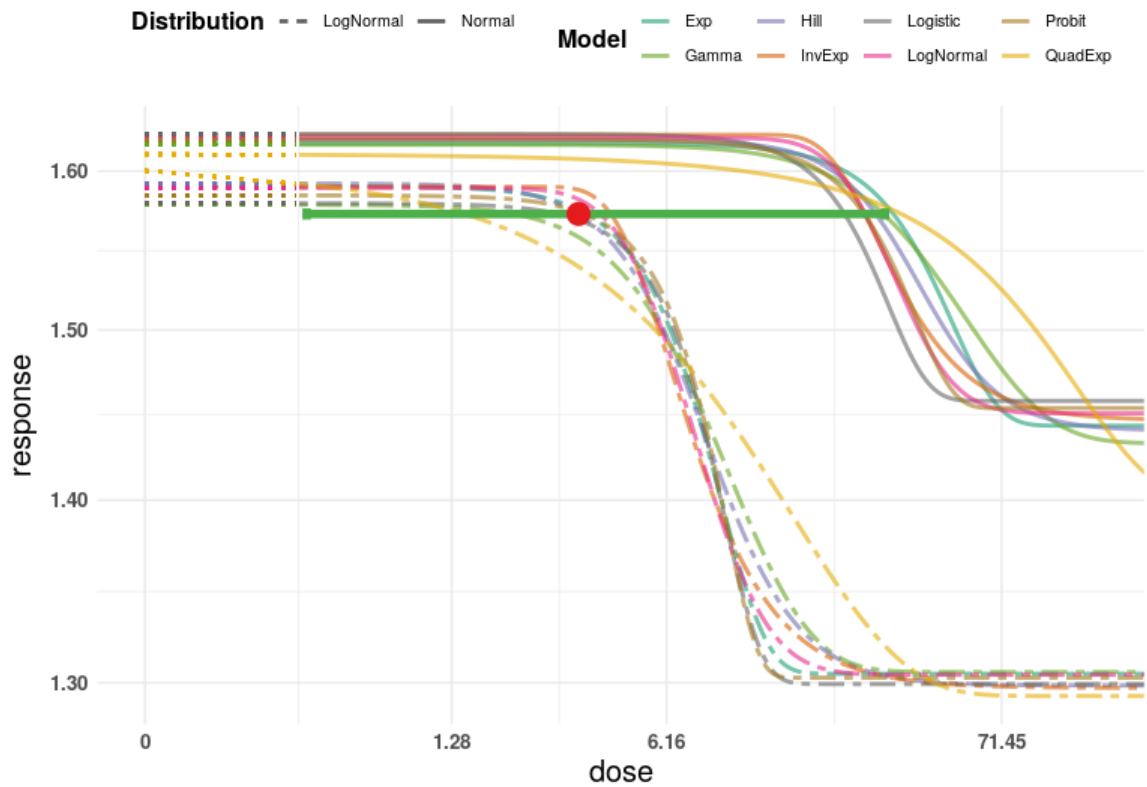
Normal distribution

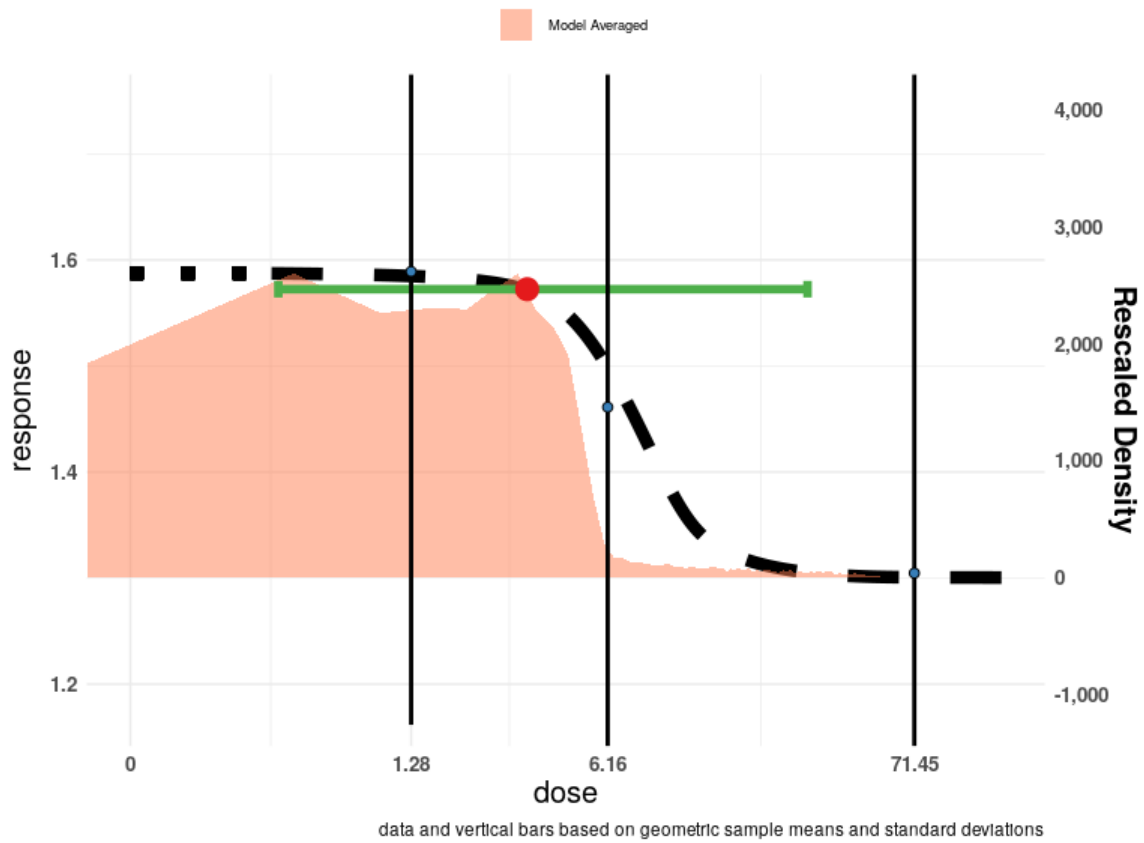


LogNormal distribution



data and vertical bars based on geometric sample means and standard deviations





Siddique et al. (2020) obstruction (lung function), relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for obstruction

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.28	16	279
6.16	30	281
71.45	52	282

The 'Value for CES' is set to 0.00060837.

Extended dose range is not applied.

Informative background prior: min: 0.05448029; the most likely: 0.05734767; max: 0.06021505. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (2022) recommendations since none of the candidate models fit the data sufficiently well, BMD/BMDL > 20 and BMDU/BMDL > 50.

Goodness of Fit

None of the models provide an adequate fit do the data (Bayes factor is 1.57e+02).

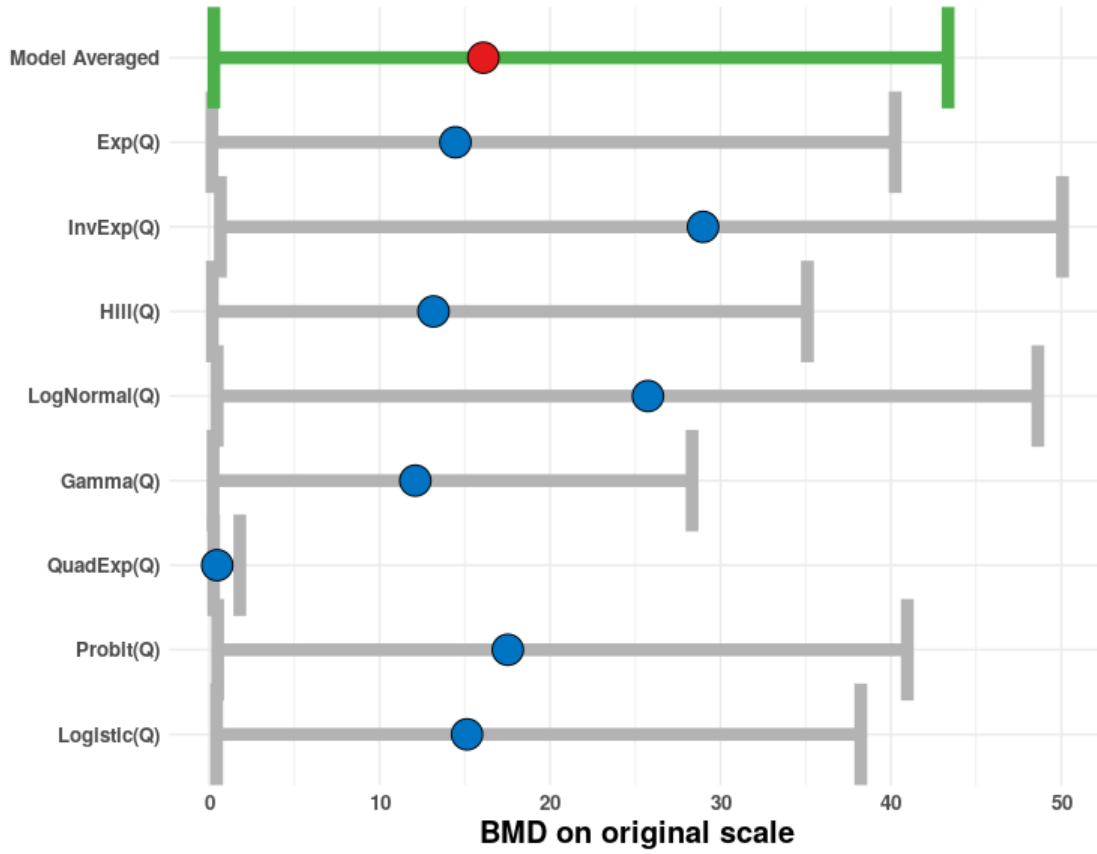
Model Averaged BMD

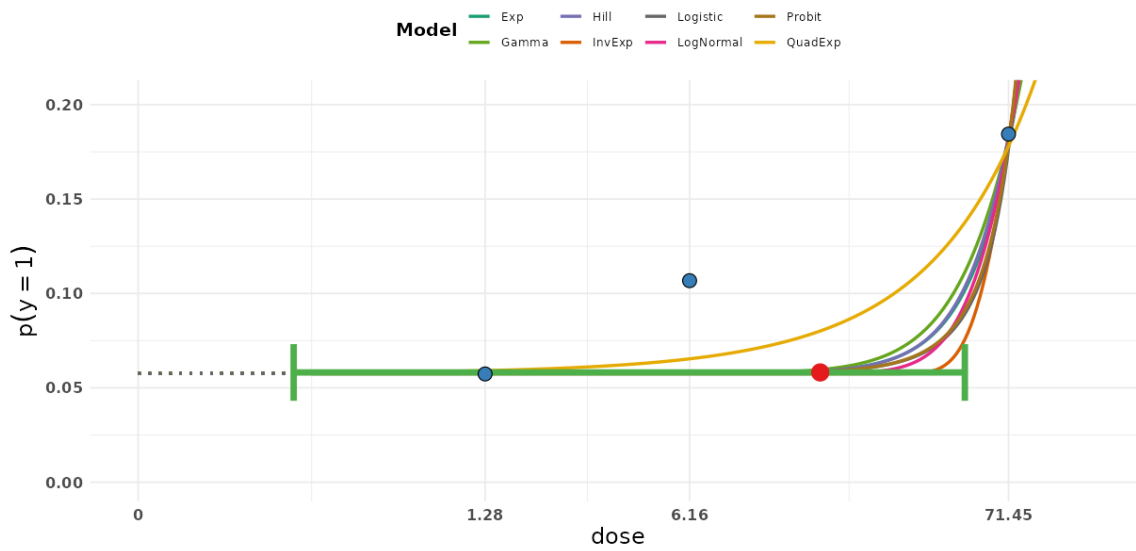
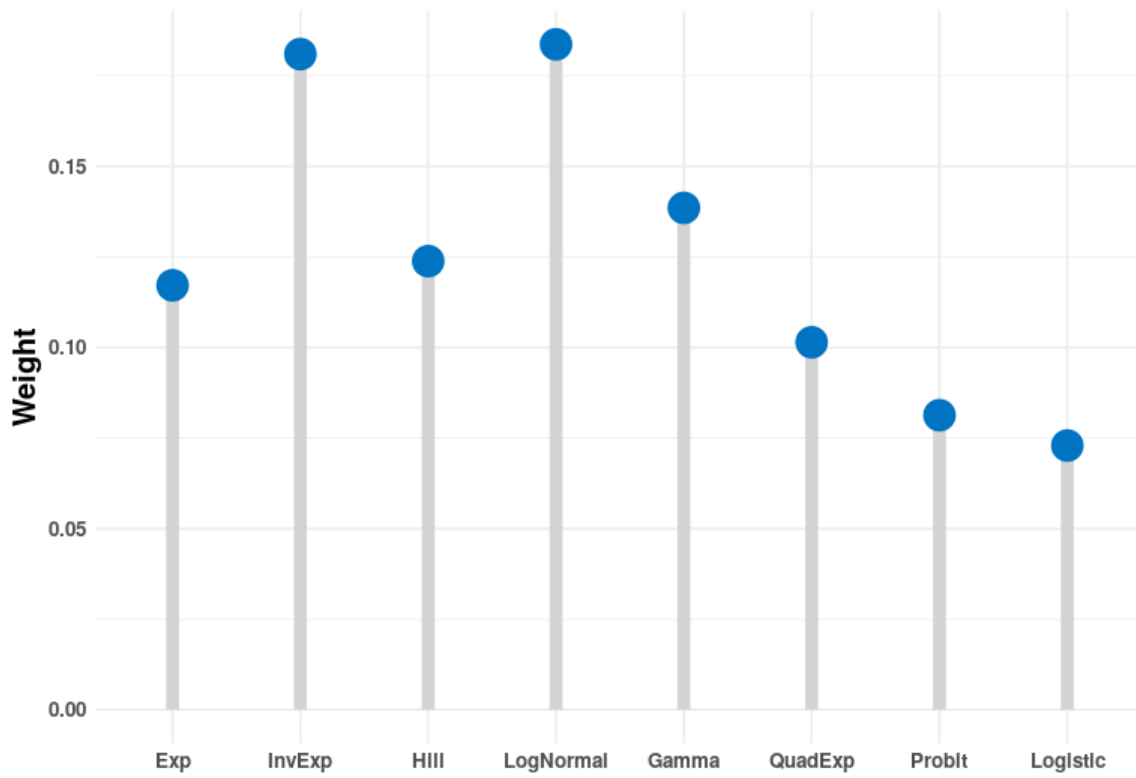
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.274	16.085	43.356

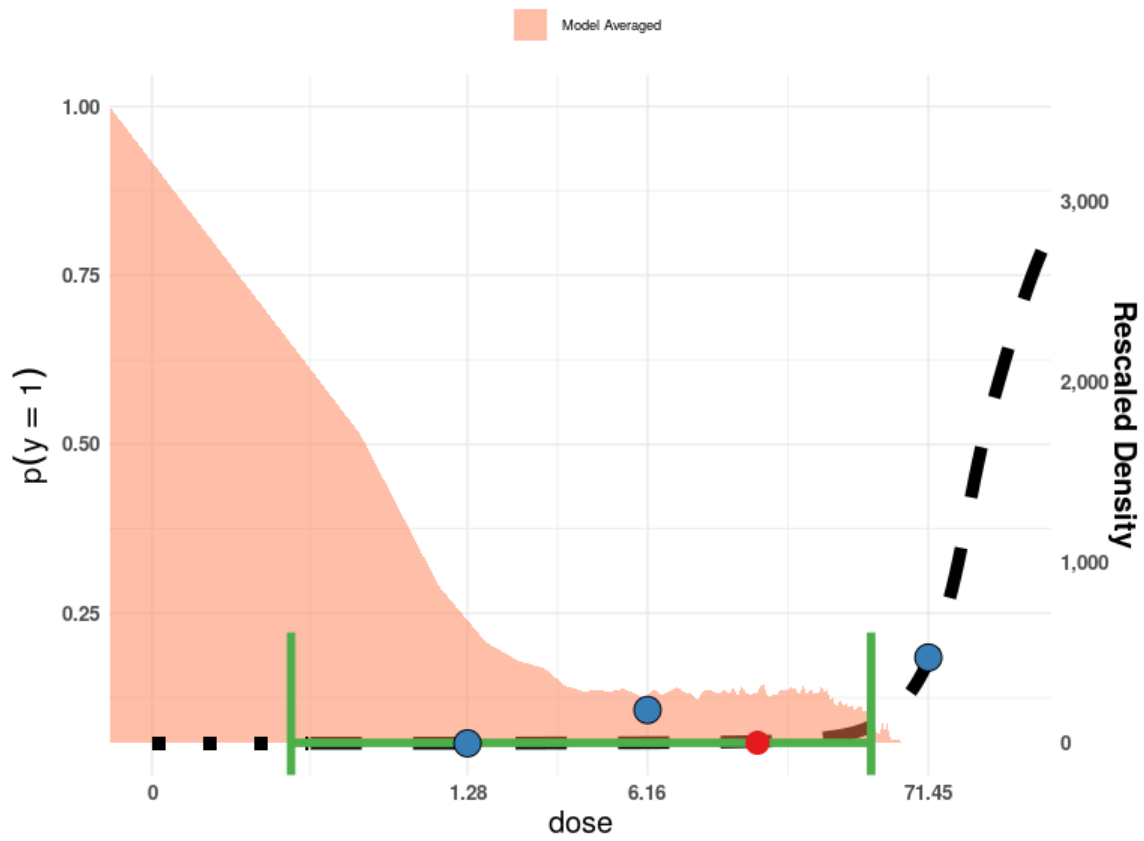
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.163	14.450	40.254	0.117	1
IE4_Q	0.656	28.978	50.070	0.181	0
H4_Q	0.181	13.162	35.104	0.124	1
LN4_Q	0.471	25.746	48.624	0.184	0
G4_Q	0.225	12.093	28.335	0.139	1
QE4_Q	0.261	0.468	1.795	0.101	1
P4_Q	0.496	17.520	40.964	0.081	0
L4_Q	0.435	15.130	38.235	0.073	0

Plots of Fitted Models







Siddique et al. (2020) reversible obstruction (lung function), relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for reversible obstruction

Data used for analysis:

Exposure, µg.kg.bw.per.day	Adj.cases	N
1.28	11	279
6.16	19	281
71.45	39	282

The 'Value for CES' is set to 0.00041045.

Extended dose range is not applied.

Informative background prior: min: 0.03548387; the most likely: 0.03942652; max: 0.04336918. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since BMD/BMDL > 20 and BMDU/BMDL > 50.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 9.78e+00).

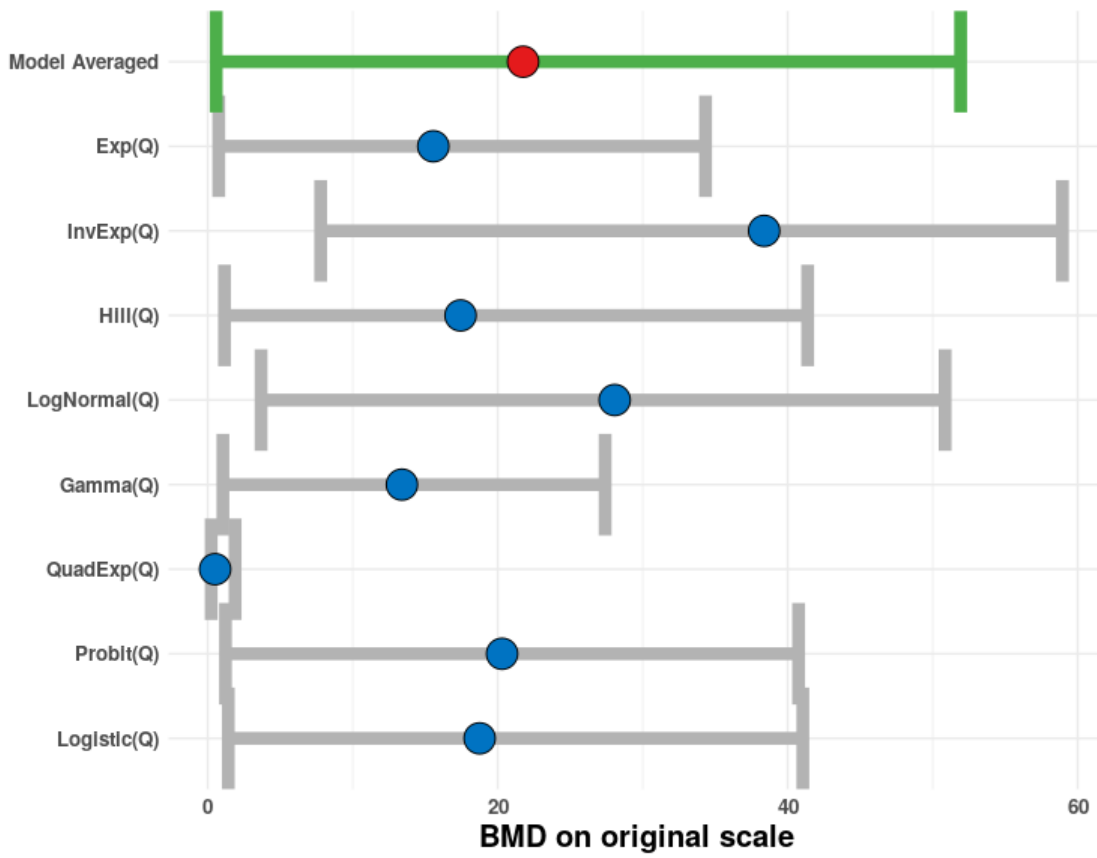
Model Averaged BMD

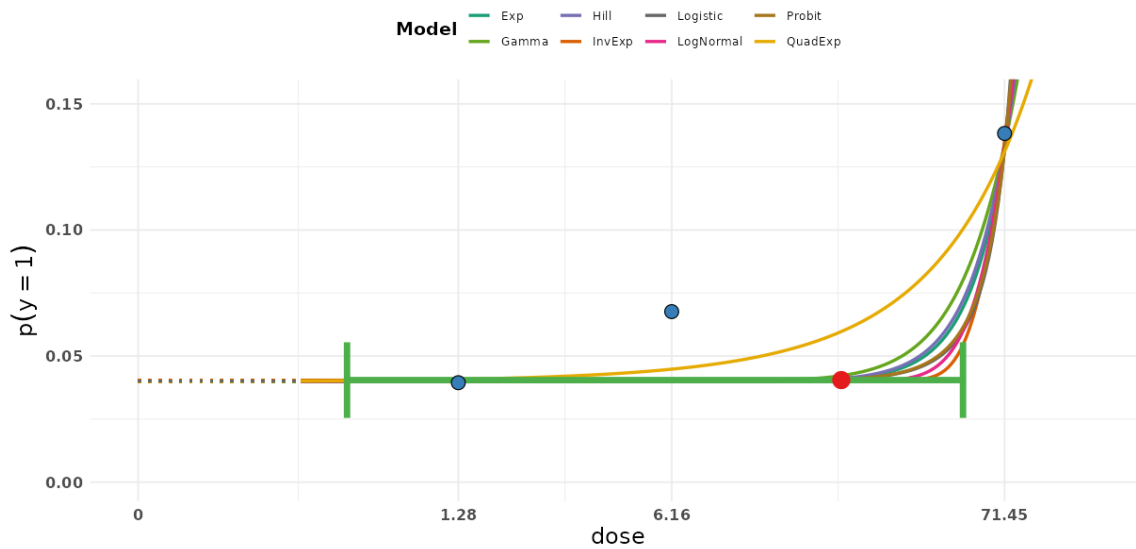
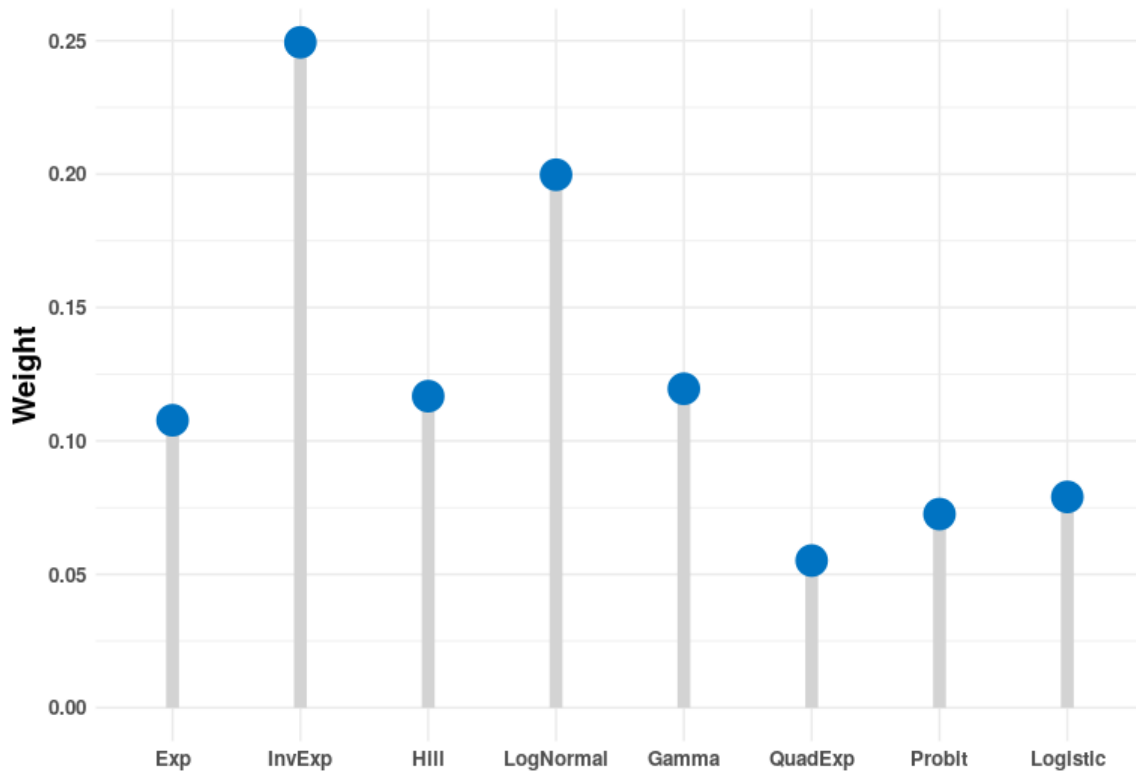
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.584	21.749	51.924

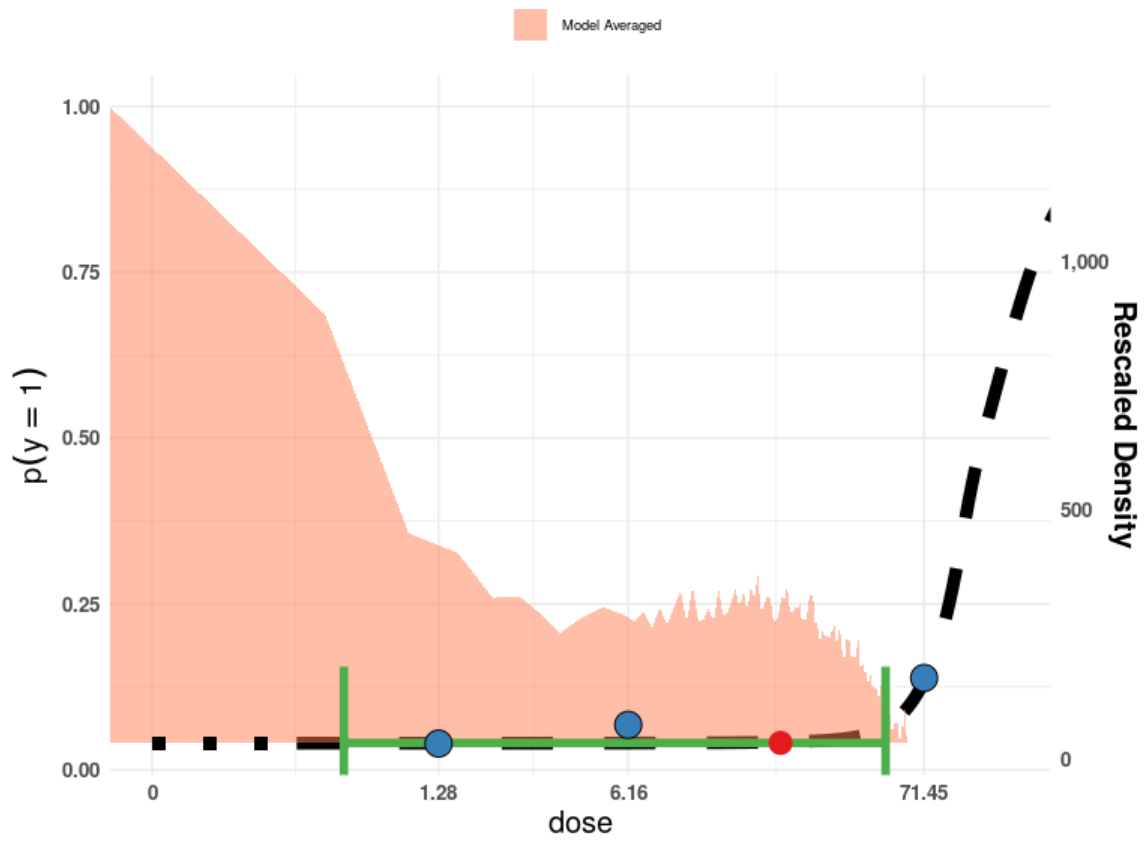
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.758	15.556	34.335	0.108	1
IE4_Q	7.788	38.375	58.948	0.249	1
H4_Q	1.155	17.436	41.375	0.117	1
LN4_Q	3.678	28.066	50.856	0.200	1
G4_Q	1.047	13.393	27.407	0.120	1
QE4_Q	0.239	0.508	1.887	0.055	1
P4_Q	1.223	20.300	40.749	0.073	1
L4_Q	1.419	18.753	41.043	0.079	1

Plots of Fitted Models







Steinmaus et al. (2013) bladder cancer, relative BMR 1%

Exposure: lifetime average, all years, based on arsenic water concentrations and water intake of 1.9L (included only in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases. for bladder cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.64	34	142031
1.71	29	132891
4.05	62	99844
5.63	107	75234

The 'Value for CES' is set to 2.39e-06.

Extended dose range is applied.

Informative background prior: min: 0.00023699; the most likely: 0.00023938; max: 0.00024178. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.42e-03).

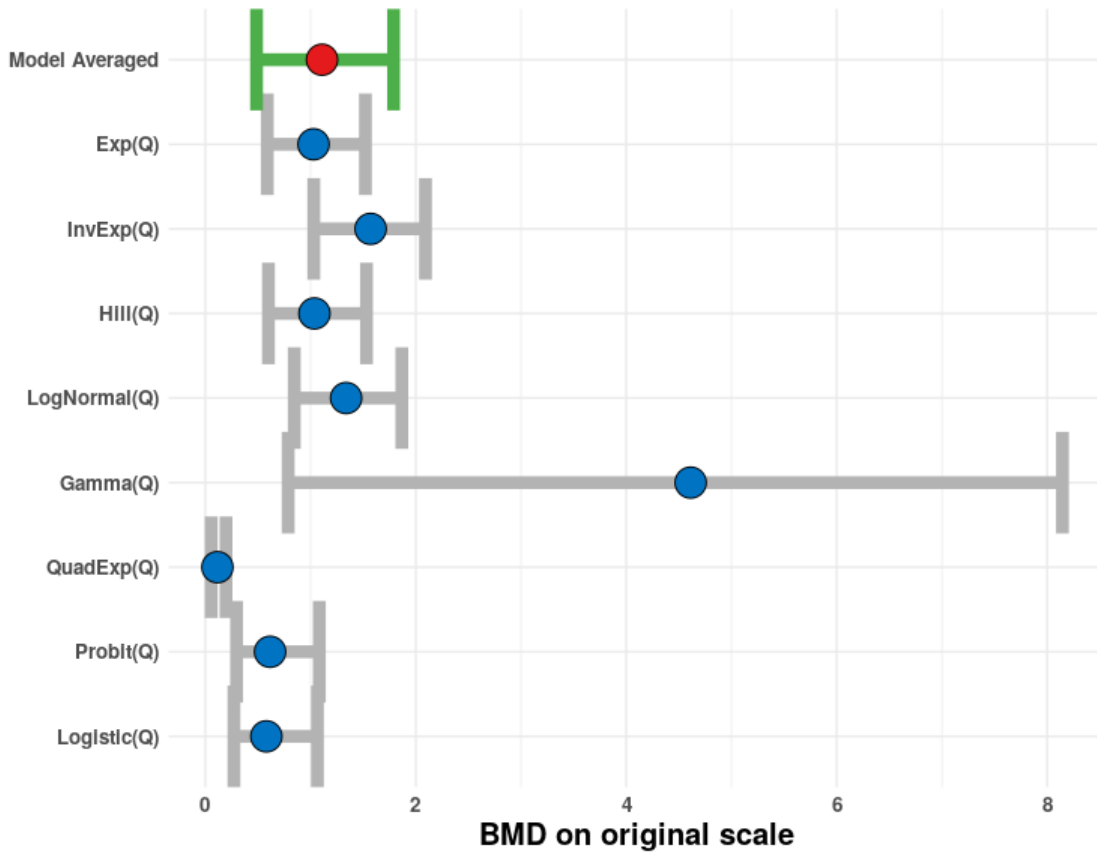
Model Averaged BMD

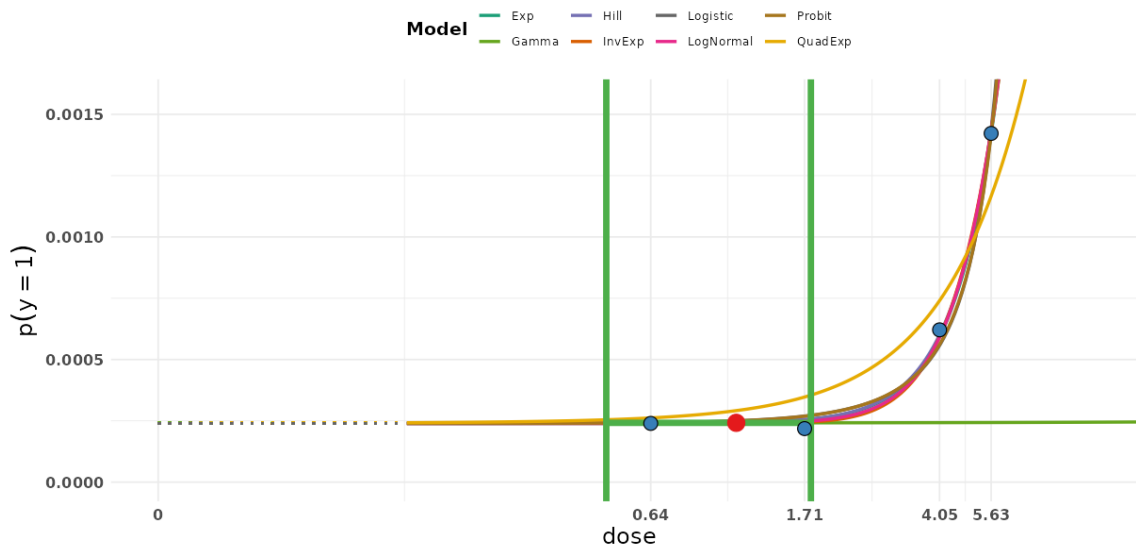
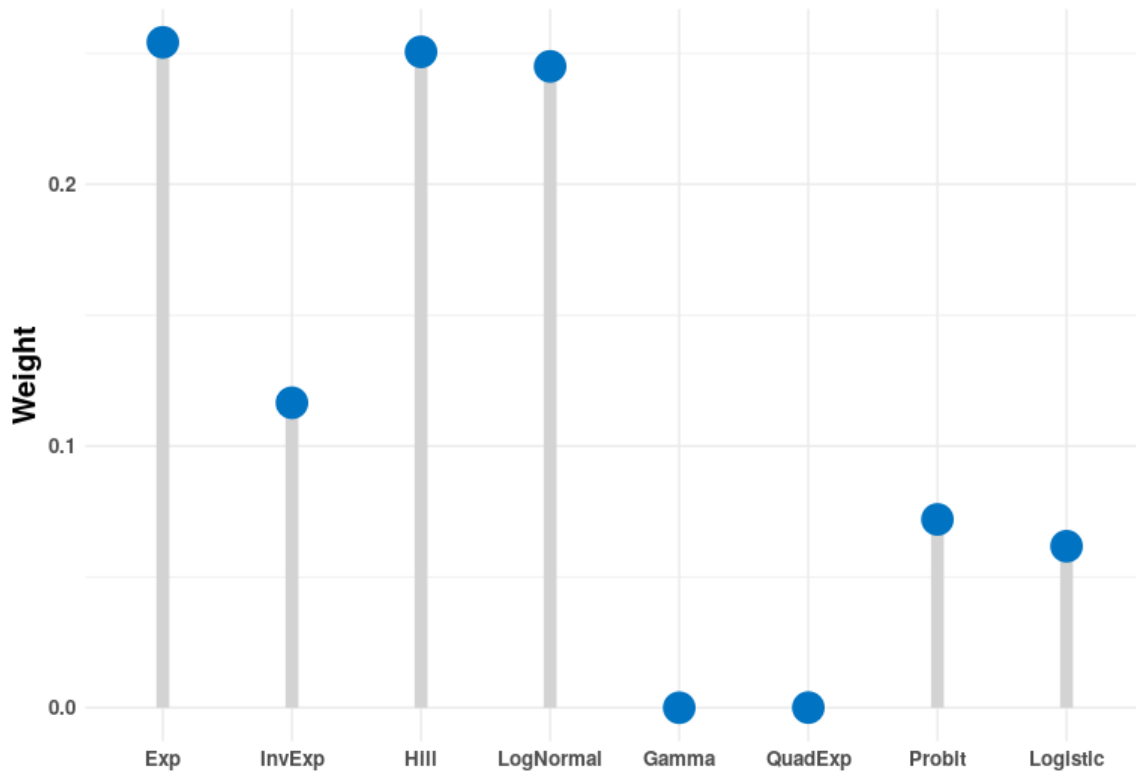
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.487	1.109	1.789

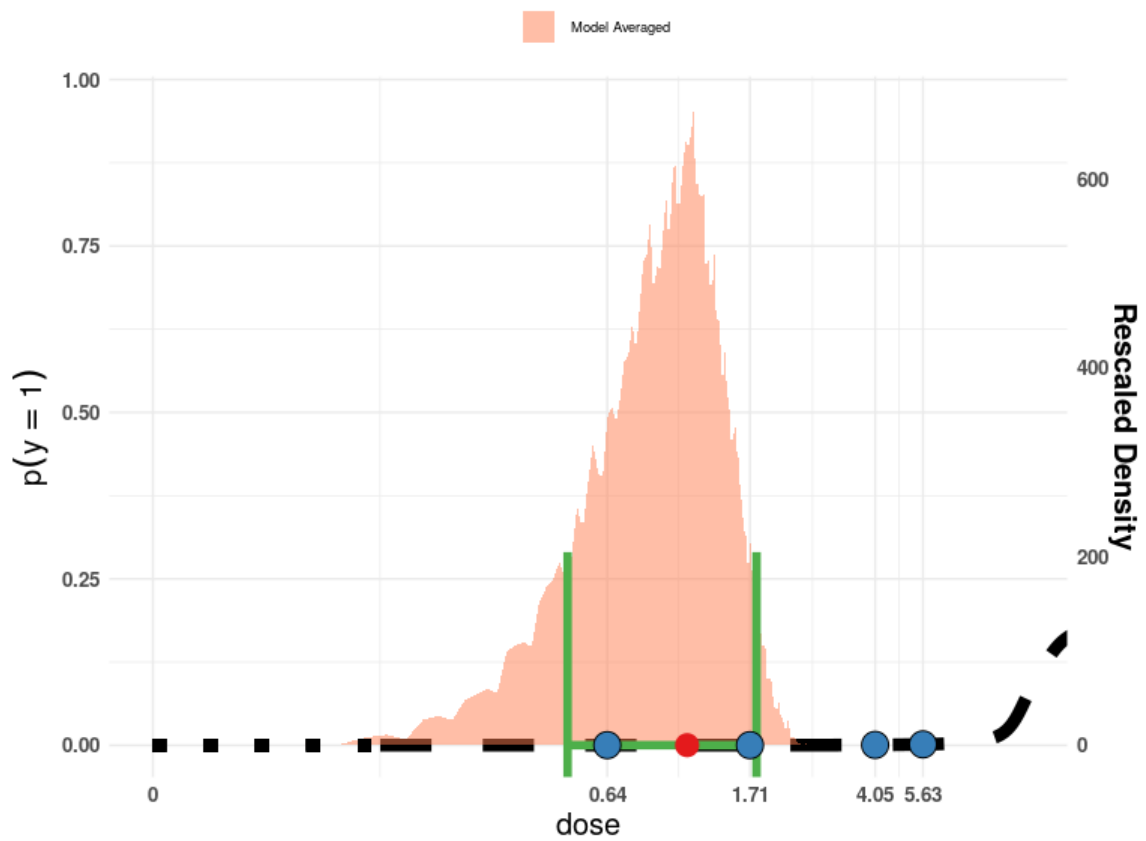
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.589	1.028	1.522	0.254	1
IE4_Q	1.031	1.571	2.093	0.117	1
H4_Q	0.600	1.037	1.532	0.251	1
LN4_Q	0.845	1.338	1.868	0.245	1
G4_Q	0.788	4.612	8.146	0.000	0
QE4_Q	0.056	0.115	0.197	0.000	1
P4_Q	0.297	0.615	1.084	0.072	1
L4_Q	0.272	0.580	1.066	0.062	1

Plots of Fitted Models







Steinmaus et al. (2013) bladder cancer, relative BMR 1%

Exposure: lifetime average, all years, based on arsenic daily intakes (the preferred exposure estimate for the study)

Data Description

The endpoint to be analyzed is: Adj.cases for bladder cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.58	32	138516
1.55	34	136406
3.46	76	108281
4.67	90	66797

The 'Value for CES' is set to 2.31e-06.

Extended dose range is applied.

Informative background prior: min: 0.00022871; the most likely: 0.00023102; max: 0.00023333. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.68e-03).

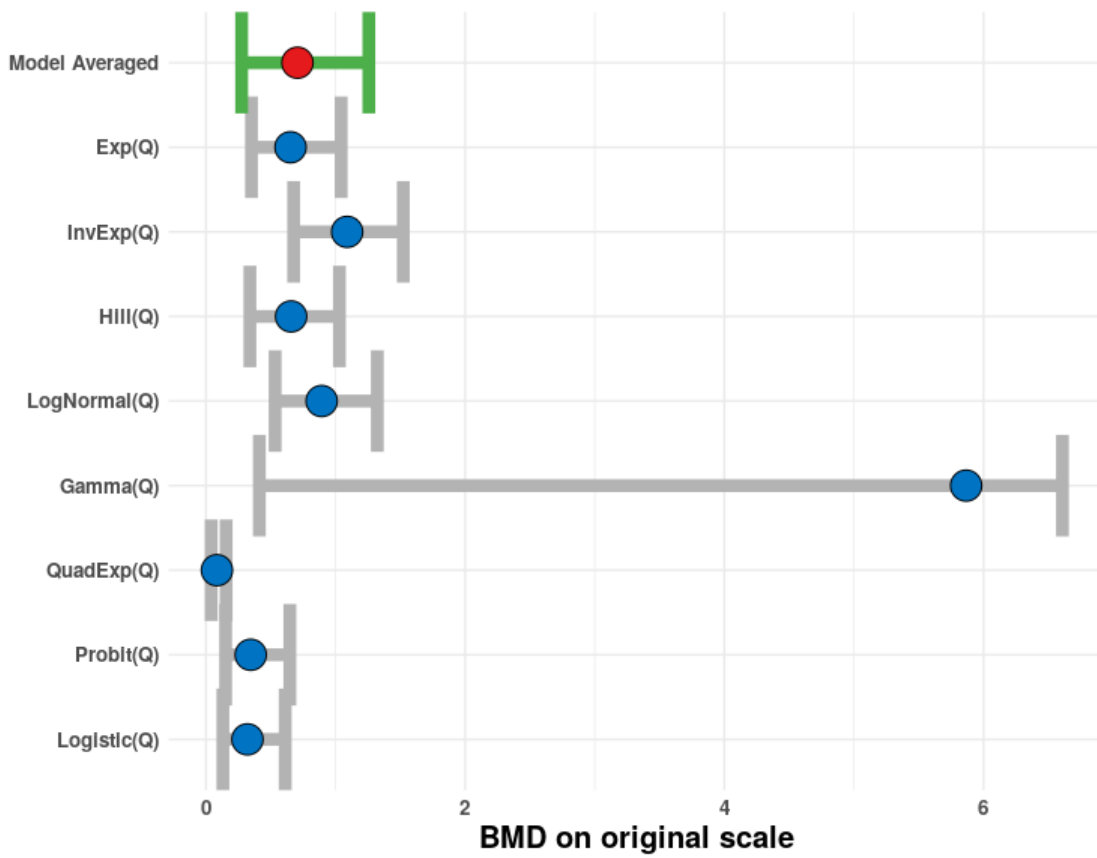
Model Averaged BMD

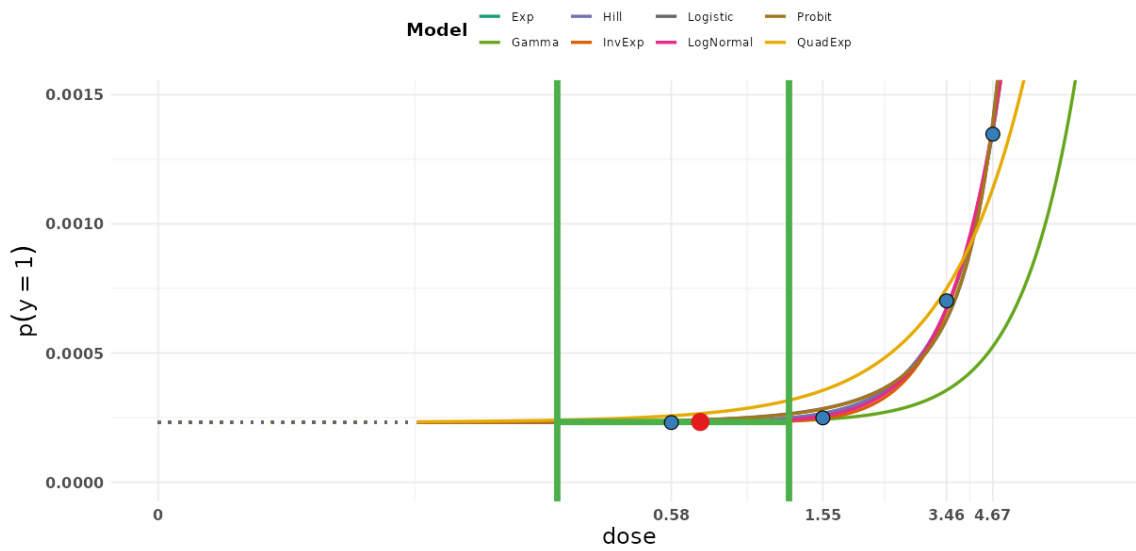
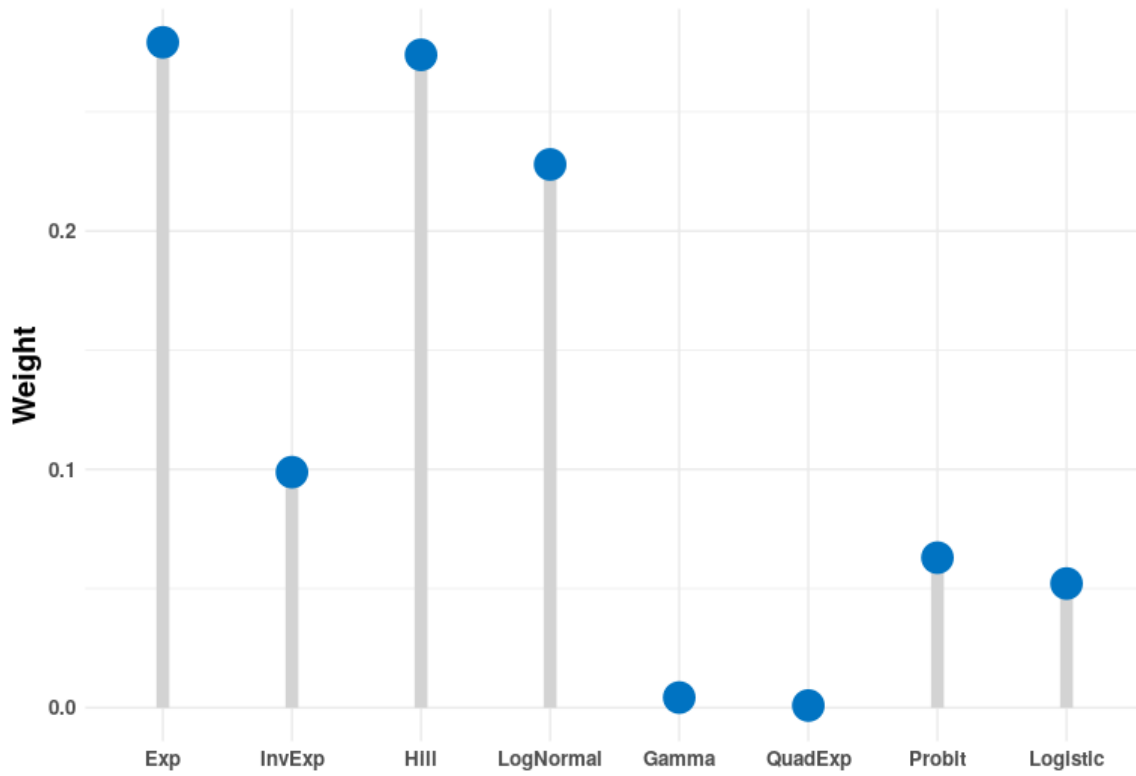
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.275	0.706	1.257

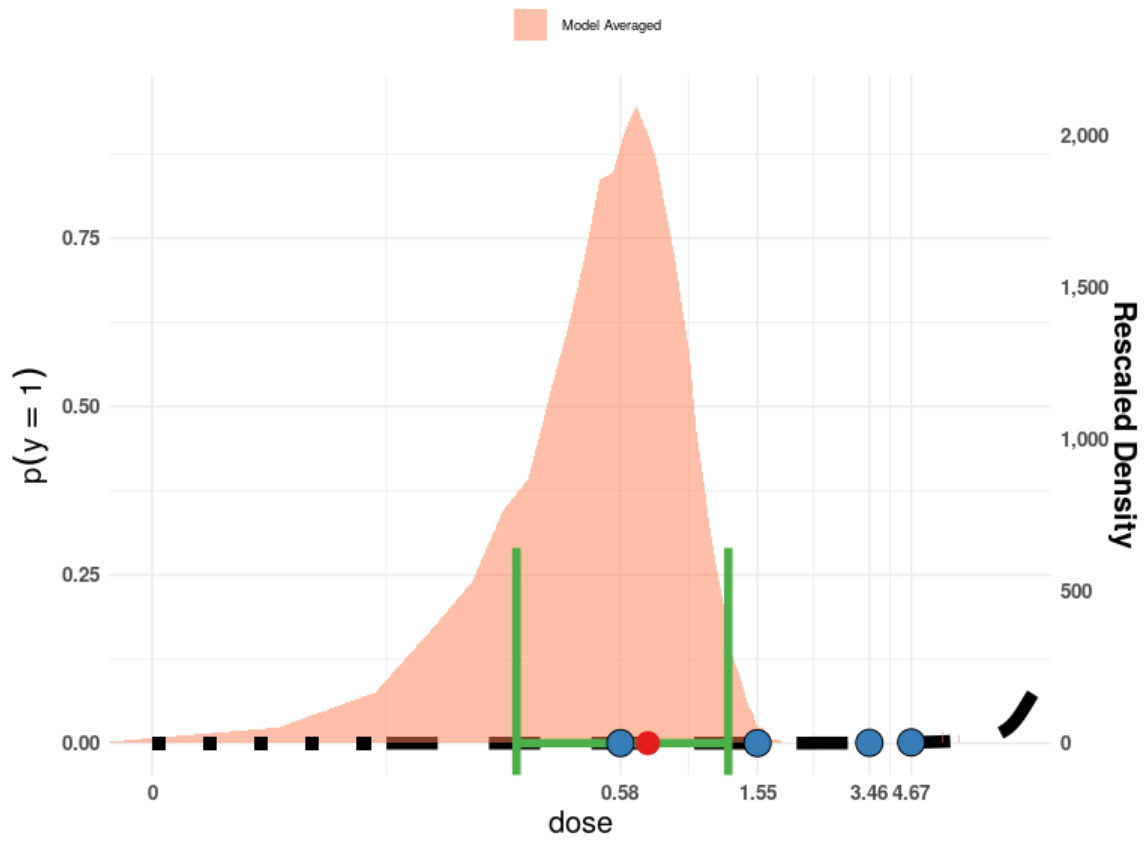
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.351	0.652	1.043	0.279	1
IE4_Q	0.677	1.089	1.523	0.099	1
H4_Q	0.339	0.657	1.030	0.274	1
LN4_Q	0.534	0.893	1.322	0.228	1
G4_Q	0.412	5.866	6.610	0.004	0
QE4_Q	0.040	0.085	0.156	0.001	1
P4_Q	0.152	0.345	0.647	0.063	1
L4_Q	0.131	0.320	0.612	0.052	1

Plots of Fitted Models







Steinmaus et al. (2013) bladder cancer, relative BMR 1%

Exposure: lifetime average before 1971, based on arsenic water concentrations and water intake of 1.9L (included only in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases for bladder cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.44	27	140802
1.66	36	135849
6.07	73	97642
9.38	95	75708

The 'Value for CES' is set to 1.92e-06.

Extended dose range is applied.

Informative background prior: min: 0.00018984; the most likely: 0.00019176; max: 0.00019368. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.85e-03).

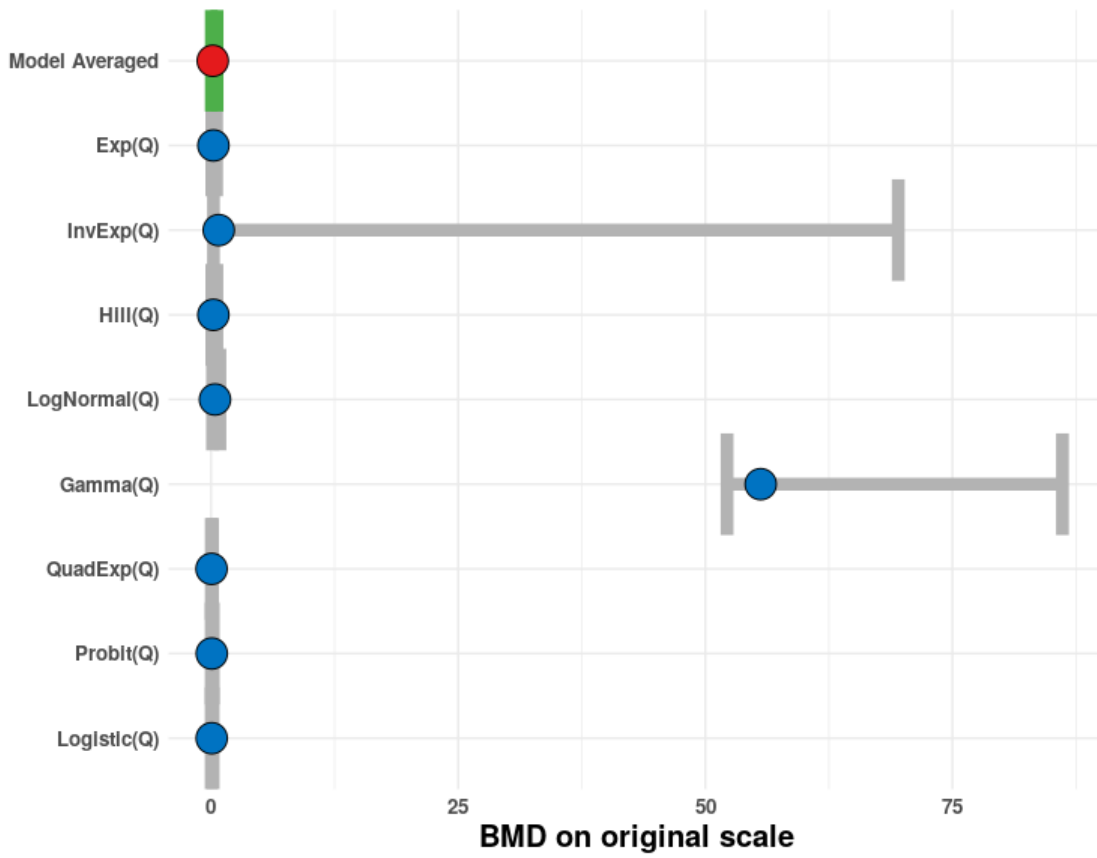
Model Averaged BMD

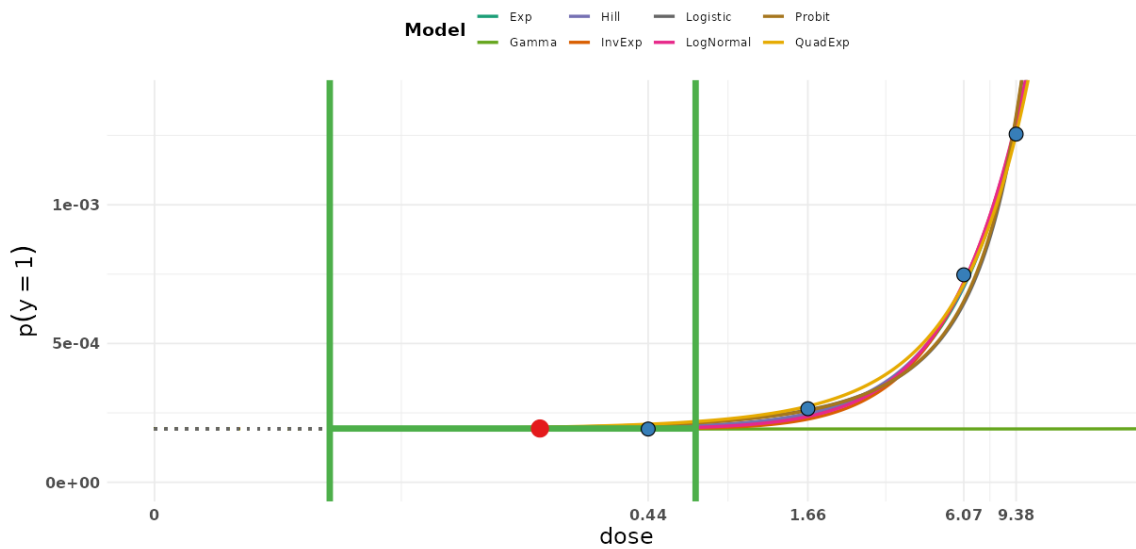
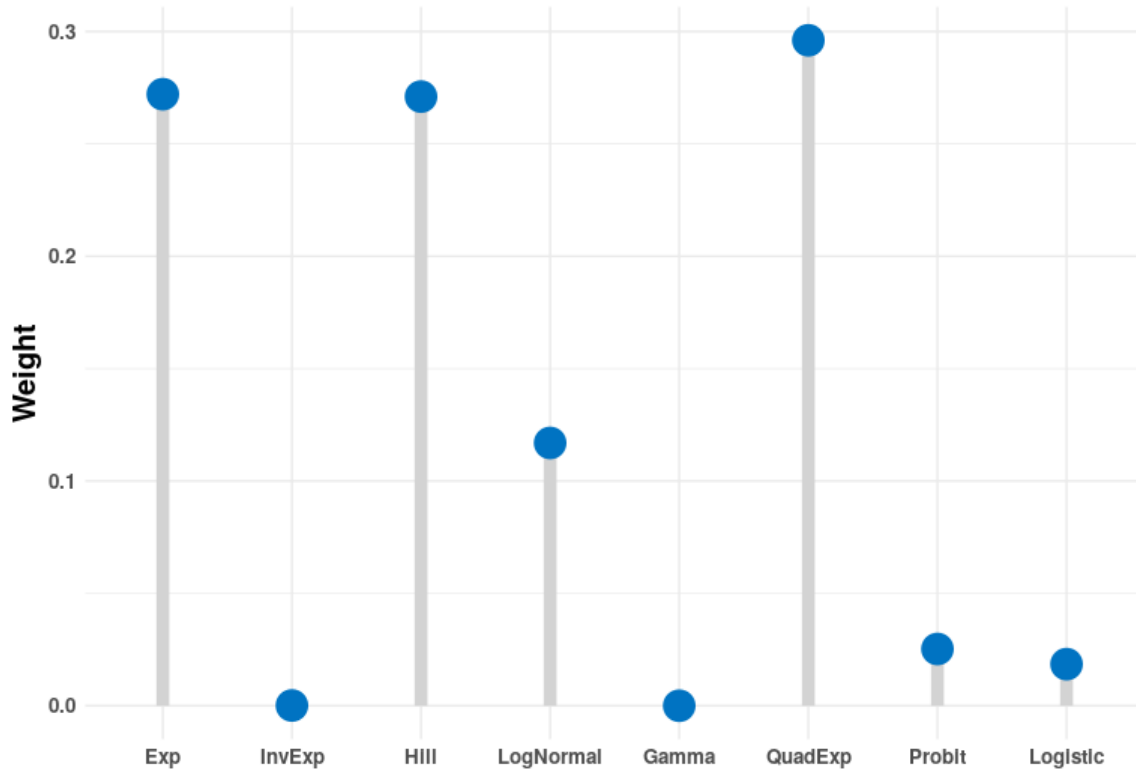
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.031	0.175	0.609

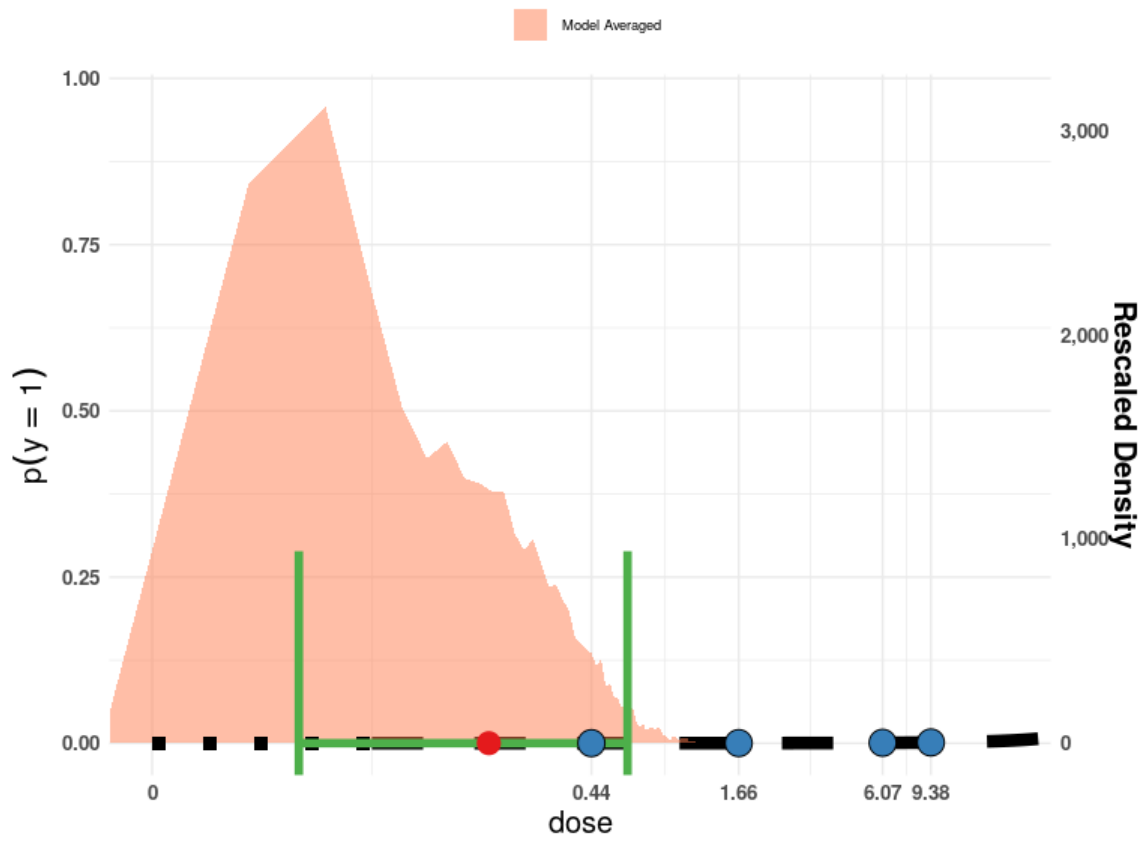
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.080	0.242	0.566	0.272	1
IE4_Q	0.245	0.779	69.518	0.000	0
H4_Q	0.079	0.236	0.593	0.271	1
LN4_Q	0.149	0.400	0.897	0.117	1
G4_Q	52.201	55.603	86.128	0.000	0
QE4_Q	0.026	0.054	0.150	0.296	1
P4_Q	0.018	0.074	0.227	0.025	1
L4_Q	0.017	0.067	0.209	0.019	1

Plots of Fitted Models







Steinmaus et al. (2013) bladder cancer, relative BMR 1%

Exposure: lifetime average before 1971, based on arsenic daily intakes (included only in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases for bladder cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.44	30	140802
1.57	36	136557
5.18	74	108962
7.79	92	63679

The 'Value for CES' is set to 2.13e-06.

Extended dose range is applied.

Informative background prior: min: 0.00020241; the most likely: 0.00021307; max: 0.00022372. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.40e-03).

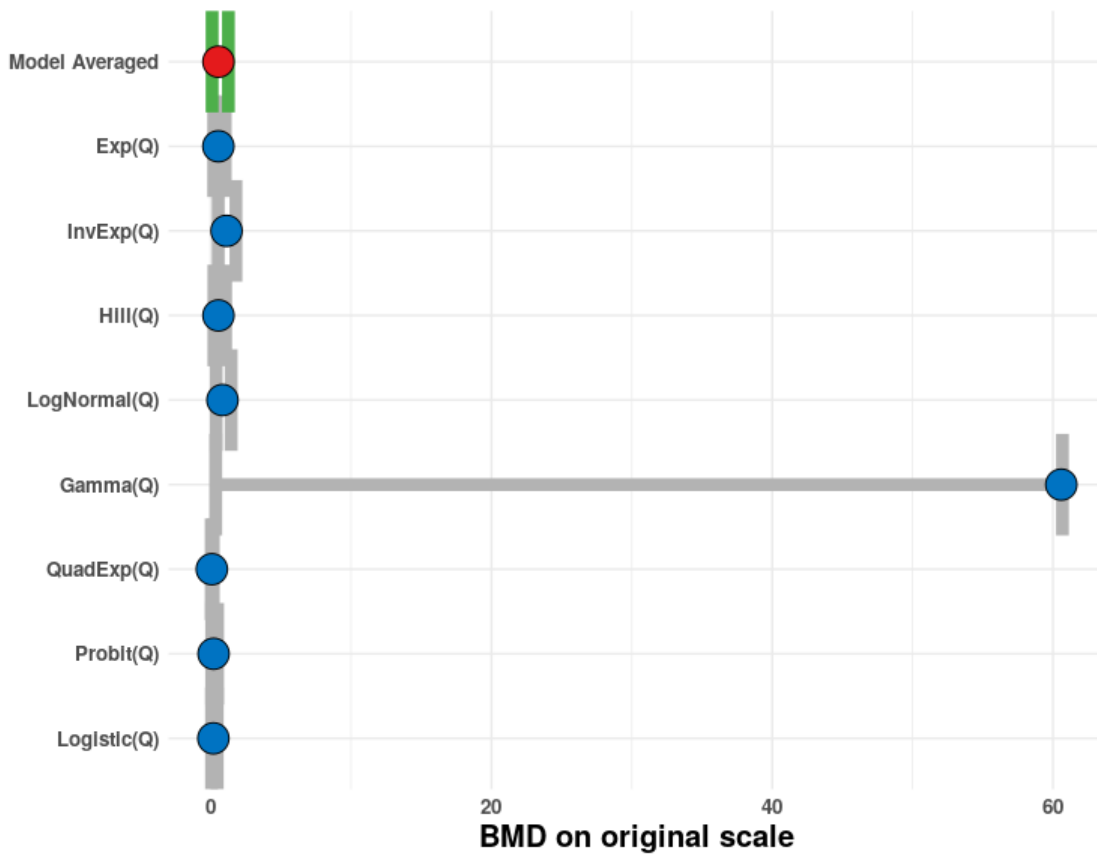
Model Averaged BMD

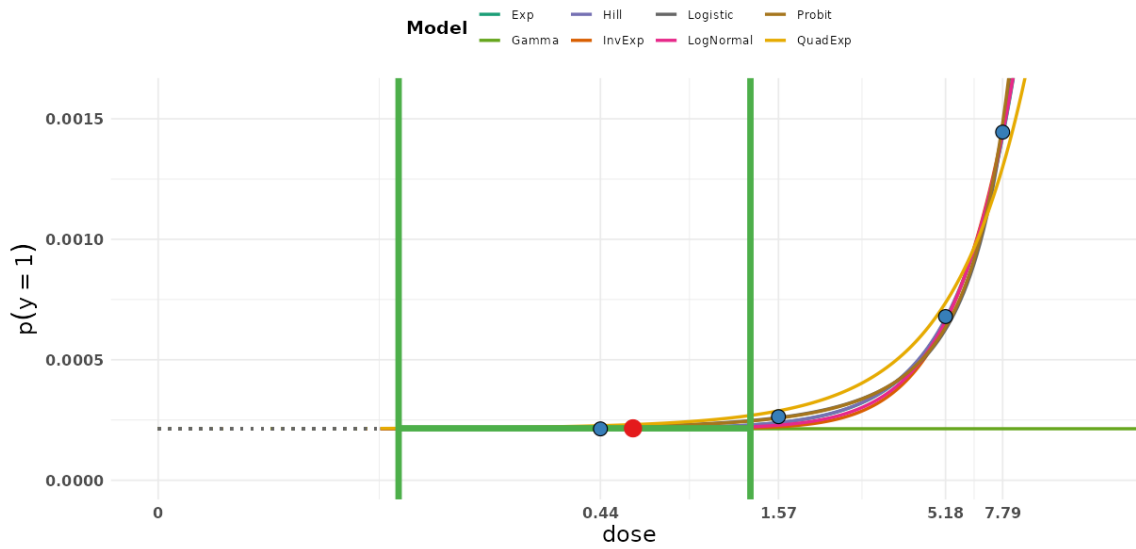
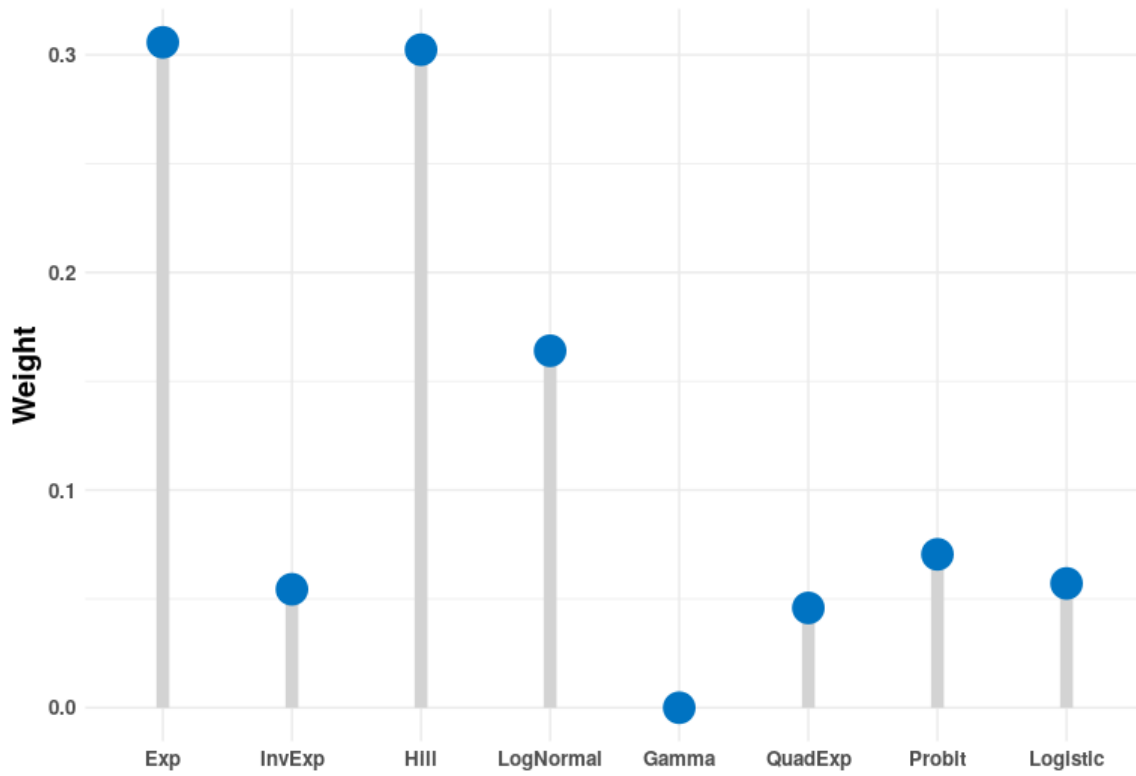
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.1	0.55	1.261

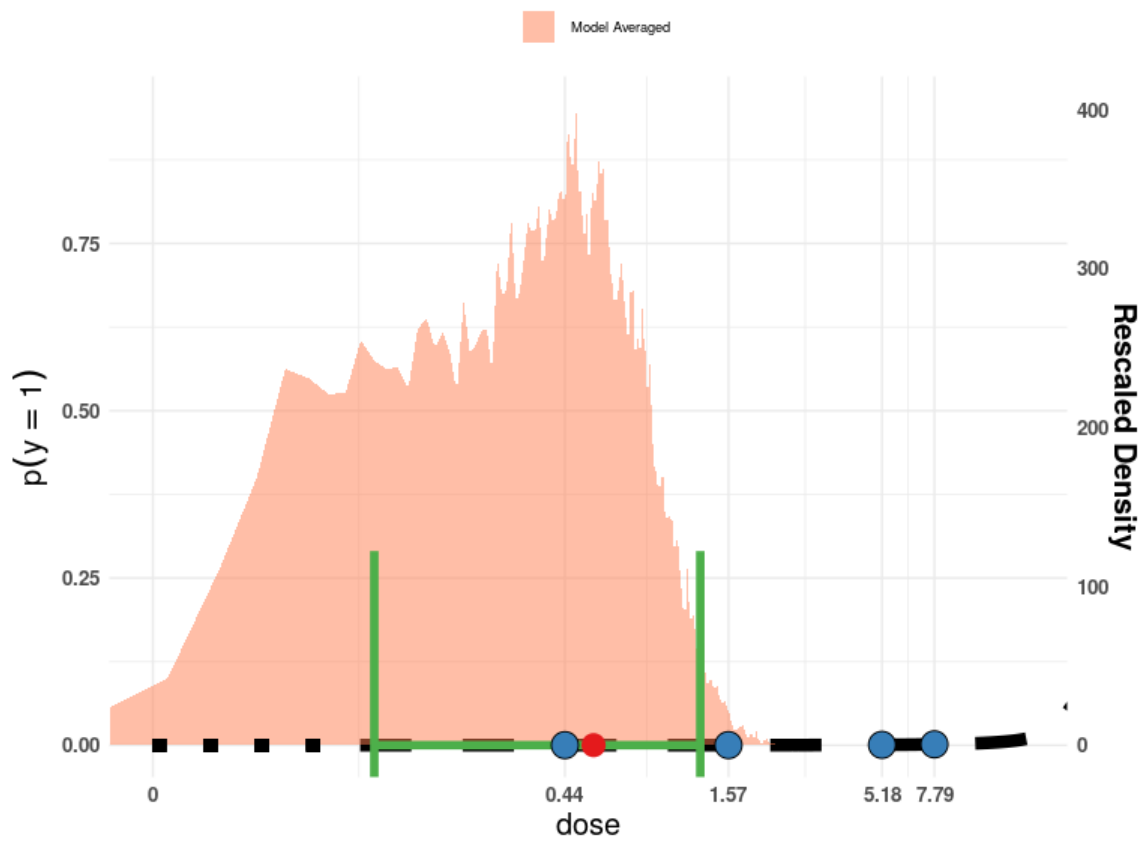
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.209	0.546	1.037	0.306	1
IE4_Q	0.538	1.128	1.799	0.054	1
H4_Q	0.226	0.552	1.065	0.302	1
LN4_Q	0.391	0.839	1.457	0.164	1
G4_Q	0.356	60.593	60.676	0.000	0
QE4_Q	0.036	0.081	0.185	0.046	1
P4_Q	0.067	0.206	0.490	0.070	1
L4_Q	0.059	0.190	0.467	0.057	1

Plots of Fitted Models







Steinmaus et al. (2013) lung cancer, relative BMR 1%

Exposure: lifetime average, all years, based on arsenic water concentrations and water intake of 1.9L (included only in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.64	64	142031
1.71	58	132891
4.05	76	99844
5.63	107	75234

The 'Value for CES' is set to 4.51e-06.

Extended dose range is applied.

Informative background prior: min: 0.00044610; the most likely: 0.00045061; max: 0.00045511. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.72e-03).

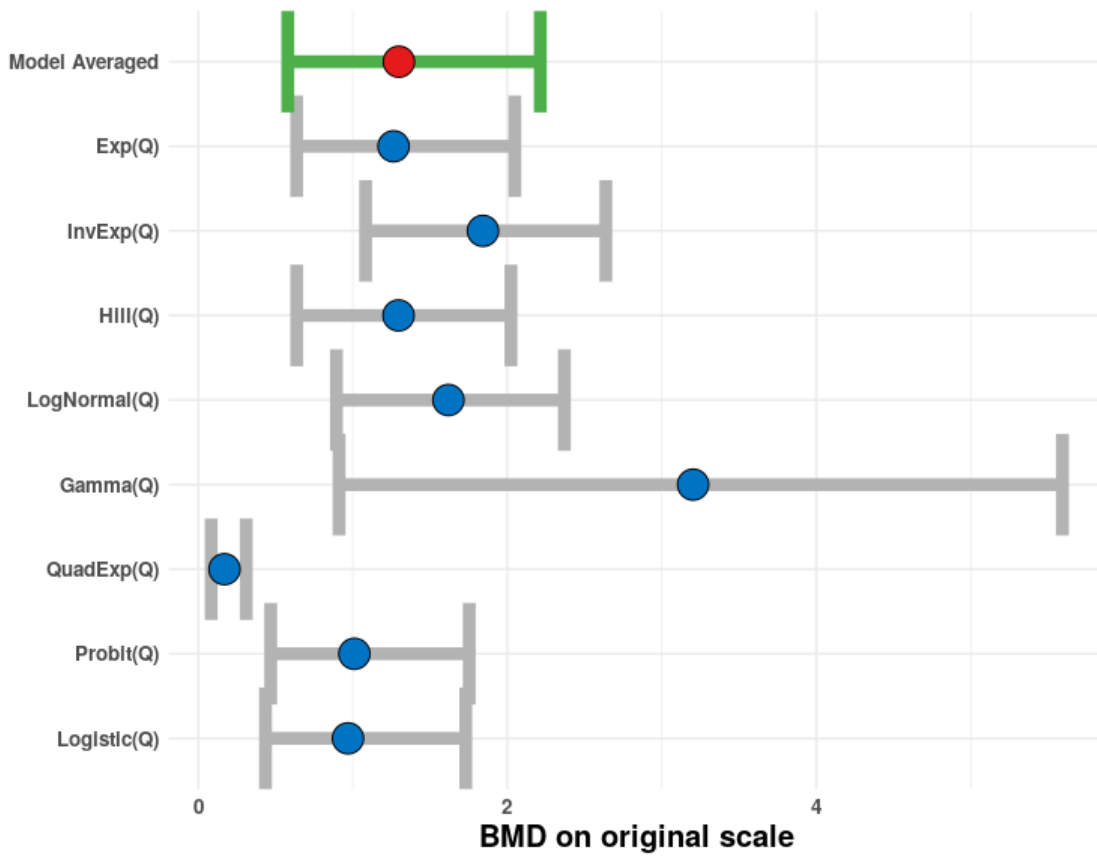
Model Averaged BMD

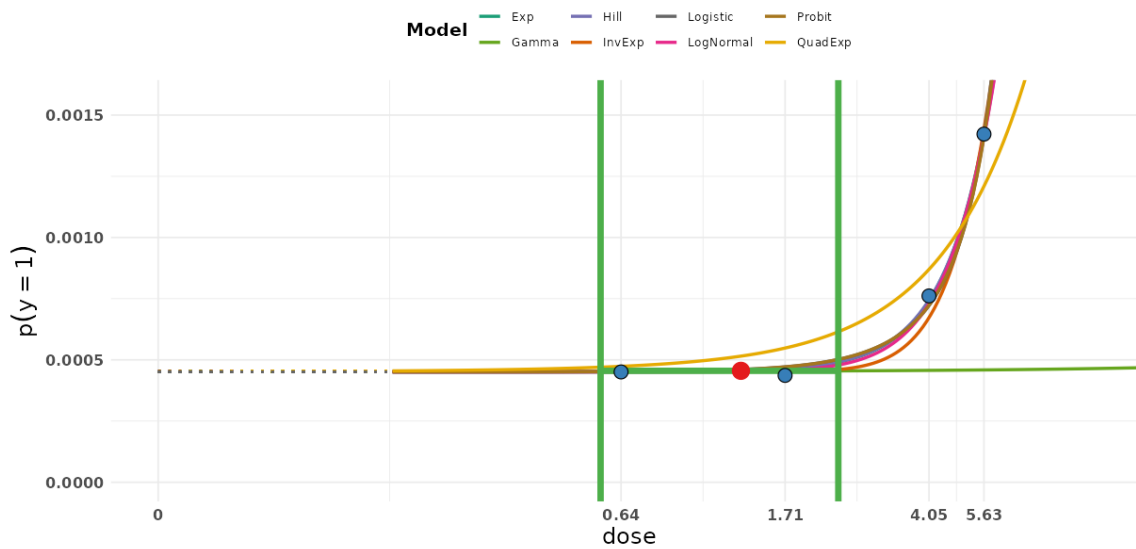
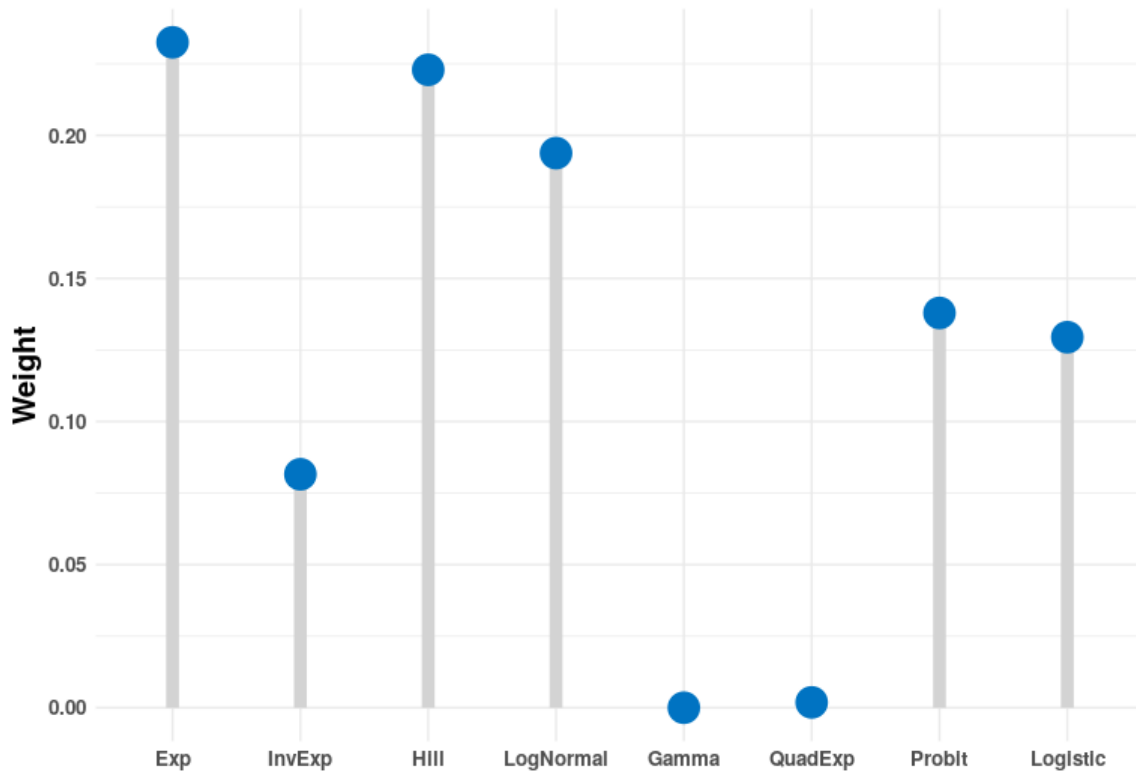
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.579	1.299	2.214

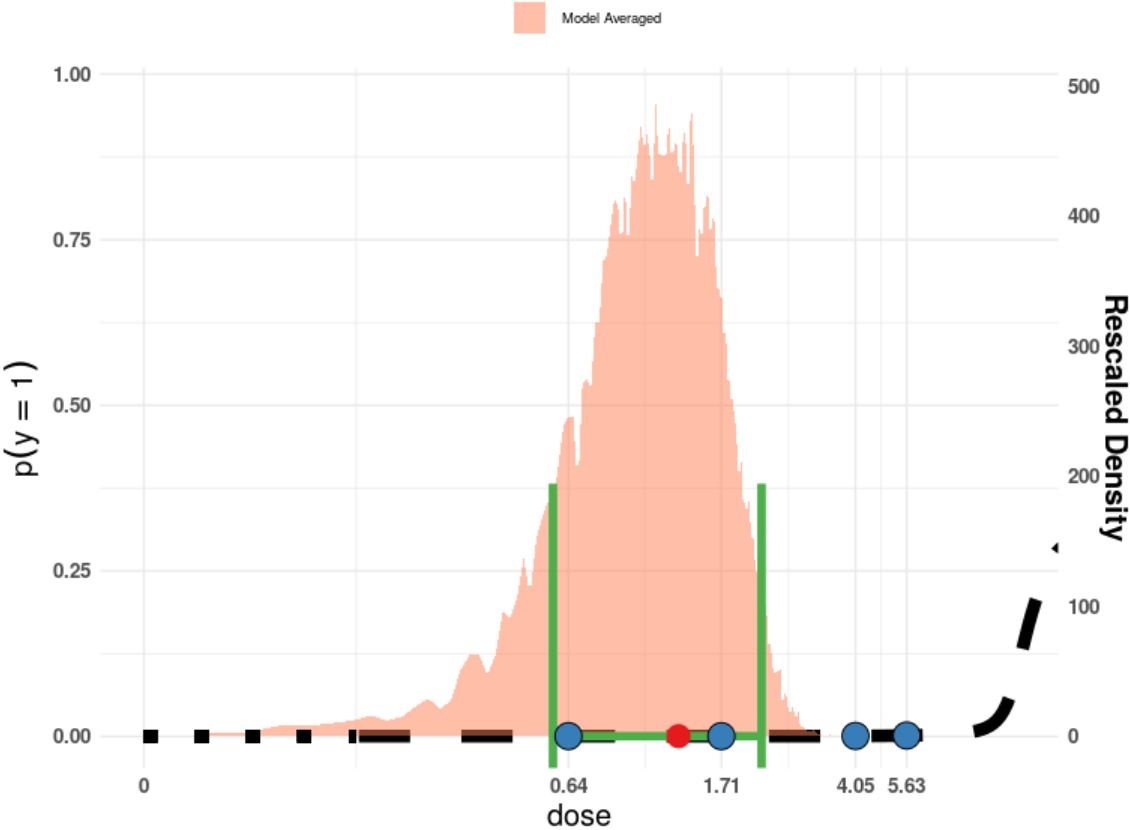
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.637	1.264	2.049	0.232	1
IE4_Q	1.083	1.843	2.638	0.082	1
H4_Q	0.637	1.296	2.024	0.223	1
LN4_Q	0.894	1.619	2.370	0.194	1
G4_Q	0.911	3.203	5.594	0.000	0
QE4_Q	0.084	0.170	0.311	0.002	1
P4_Q	0.469	1.010	1.754	0.138	1
L4_Q	0.435	0.969	1.731	0.129	1

Plots of Fitted Models







Steinmaus et al. (2013) lung cancer, relative BMR 1%

Exposure: lifetime average, all years, based on arsenic daily intakes (the preferred exposure estimate for the study)

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.58	70	138516
1.55	60	136406
3.46	68	108281
4.67	107	66797

The 'Value for CES' is set to 5.06e-06.

Extended dose range is applied.

Informative background prior: min: 0.00042955; the most likely: 0.00050536; max: 0.00058116. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.62e-03).

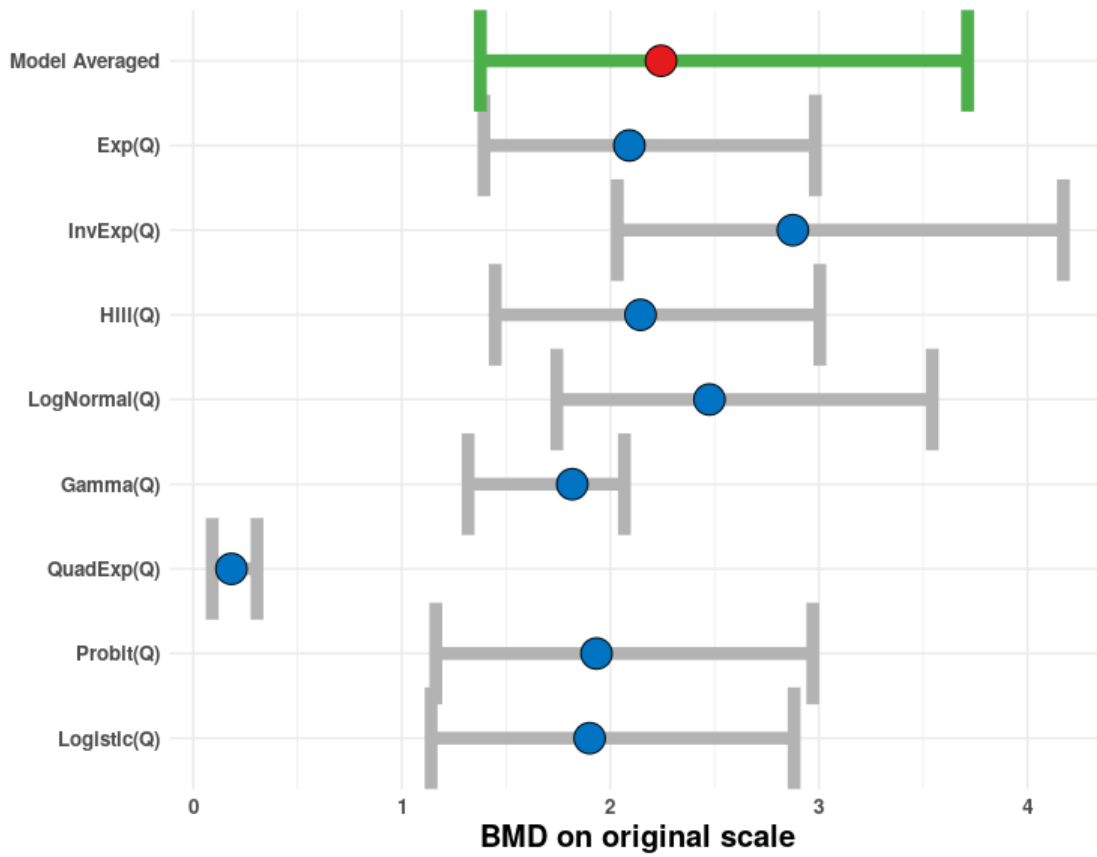
Model Averaged BMD

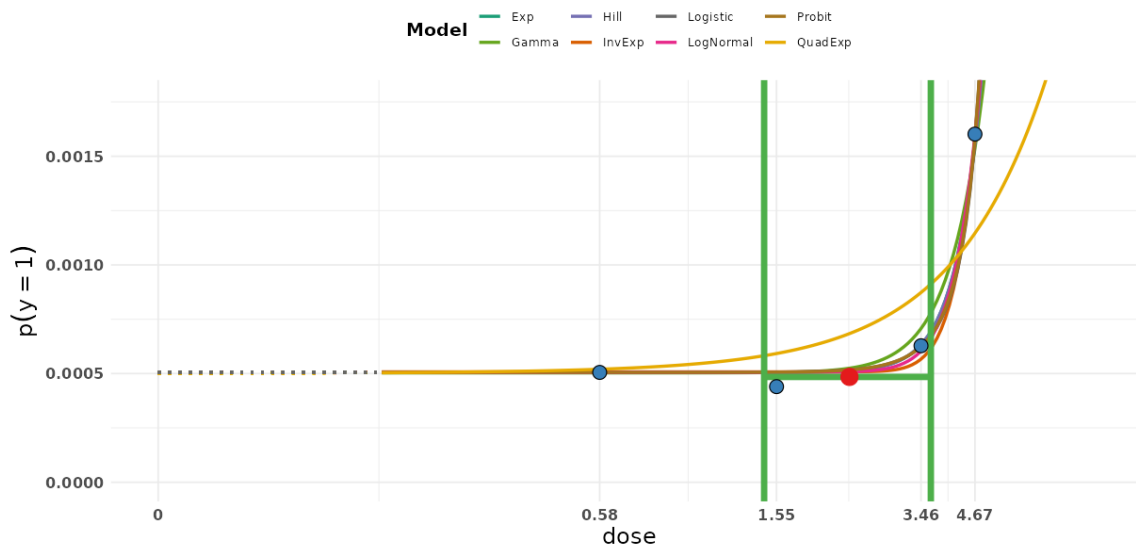
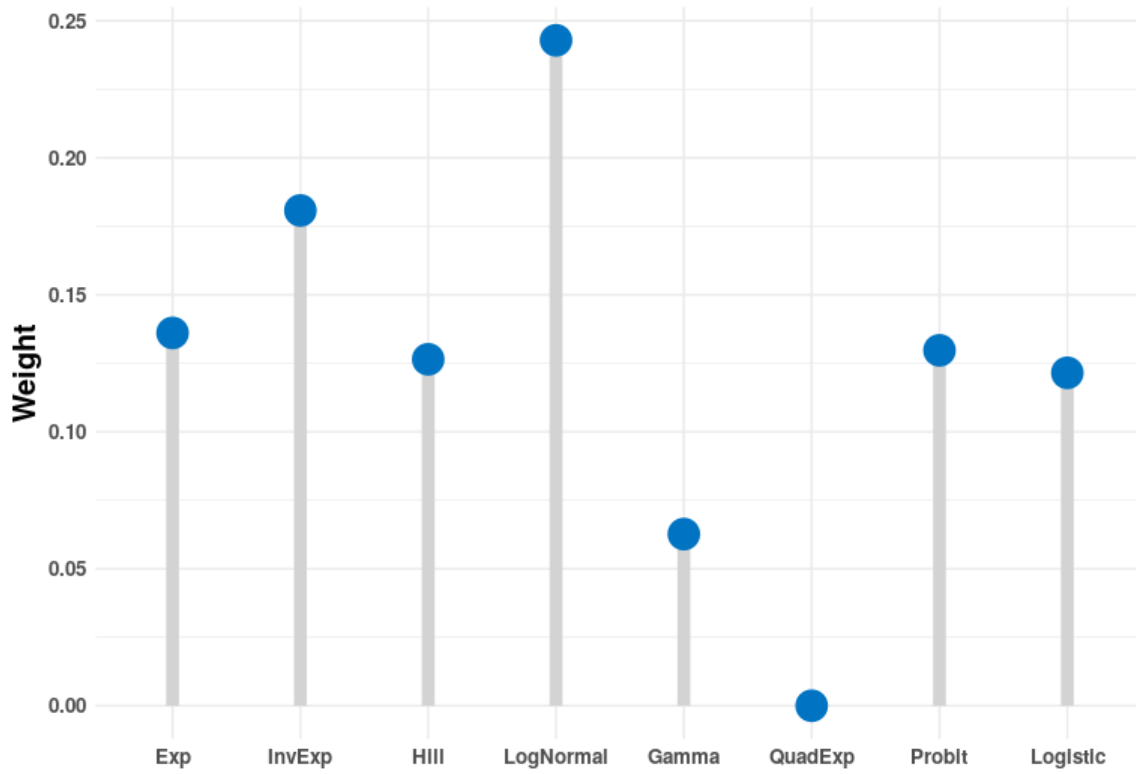
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	1.377	2.243	3.713

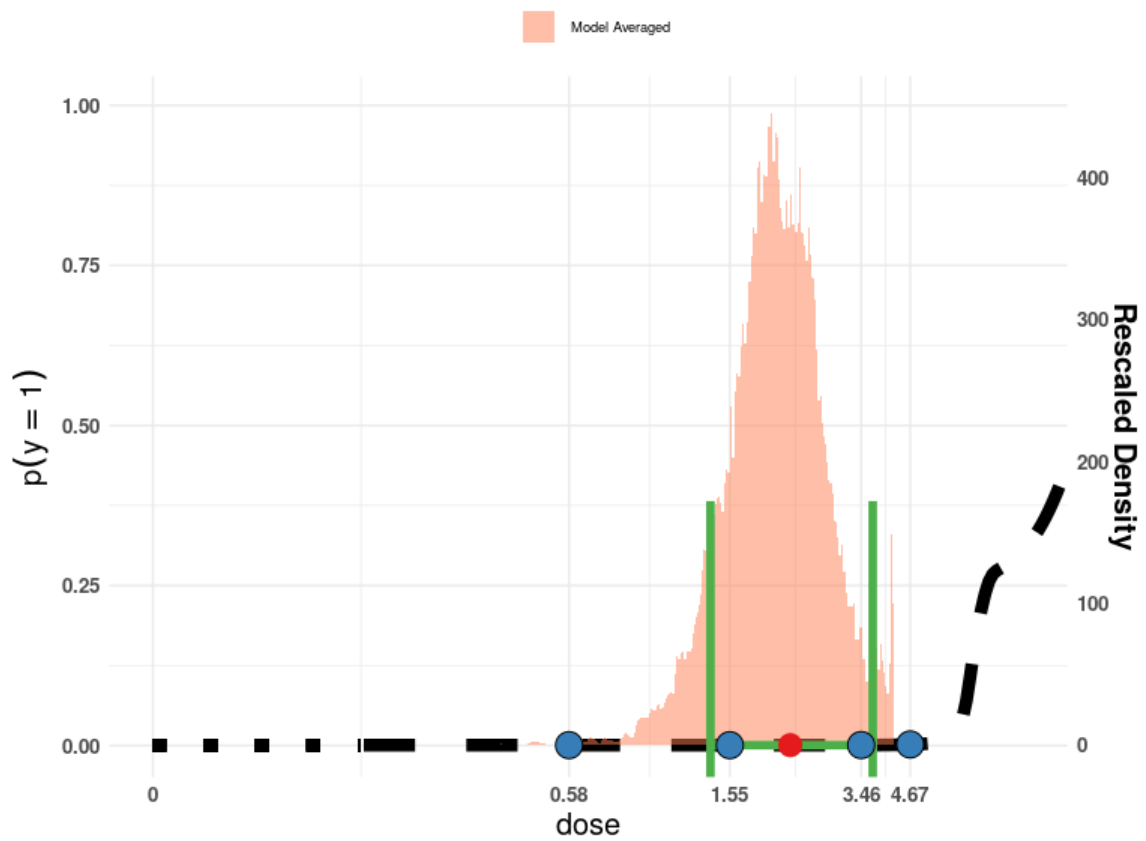
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	1.394	2.091	2.983	0.136	1
IE4_Q	2.033	2.875	4.173	0.181	1
H4_Q	1.448	2.145	3.005	0.126	1
LN4_Q	1.744	2.475	3.544	0.243	1
G4_Q	1.318	1.817	2.067	0.063	1
QE4_Q	0.091	0.183	0.306	0.000	1
P4_Q	1.163	1.934	2.971	0.130	1
L4_Q	1.141	1.901	2.881	0.122	1

Plots of Fitted Models







Steinmaus et al. (2013) lung cancer, relative BMR 1%

Exposure: lifetime average before 1971, based on arsenic water concentrations and water intake of 1.9L (included only in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.44	51	140802
1.66	62	135849
6.07	71	97642
9.38	118	75708

The 'Value for CES' is set to 3.62e-06.

Extended dose range is applied.

Informative background prior: min: 0.00035859; the most likely: 0.00036221; max: 0.00036583. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

The results do not fulfill the EFSA BMD guidance (EFSA Scientific Committee, 2022) recommendations since BMDU/BMDL > 50.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 3.36e-03).

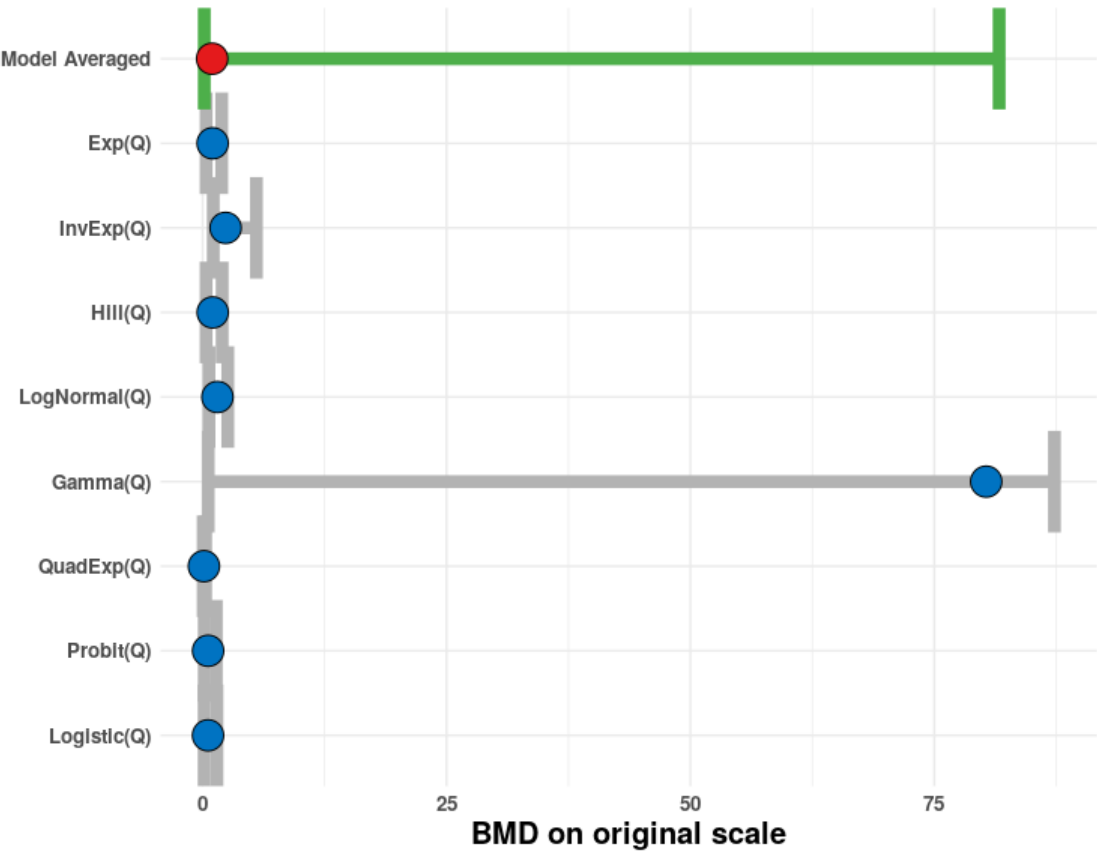
Model Averaged BMD

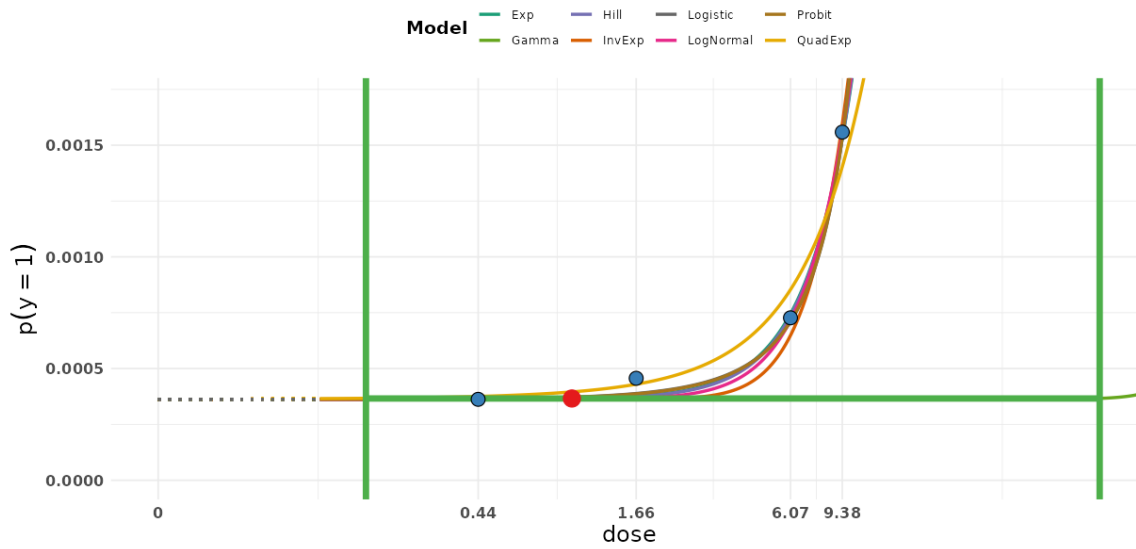
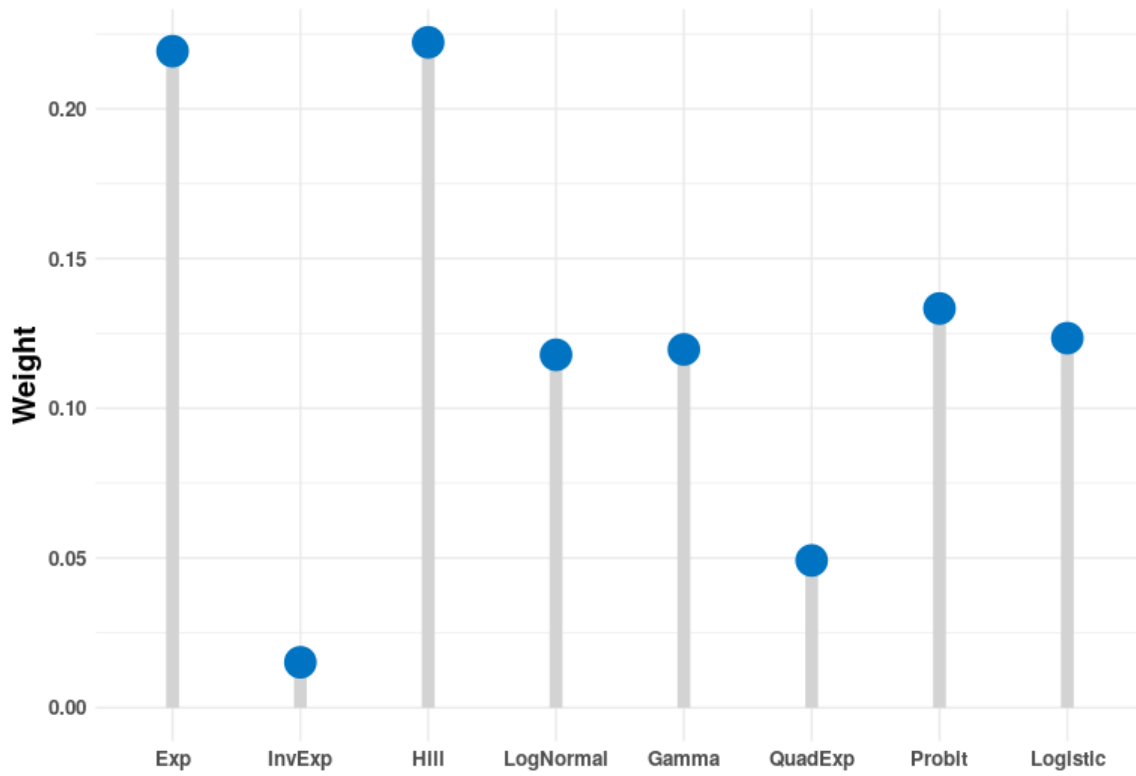
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.171	0.979	81.644

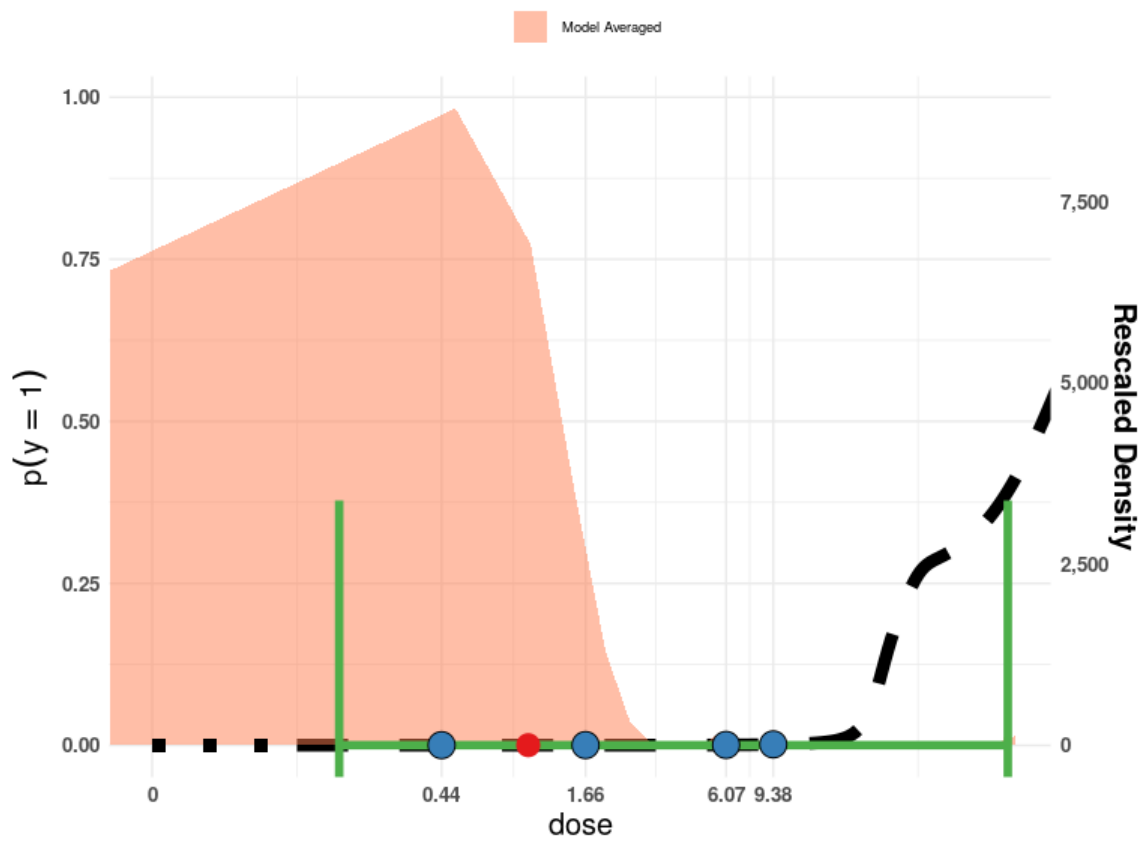
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.363	1.027	1.959	0.219	1
IE4_Q	1.092	2.357	5.514	0.015	0
H4_Q	0.359	1.034	2.005	0.222	1
LN4_Q	0.651	1.520	2.581	0.118	1
G4_Q	0.578	80.320	87.313	0.120	0
QE4_Q	0.061	0.135	0.308	0.049	1
P4_Q	0.169	0.564	1.404	0.133	1
L4_Q	0.158	0.556	1.469	0.123	1

Plots of Fitted Models







Steinmaus et al. (2013) lung cancer, relative BMR 1%

Exposure: lifetime average before 1971, based on arsenic daily intakes (included only in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.44	54	140802
1.57	62	136557
5.18	68	108962
7.79	119	63679

The 'Value for CES' is set to 3.84e-06.

Extended dose range is applied.

Informative background prior: min: 0.00037968; the most likely: 0.00038352; max: 0.00038735. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.50e-03).

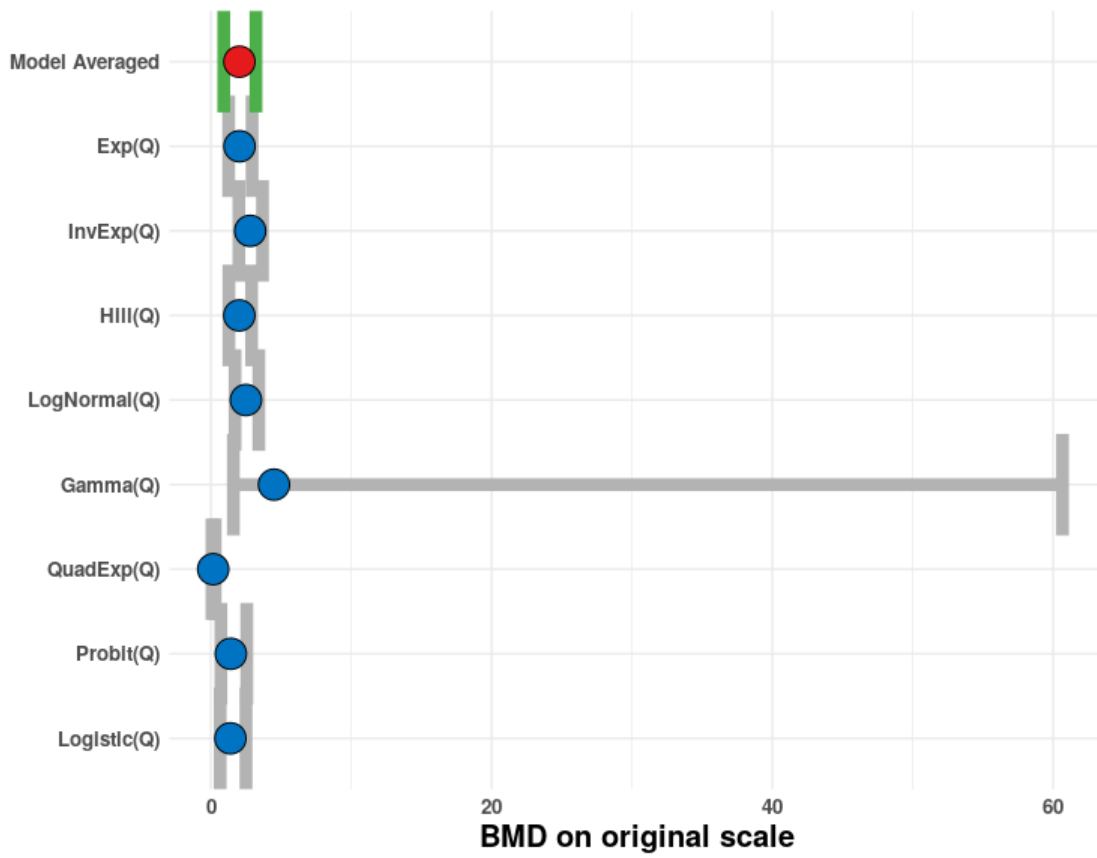
Model Averaged BMD

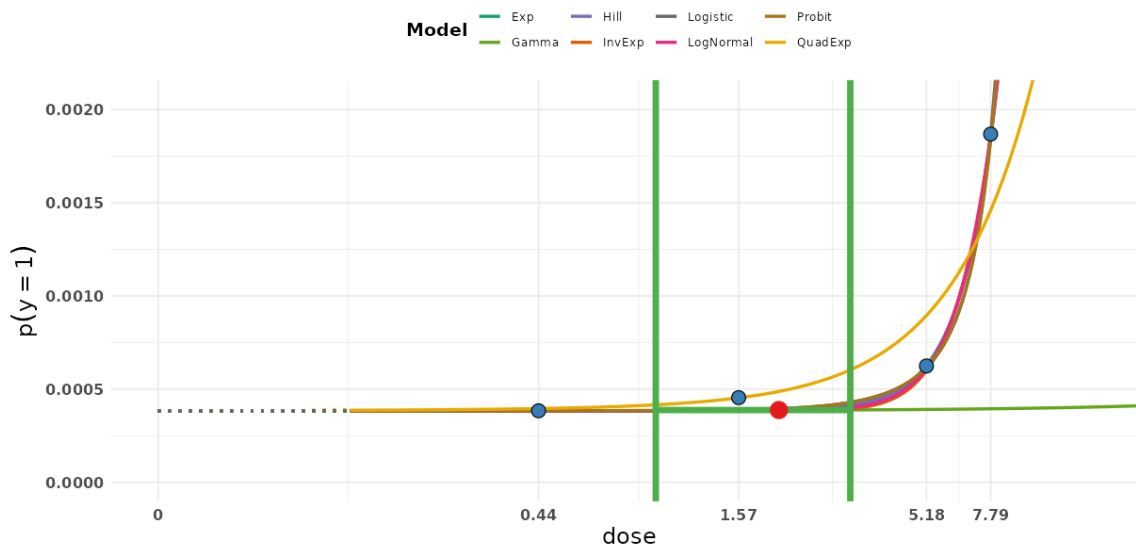
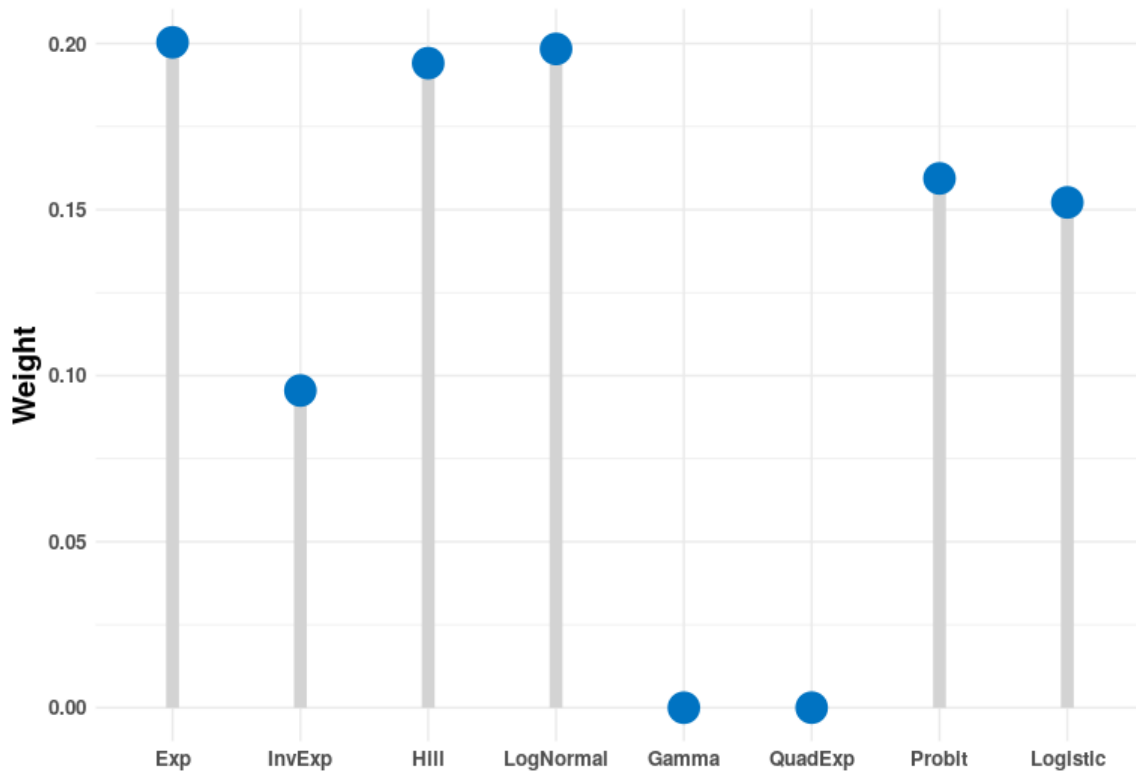
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.917	2.031	3.211

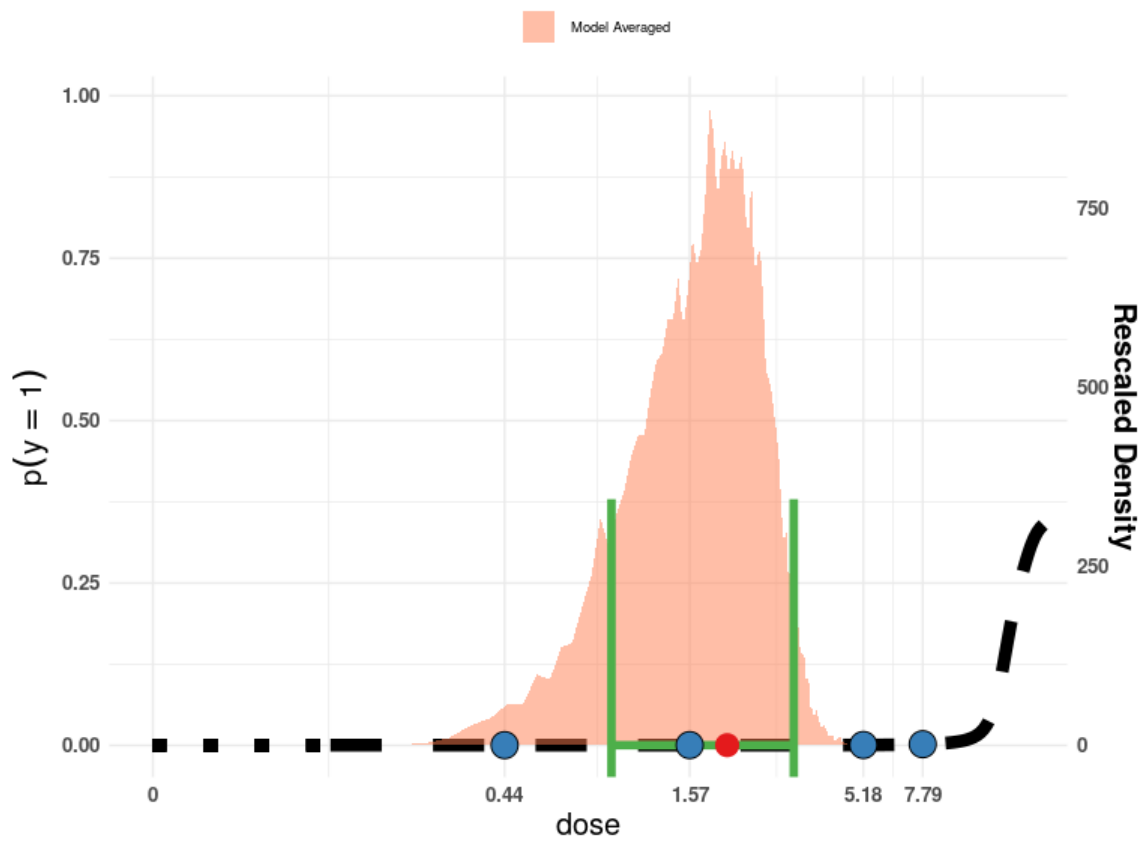
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	1.268	2.042	2.936	0.200	1
IE4_Q	1.996	2.802	3.676	0.096	1
H4_Q	1.284	2.026	2.899	0.194	1
LN4_Q	1.719	2.498	3.414	0.198	1
G4_Q	1.601	4.493	60.664	0.000	0
QE4_Q	0.078	0.164	0.305	0.000	1
P4_Q	0.712	1.426	2.557	0.159	1
L4_Q	0.661	1.393	2.500	0.152	1

Plots of Fitted Models







Steinmaus et al. (2014a) lung cancer, relative BMR 1%

Exposure: lifetime average, based on arsenic daily intakes (only included in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.32	27	80469
0.53	28	74219
1.58	37	70313

The 'Value for CES' is set to 3.36e-06.

Extended dose range is not applied.

Informative background prior: min: 0.00033218; the most likely: 0.00033553; max: 0.00033889. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 4.01e+00).

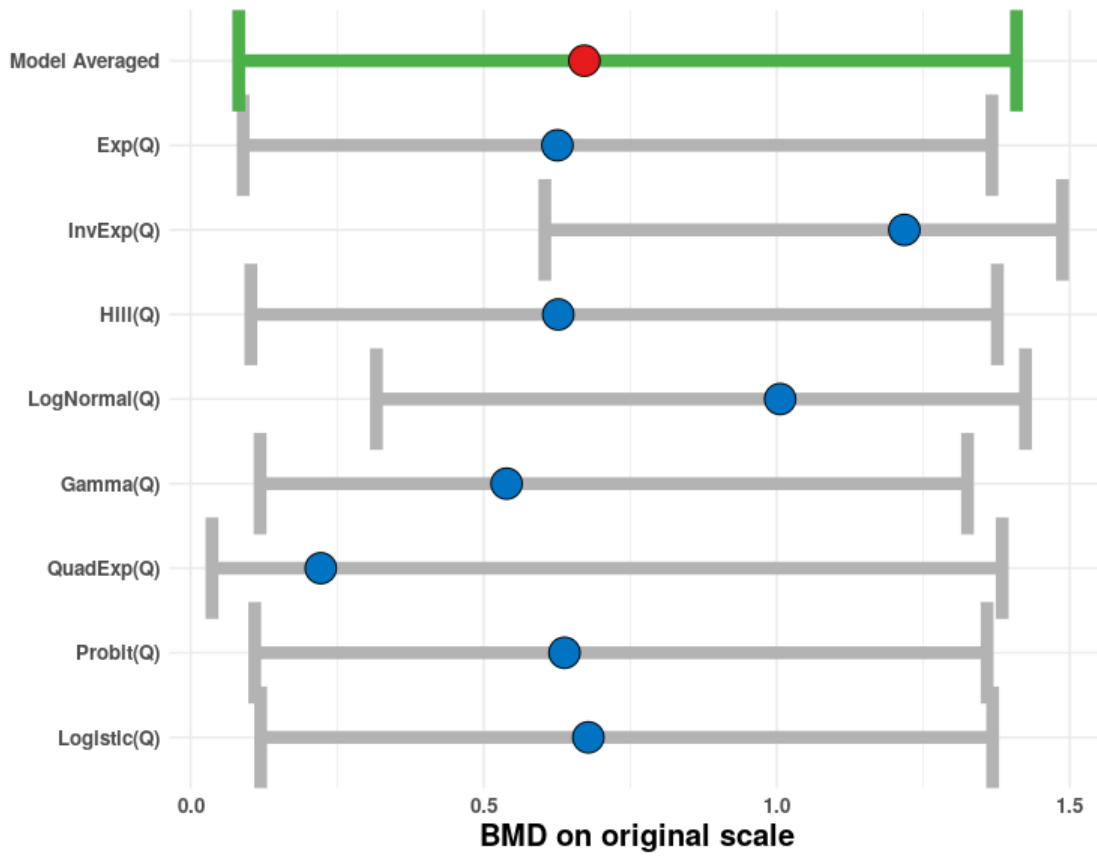
Model Averaged BMD

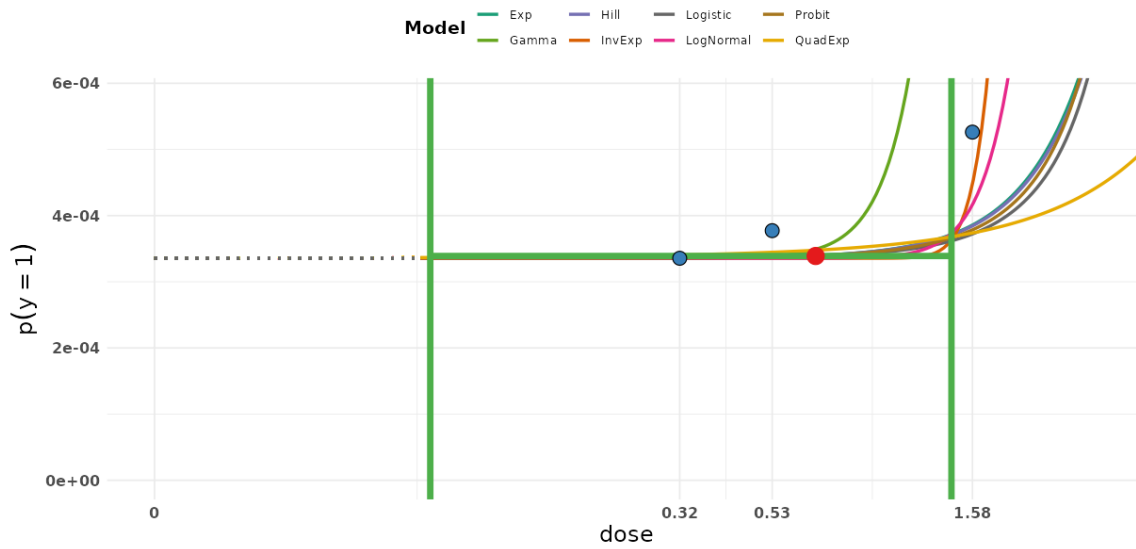
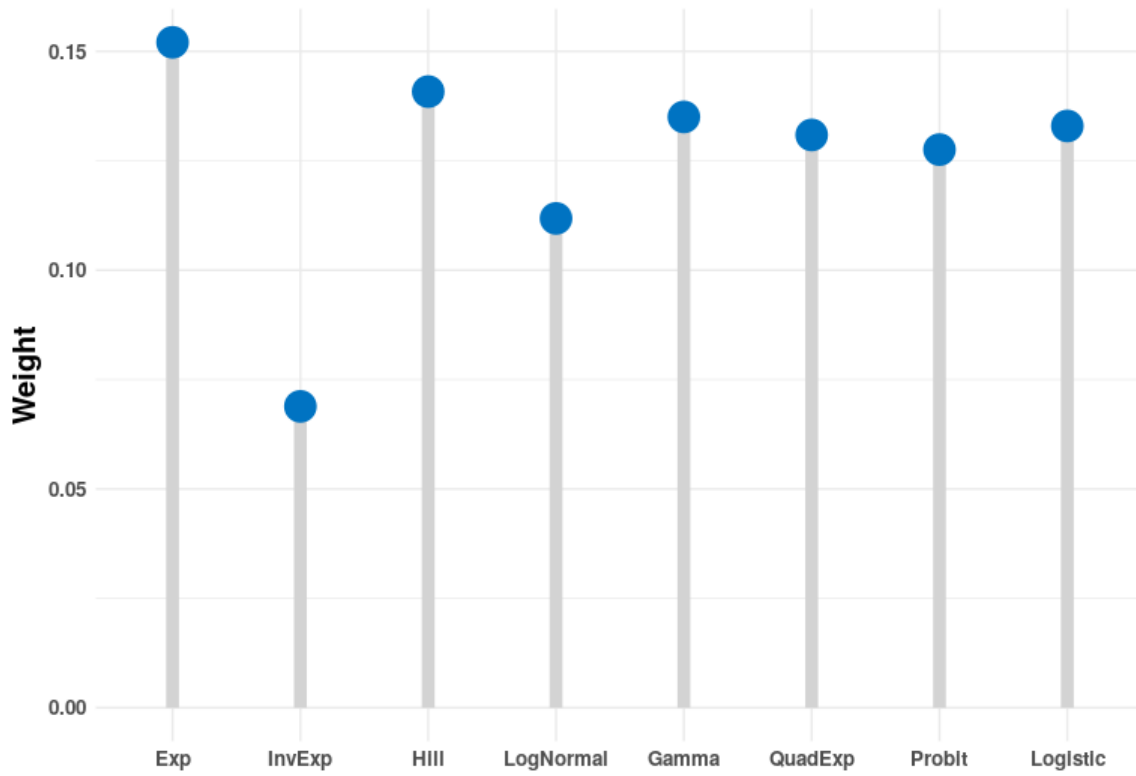
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.082	0.672	1.409

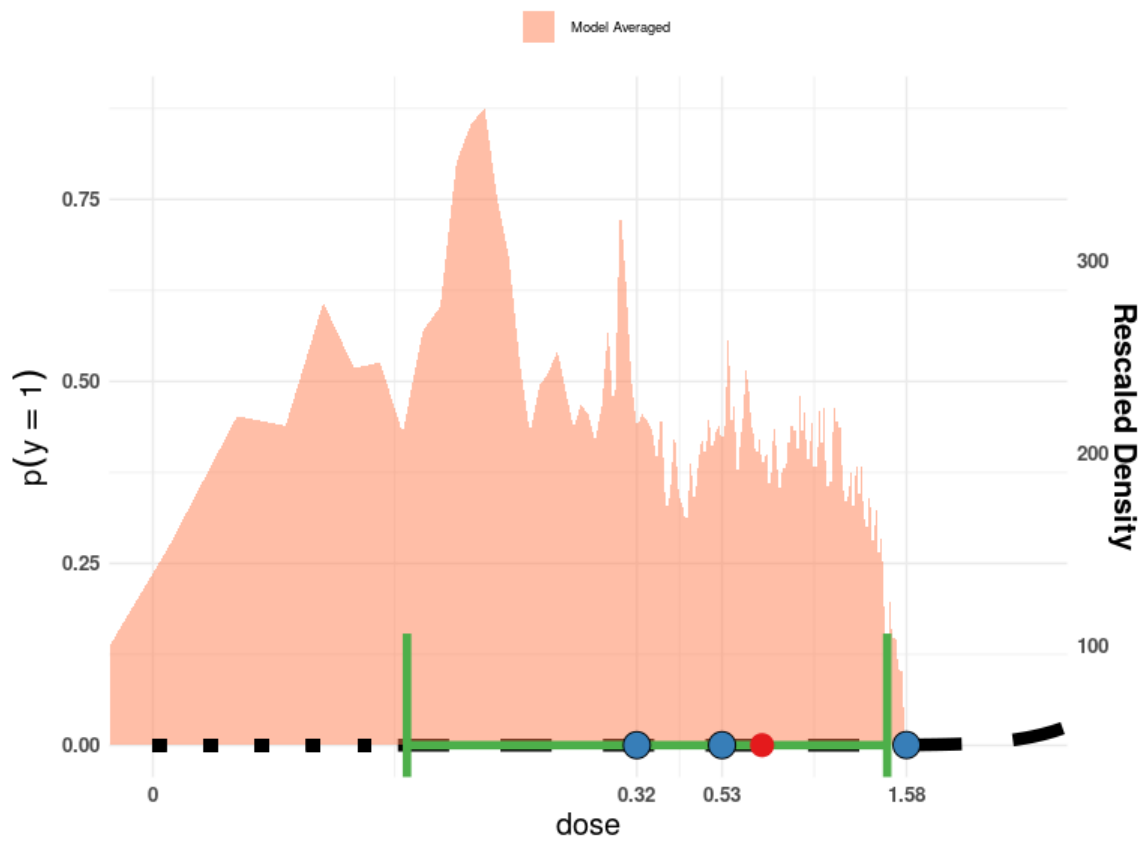
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.090	0.626	1.367	0.152	1
IE4_Q	0.604	1.218	1.488	0.069	1
H4_Q	0.103	0.627	1.376	0.141	1
LN4_Q	0.317	1.006	1.424	0.112	1
G4_Q	0.119	0.539	1.326	0.135	0
QE4_Q	0.036	0.222	1.385	0.131	1
P4_Q	0.109	0.638	1.359	0.128	1
L4_Q	0.120	0.679	1.368	0.133	1

Plots of Fitted Models







Steinmaus et al. (2014a) lung cancer, relative BMR 1%

Exposure: the highest 5-year average, based on arsenic daily intakes (the preferred exposure estimate for the study)

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.36	25	79688
0.70	30	77344
2.00	37	67969

The 'Value for CES' is set to 3.14e-06.

Extended dose range is not applied.

Informative background prior: min: 0.00031059; the most likely: 0.00031372; max: 0.00031686. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 3.76e+00).

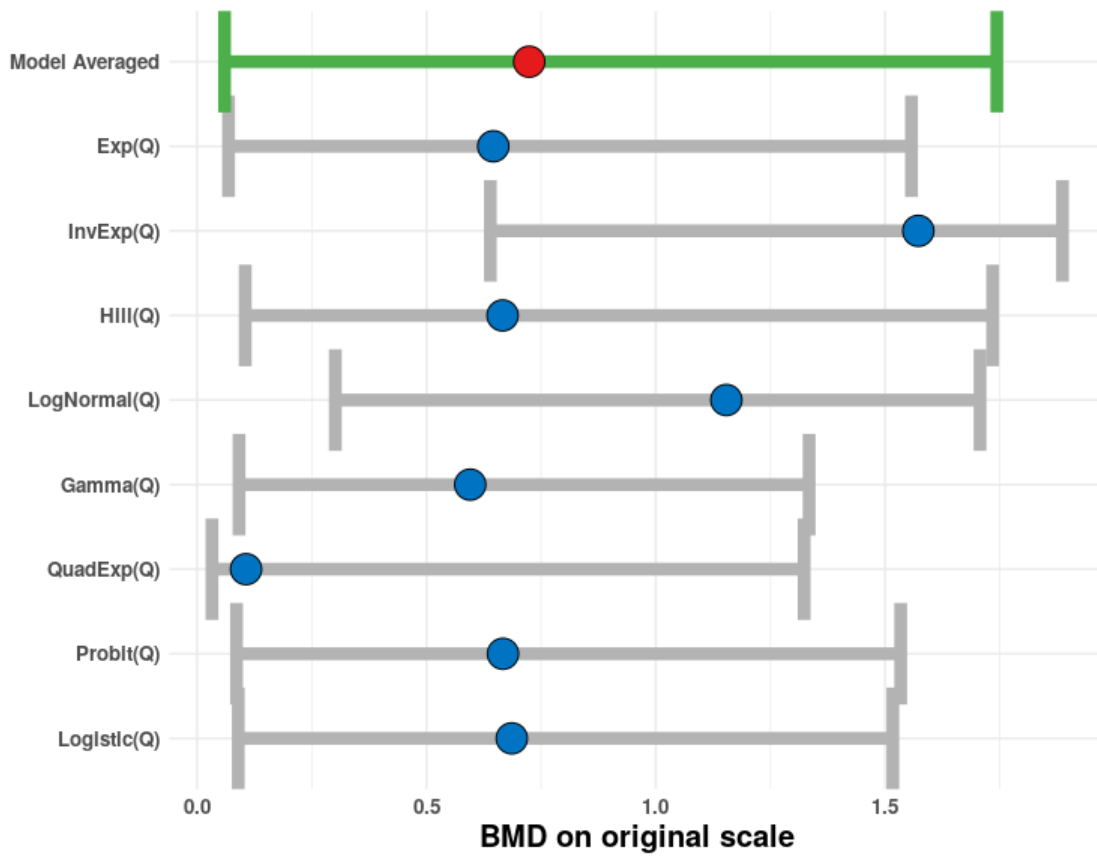
Model Averaged BMD

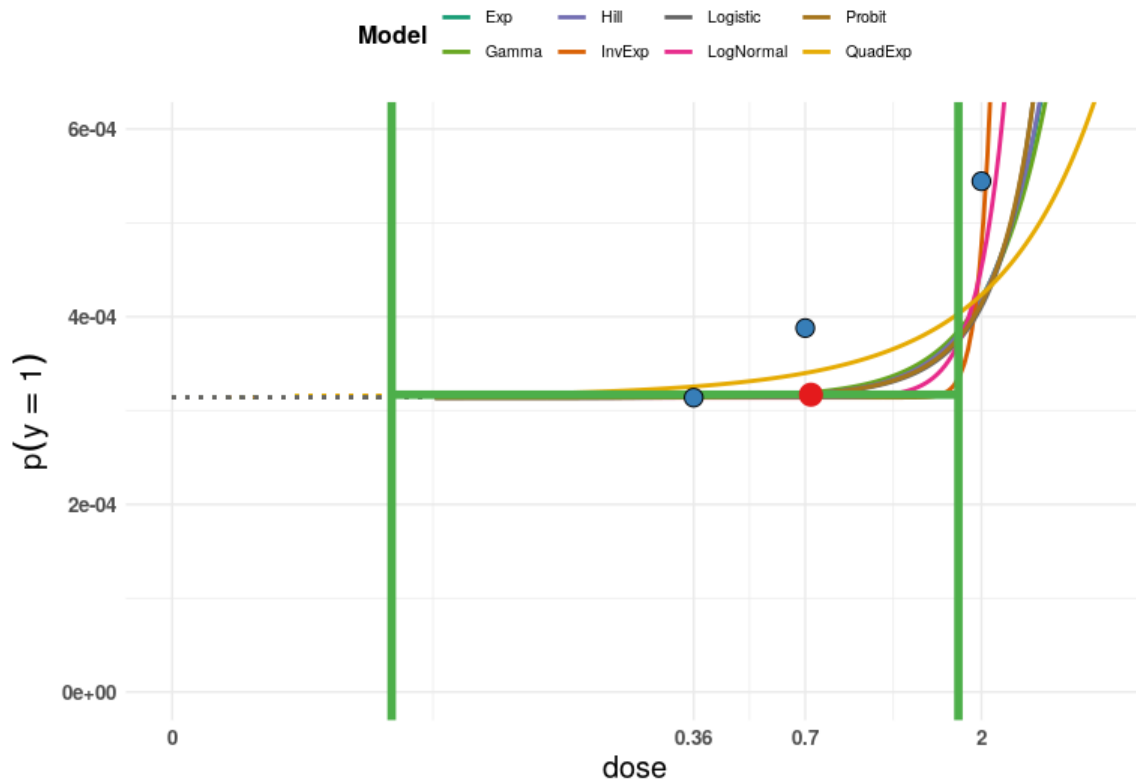
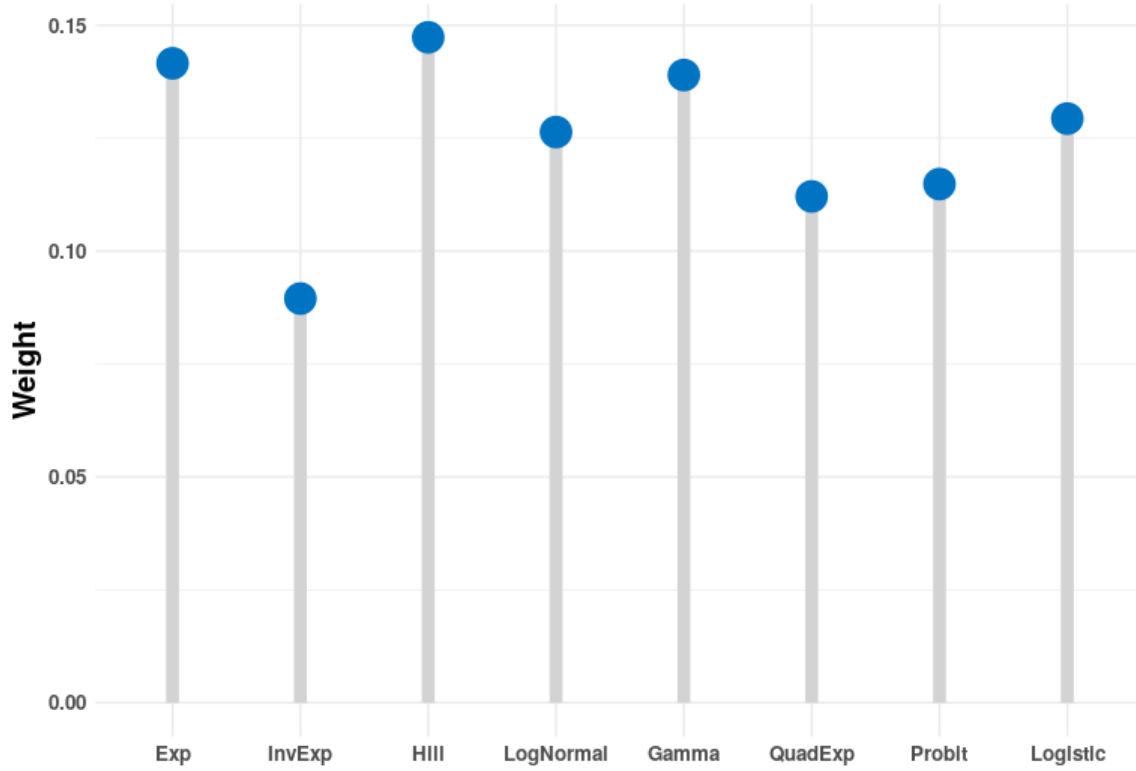
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.06	0.724	1.744

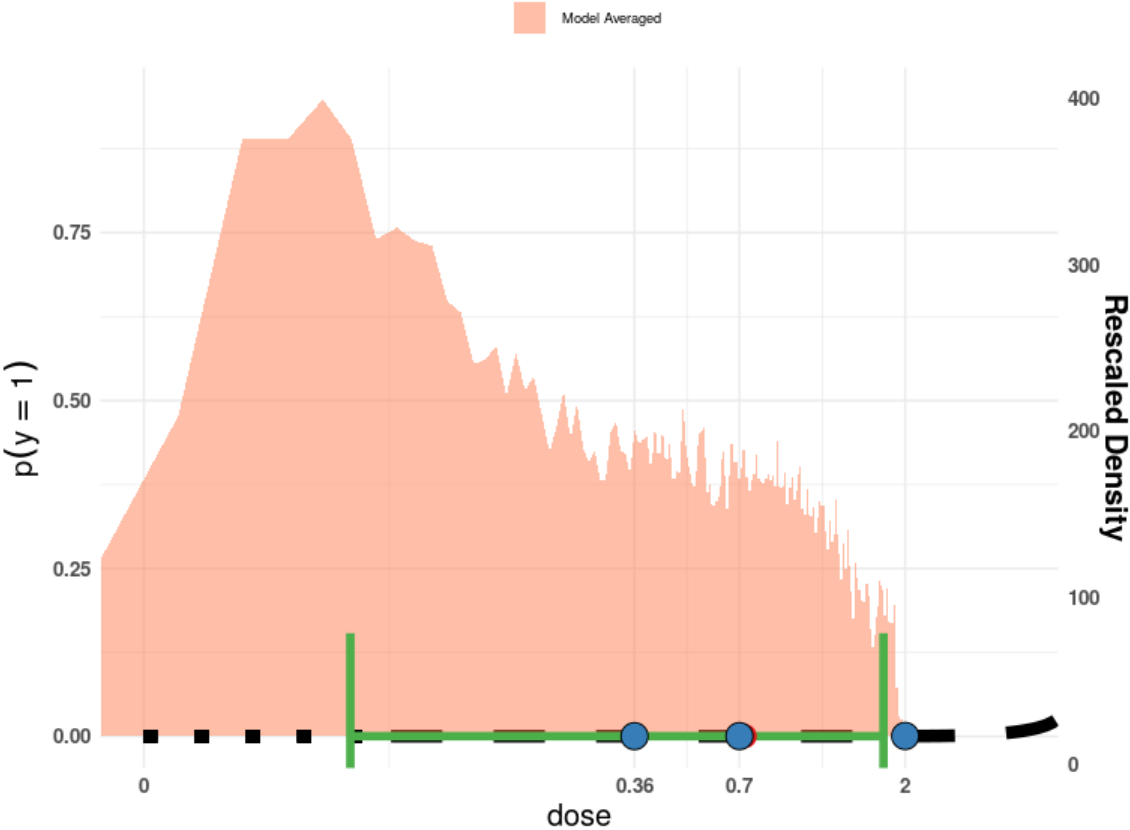
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.068	0.646	1.558	0.142	1
IE4_Q	0.639	1.572	1.887	0.089	0
H4_Q	0.105	0.666	1.735	0.147	1
LN4_Q	0.301	1.154	1.707	0.126	1
G4_Q	0.091	0.595	1.334	0.139	1
QE4_Q	0.032	0.106	1.323	0.112	1
P4_Q	0.086	0.667	1.534	0.115	0
L4_Q	0.089	0.686	1.517	0.129	1

Plots of Fitted Models







Steinmaus et al. (2014a) lung cancer, relative BMR 1%

Exposure: the highest year, based on arsenic daily intakes (included only in the uncertainty analysis)

Data Description

The endpoint to be analyzed is: Adj.cases for lung cancer

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.39	23	80469
0.84	31	76563
1.19	38	67969

The 'Value for CES' is set to 2.86e-06.

Extended dose range is not applied.

Informative background prior: min: 0.00027153; the most likely: 0.00028582; max: 0.00030012. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.12e+00).

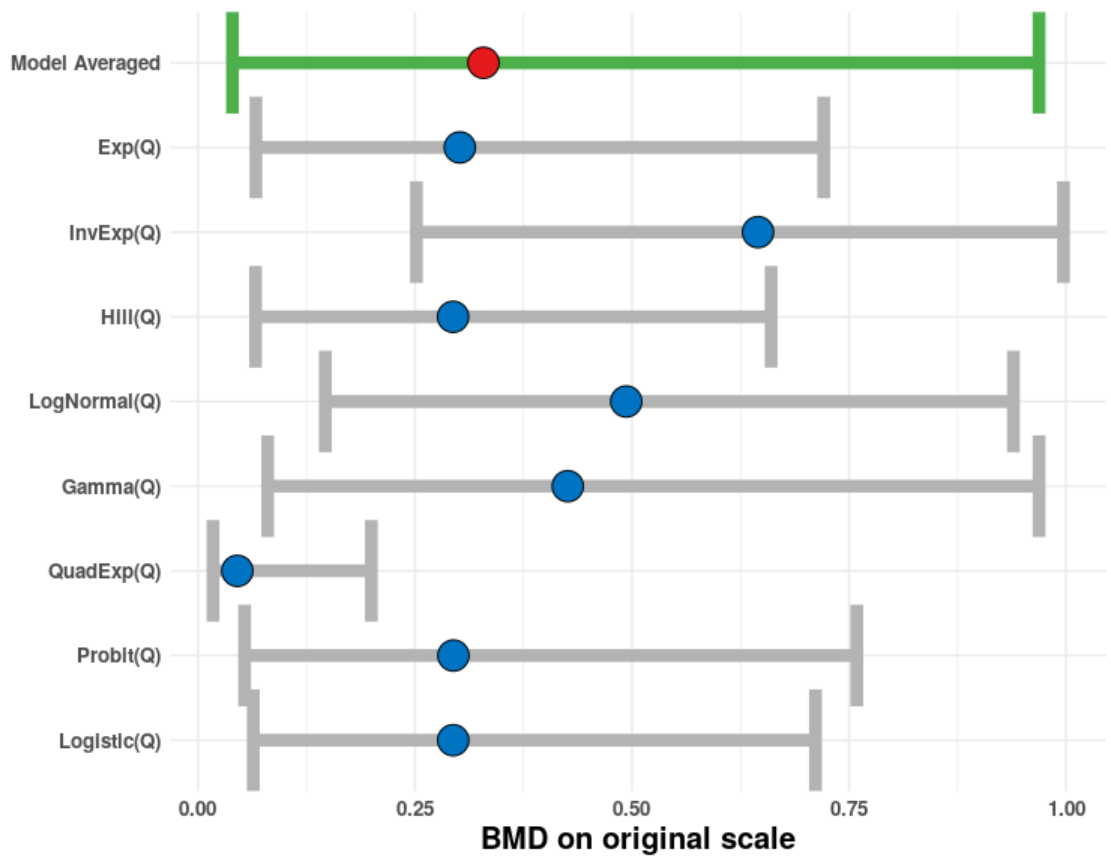
Model Averaged BMD

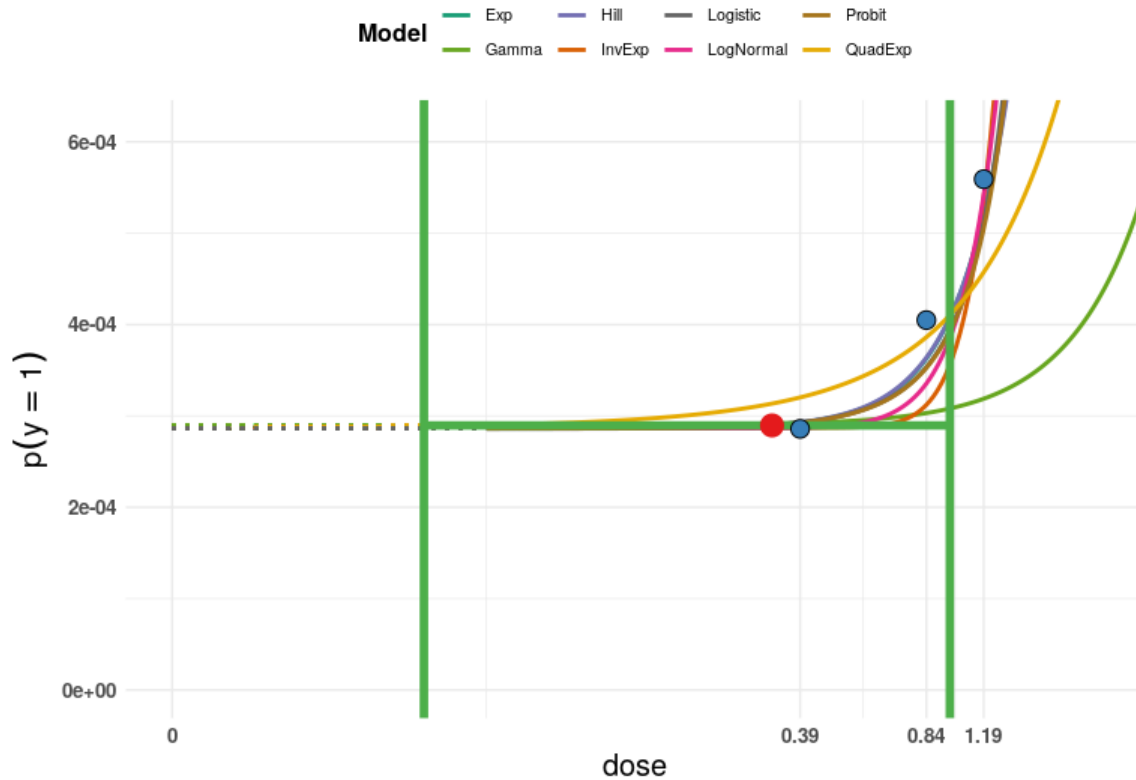
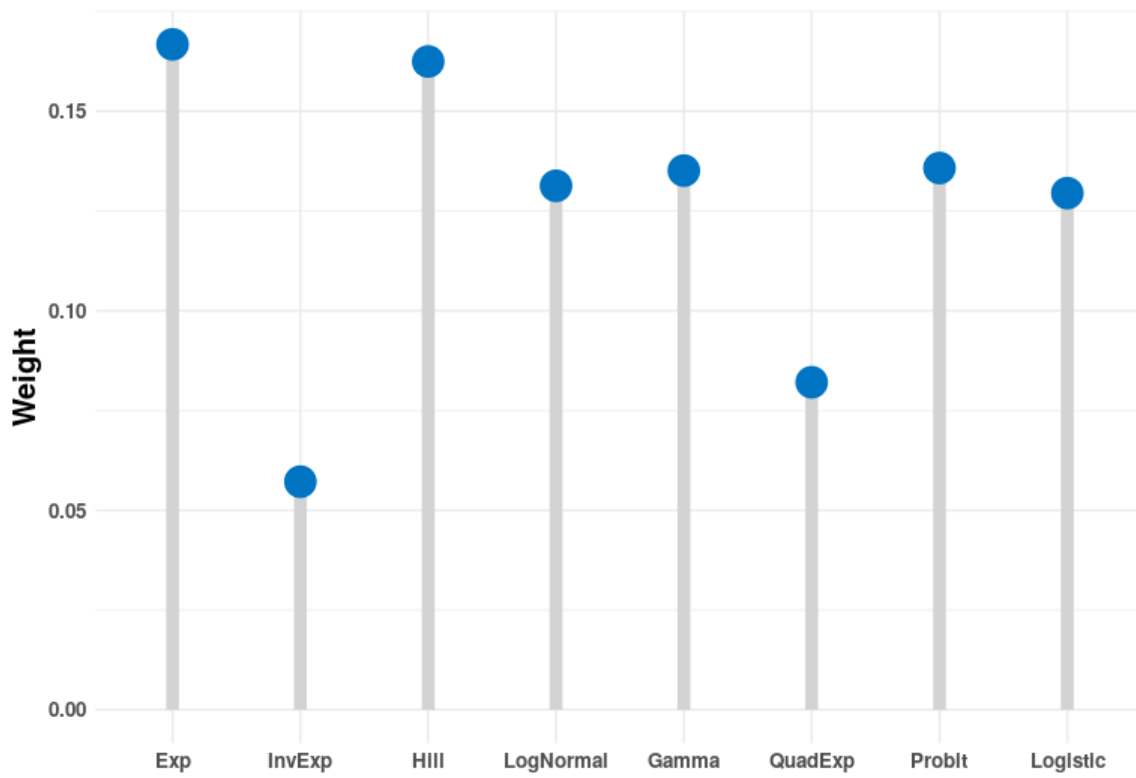
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.04	0.329	0.969

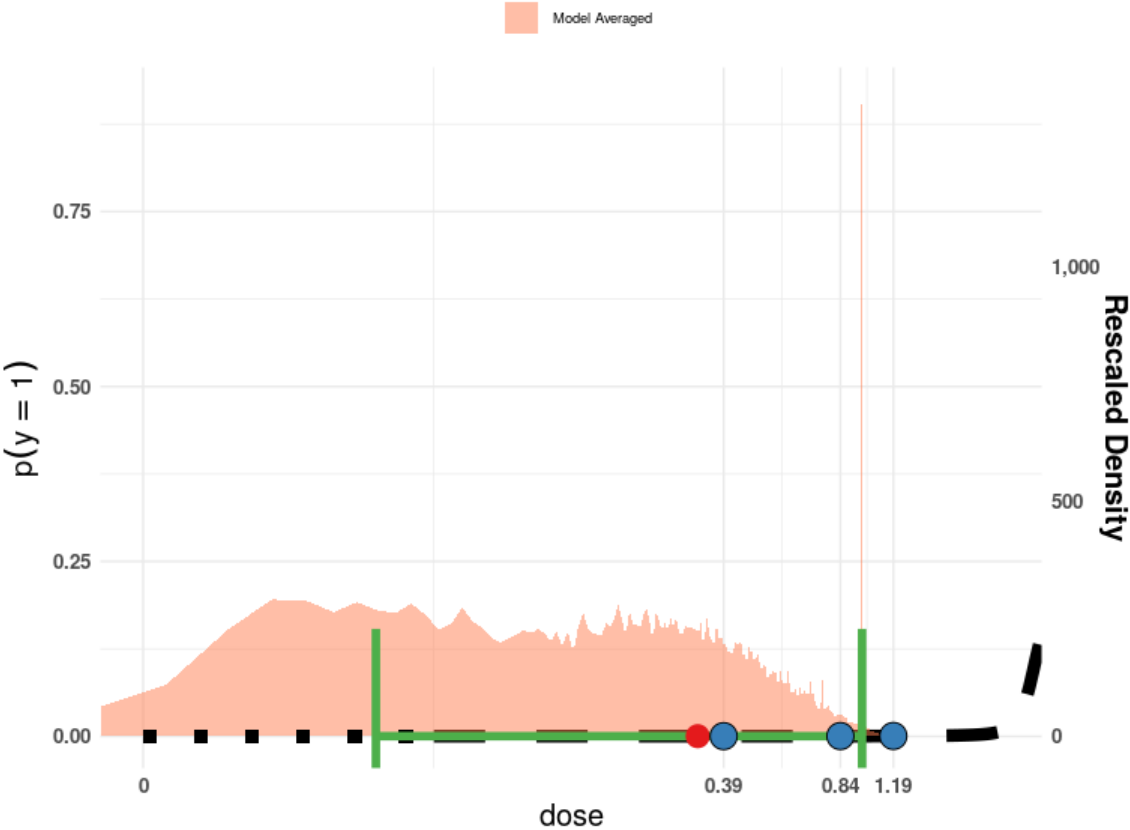
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.067	0.302	0.721	0.167	1
IE4_Q	0.252	0.645	0.997	0.057	1
H4_Q	0.066	0.294	0.660	0.162	1
LN4_Q	0.147	0.493	0.939	0.131	1
G4_Q	0.080	0.426	0.969	0.135	0
QE4_Q	0.017	0.045	0.200	0.082	1
P4_Q	0.054	0.294	0.759	0.136	1
L4_Q	0.064	0.294	0.711	0.129	1

Plots of Fitted Models







Vahter et al. (2020) full developmental score, mothers u-tiAs at GW 8, BMR 1%

Data Description

The endpoint to be analyzed is: Full.development.score

Data used for analysis:

Exposure	Full.development.score	SD	N
1.53	141	34	294
1.89	135	33	293
2.47	126	34	294
4.62	127	31	293
7.02	132	31	293

The 'Value for CES' is set to 0.01.

Extended dose range is applied.

Informative background prior: min: 127; the most likely: 141; max: 155. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Check for constant variance coefficient of variation

Distributional assumption of constant variance are met, Bartlett test p-value is 0.2801

Distributional assumption of constant variance (on log-scale) are met, Bartlett test p-value is 0.1741

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.50e+00).

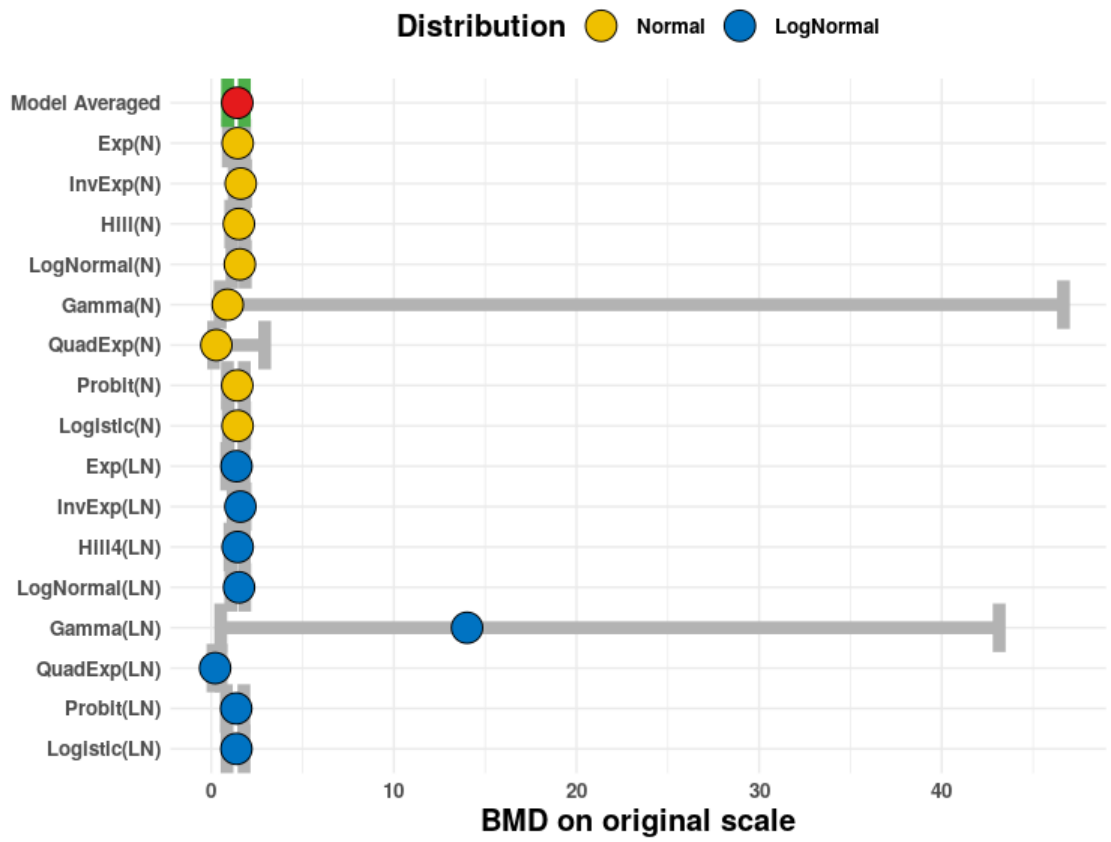
Model Averaged BMD

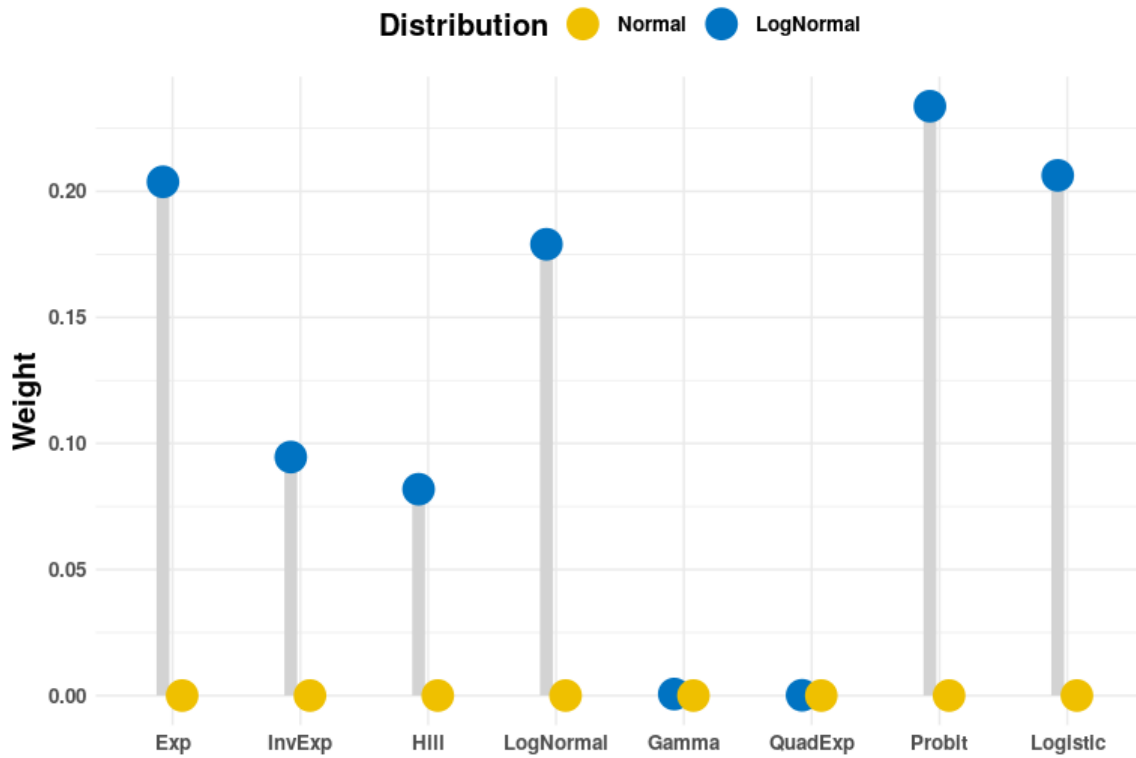
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.896	1.427	1.815

Estimated BMDs per model

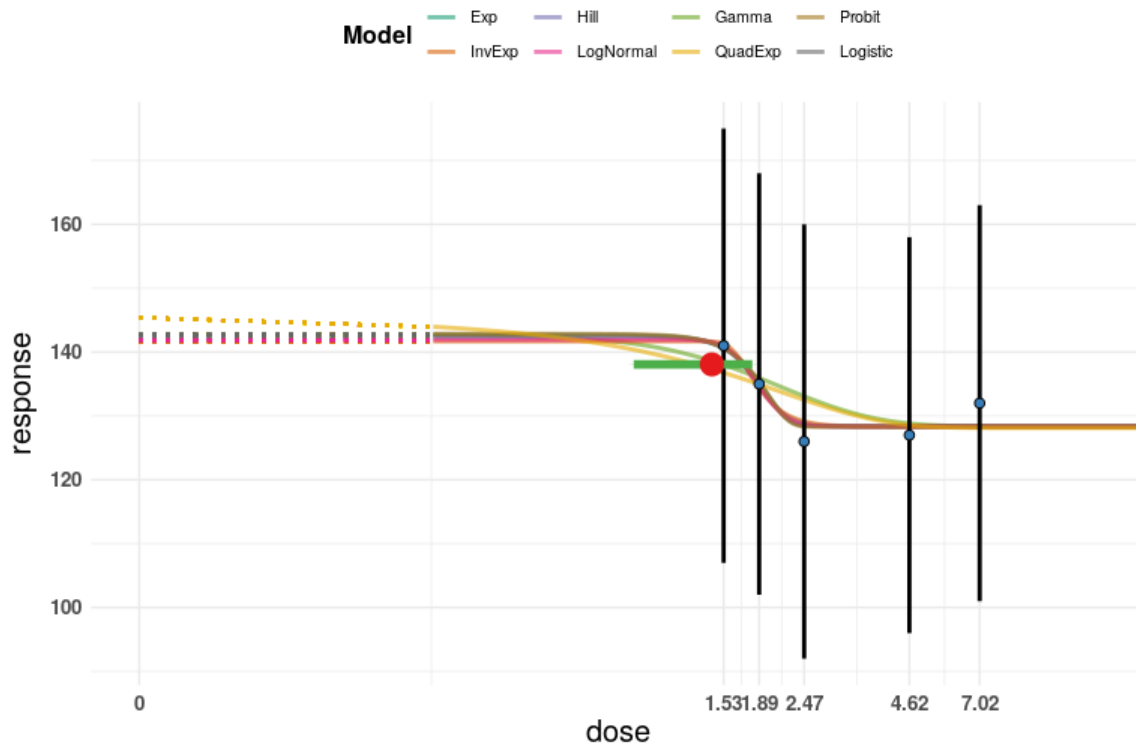
Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_N	0.928	1.451	1.830	0.000	1
IE4_N	1.251	1.616	1.876	0.000	1
H4_N	1.067	1.512	1.821	0.000	1
LN4_N	1.134	1.565	1.864	0.000	1
G4_N	0.484	0.901	46.667	0.000	0
QE4_N	0.127	0.279	2.925	0.000	1
P4_N	0.884	1.426	1.811	0.000	1
L4_N	0.926	1.443	1.828	0.000	1
E4_LN	0.843	1.382	1.790	0.204	1
IE4_LN	1.193	1.594	1.849	0.095	1
H4_LN	1.022	1.447	1.812	0.082	1
LN4_LN	1.069	1.521	1.834	0.179	1
G4_LN	0.518	14.006	43.147	0.001	0
QE4_LN	0.095	0.210	0.536	0.000	1
P4_LN	0.828	1.366	1.786	0.234	1
L4_LN	0.863	1.376	1.797	0.206	1

Plots of Fitted Models

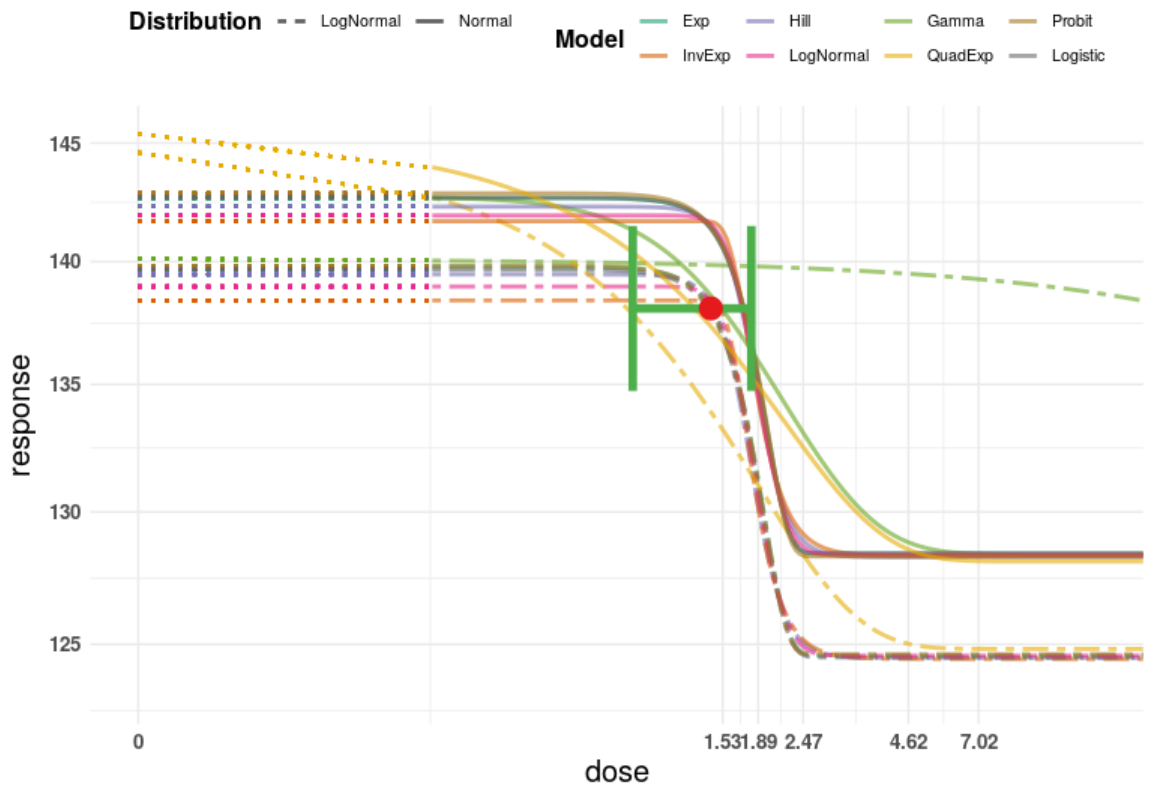
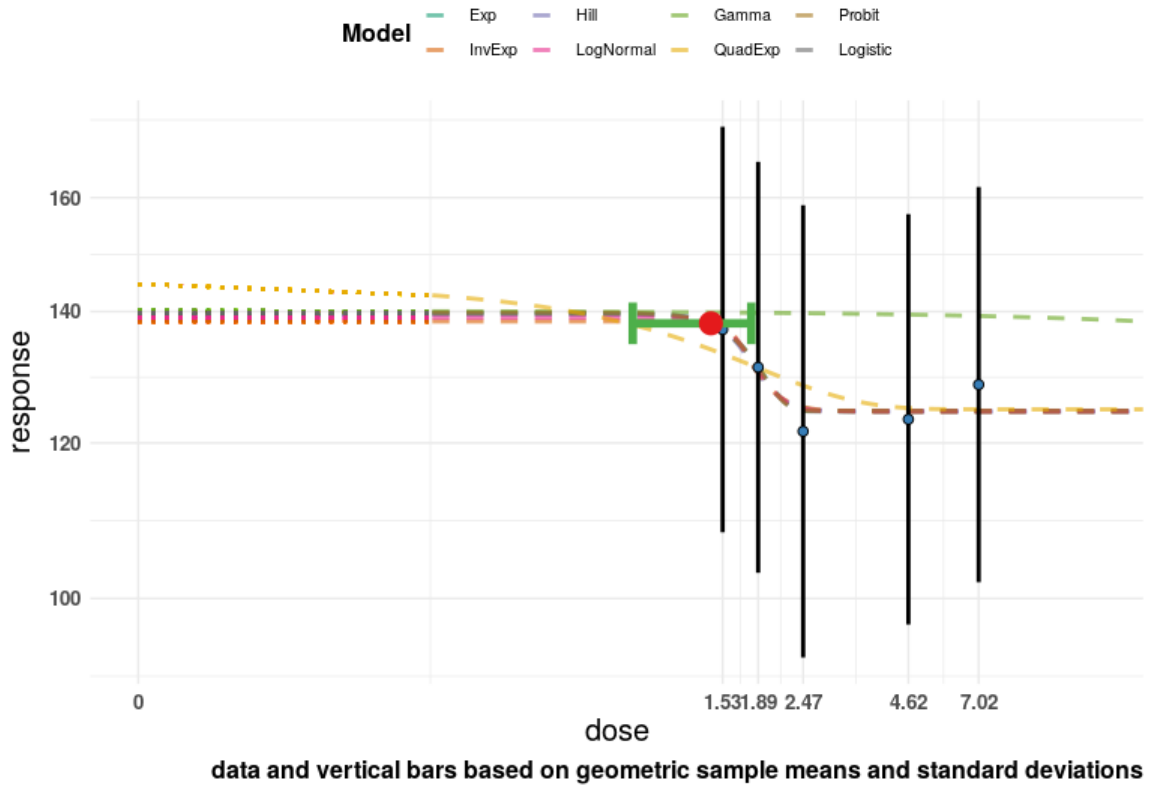


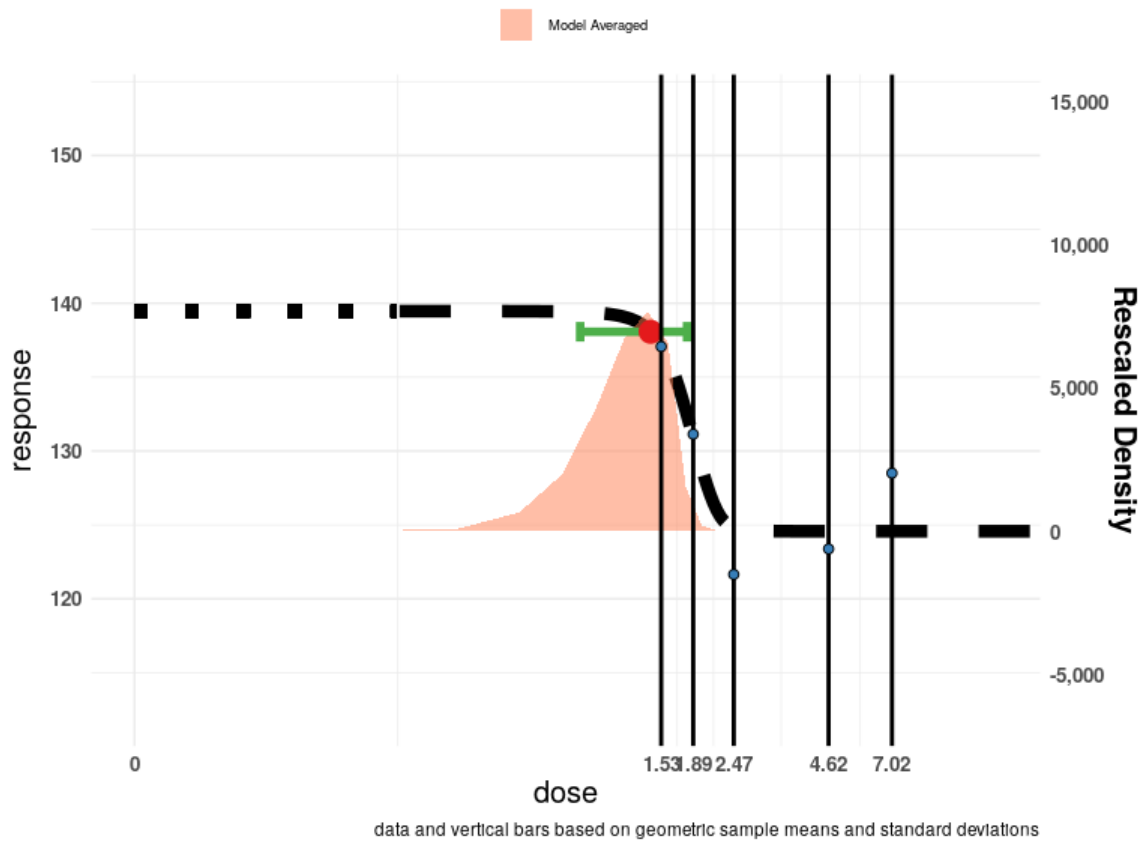


Normal distribution



LogNormal distribution





Vahter et al. (2020), full developmental score, children u-tiAs 10 years, BMR 1%

Data Description

The endpoint to be analyzed is: Full.development.score

Data used for analysis:

Exposure	Full.development.score	SD	N
0.98	141	34	305
1.57	135	33	305
2.49	126	34	304
4.52	127	31	305
11.52	132	31	304

The 'Value for CES' is set to 0.01.

Extended dose range is applied.

Informative background prior: min: 127; the most likely; 141; max: 155. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Check for constant variance coefficient of variation

Distributional assumption of constant variance are met, Bartlett test p-value is 0.2613

Distributional assumption of constant variance (on log-scale) are met, Bartlett test p-value is 0.1598

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.67e+00).

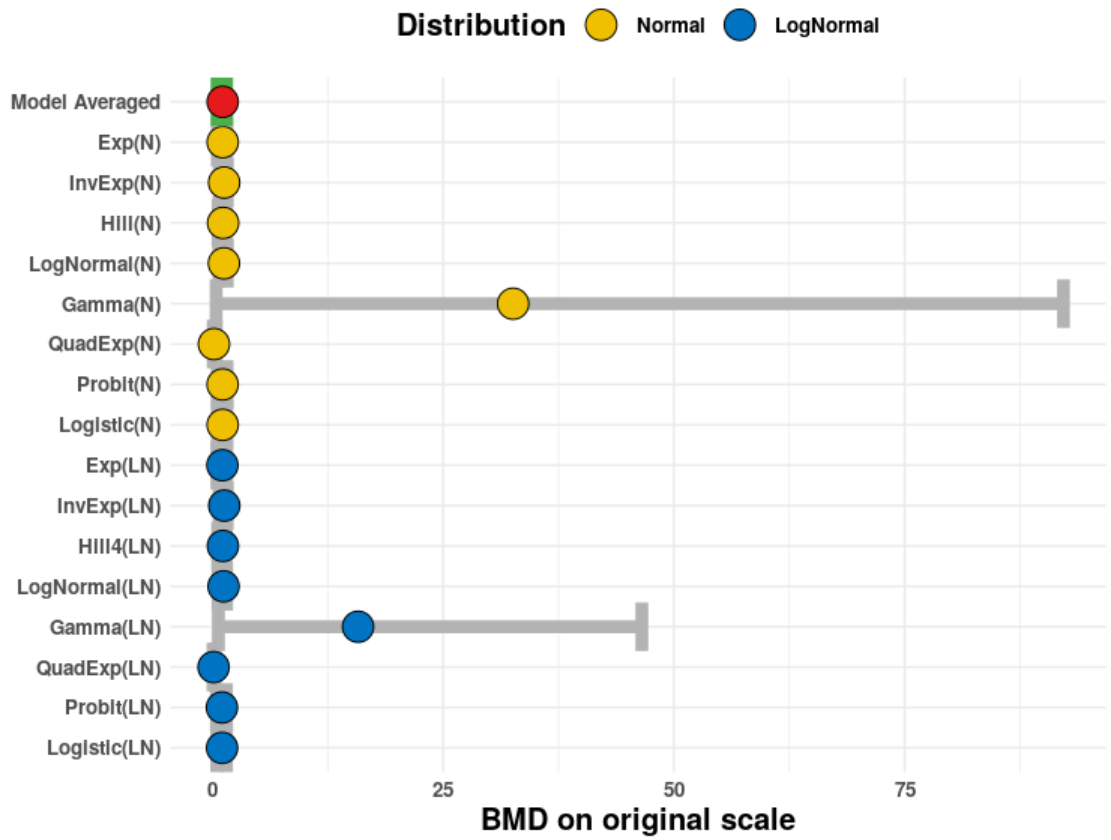
Model Averaged BMD

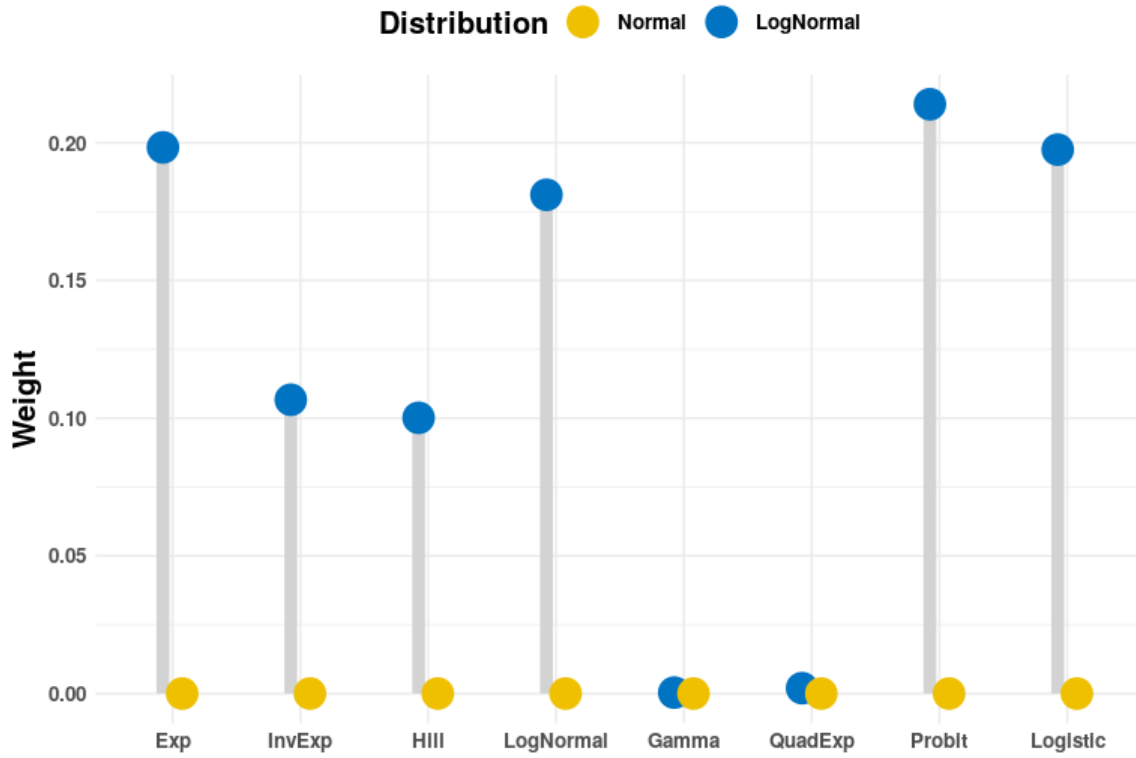
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.503	1.119	1.545

Estimated BMDs per model

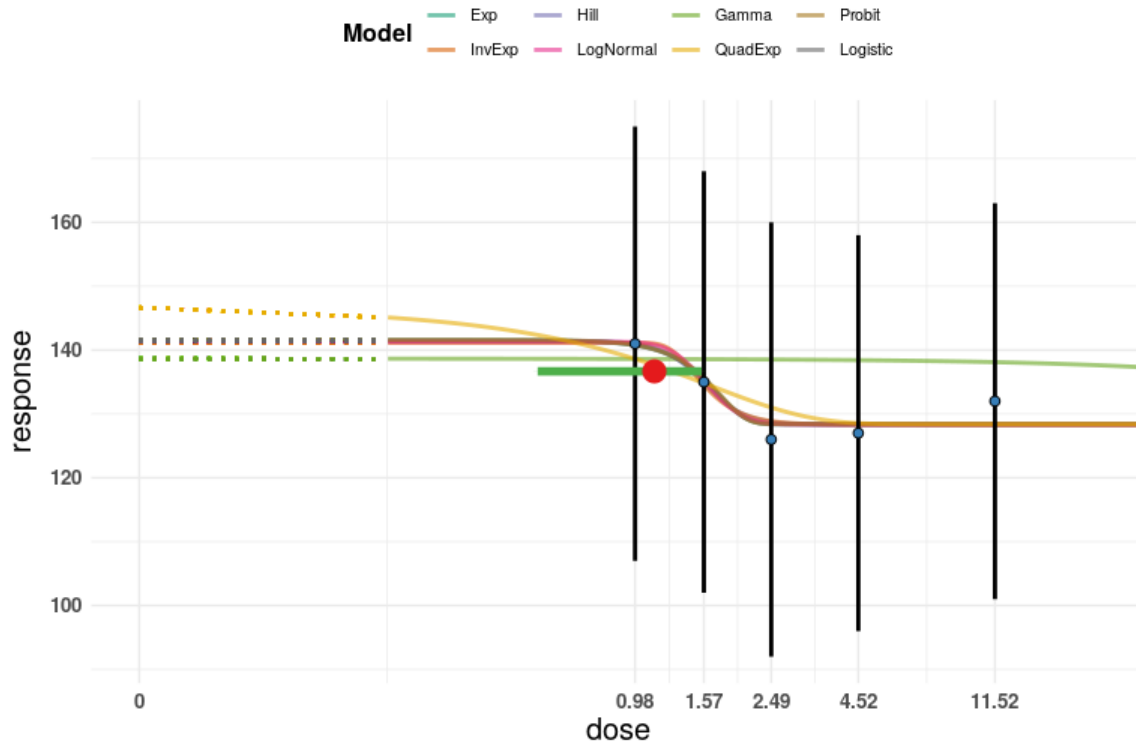
Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_N	0.536	1.123	1.575	0.000	1
IE4_N	0.770	1.276	1.601	0.000	1
H4_N	0.628	1.163	1.549	0.000	1
LN4_N	0.721	1.251	1.618	0.000	1
G4_N	0.407	32.585	92.211	0.000	0
QE4_N	0.089	0.170	0.392	0.000	1
P4_N	0.531	1.110	1.593	0.000	1
L4_N	0.541	1.116	1.564	0.000	1
E4_LN	0.485	1.088	1.552	0.198	1
IE4_LN	0.761	1.288	1.610	0.107	1
H4_LN	0.583	1.142	1.513	0.100	1
LN4_LN	0.611	1.211	1.545	0.181	1
G4_LN	0.658	15.784	46.530	0.000	0
QE4_LN	0.066	0.128	0.294	0.002	1
P4_LN	0.435	1.036	1.529	0.214	1
L4_LN	0.467	1.052	1.535	0.198	1

Plots of Fitted Models

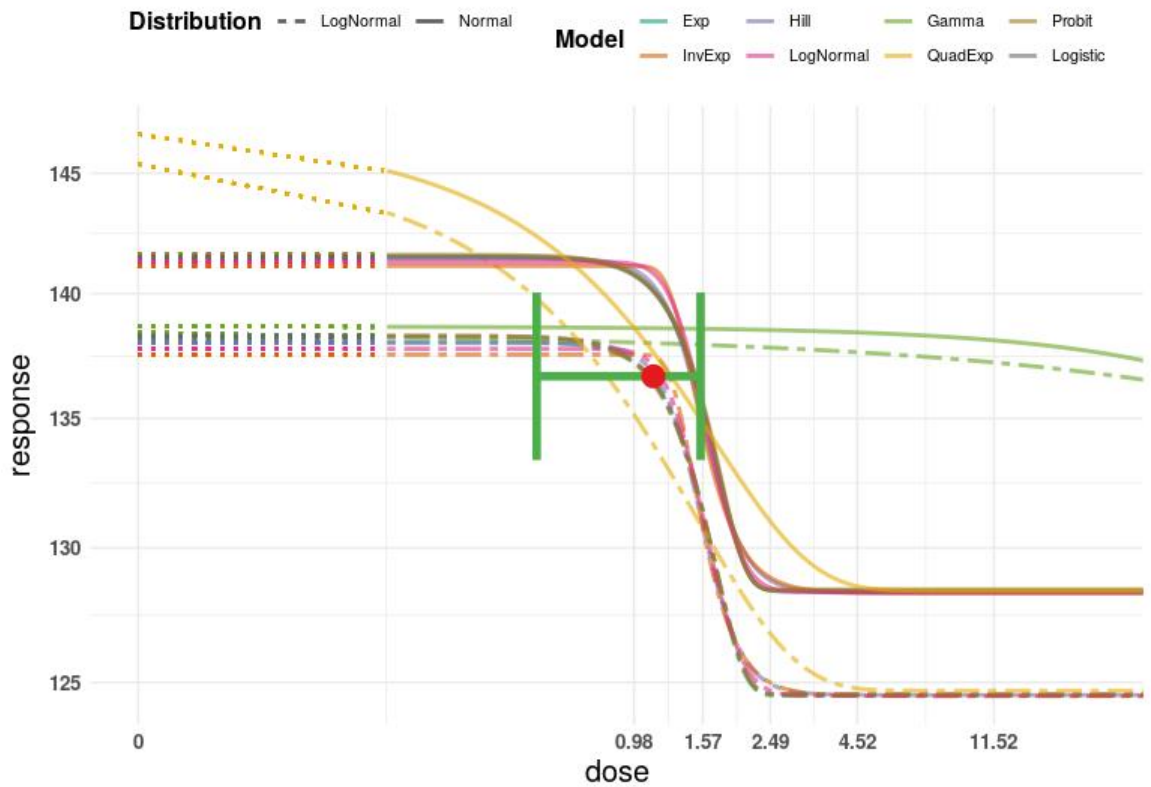
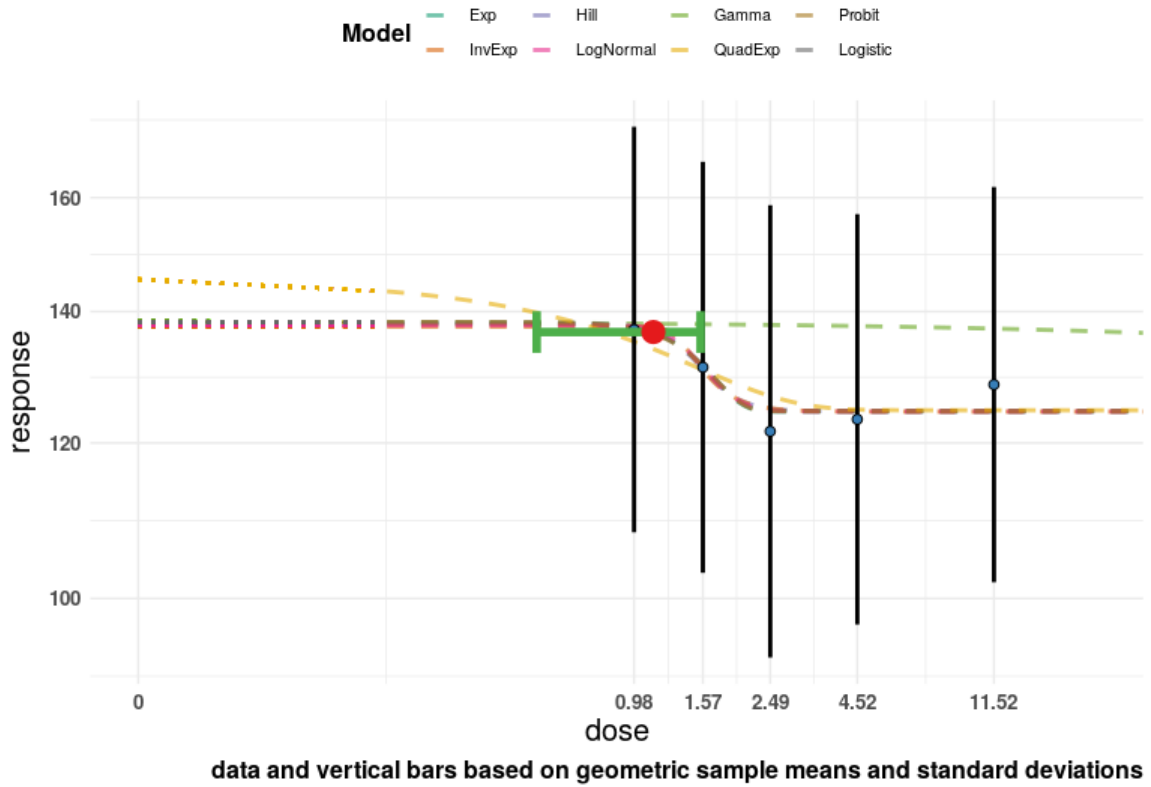


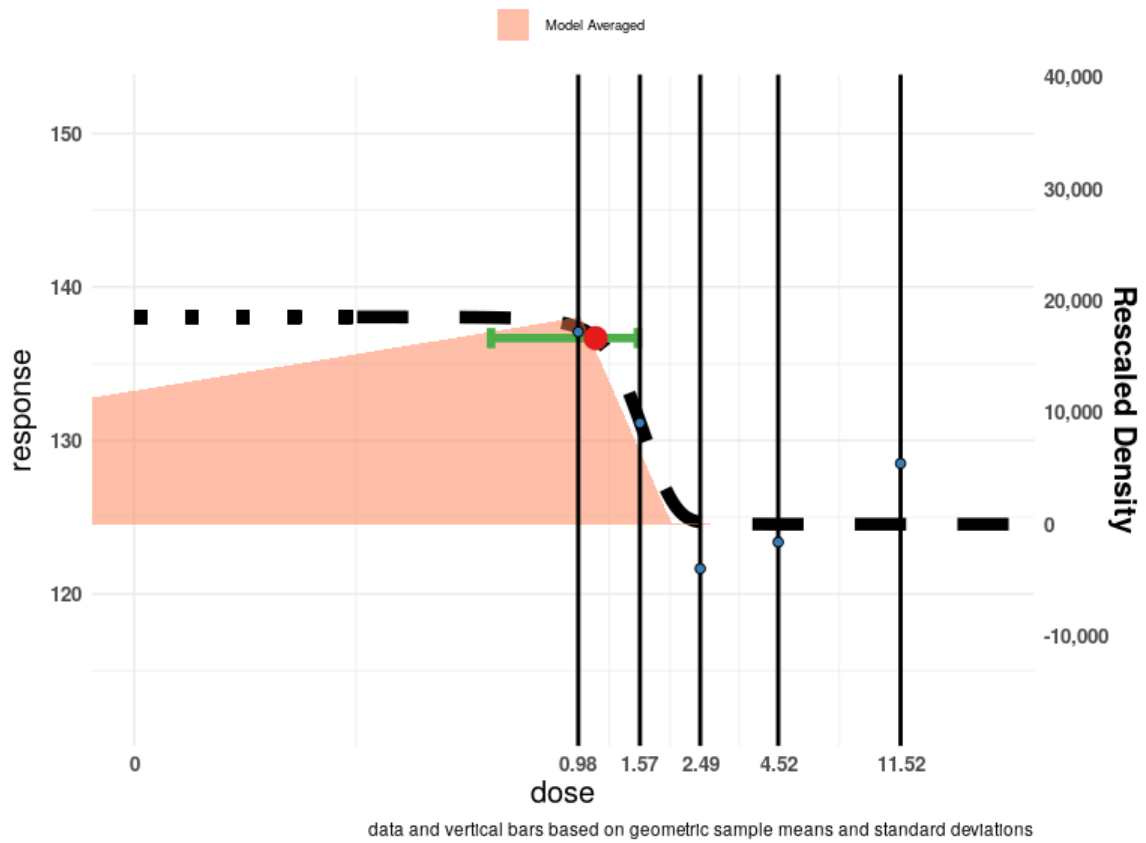


Normal distribution



LogNormal distribution





Wade et al. (2015) ischemic heart disease, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for ischemic heart disease

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.93	124	100735
2.02	146	96324
2.84	15	2941

The 'Value for CES' is set to 1.232e-05.

Extended dose range is applied.

Informative background prior: min: 0.00104631; the most likely: 0.00123095; max: 0.00141560. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 1.02e+00).

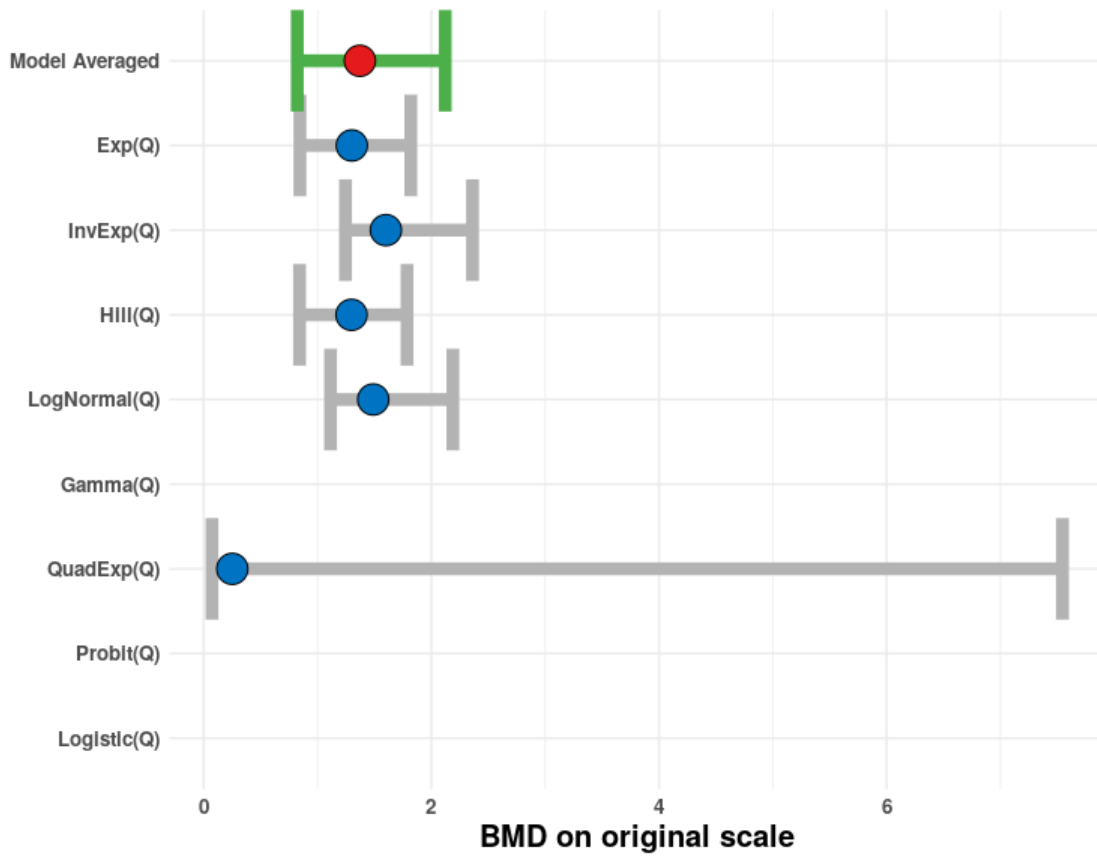
Model Averaged BMD

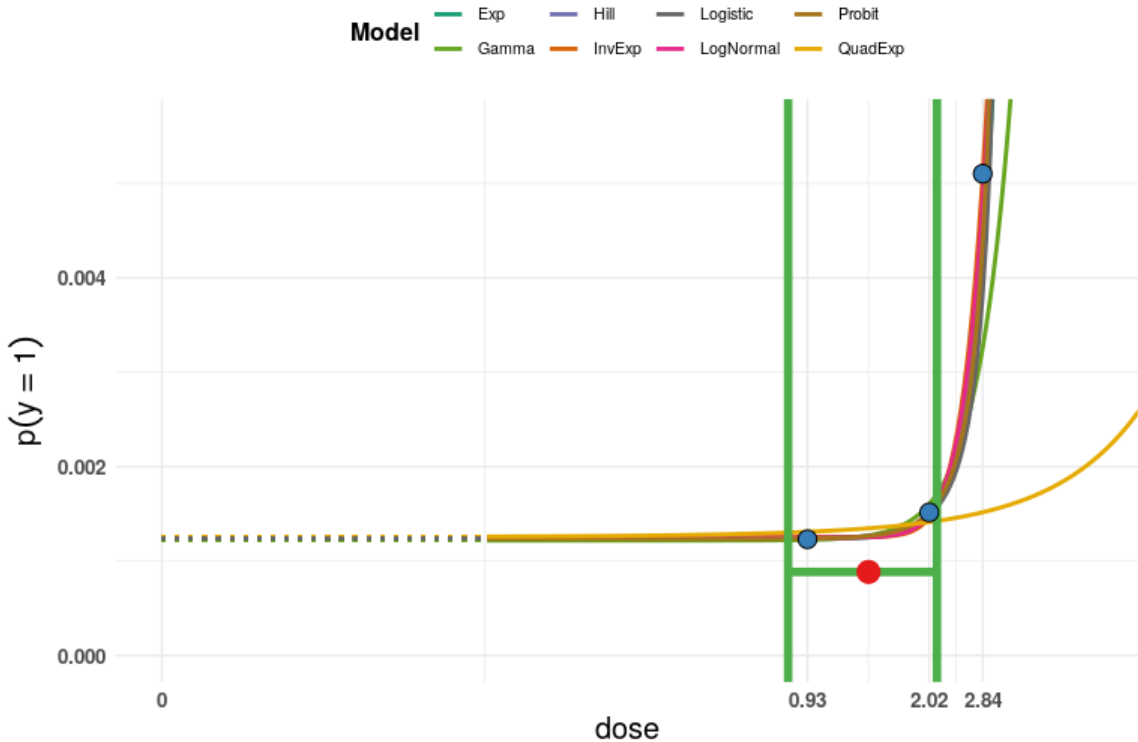
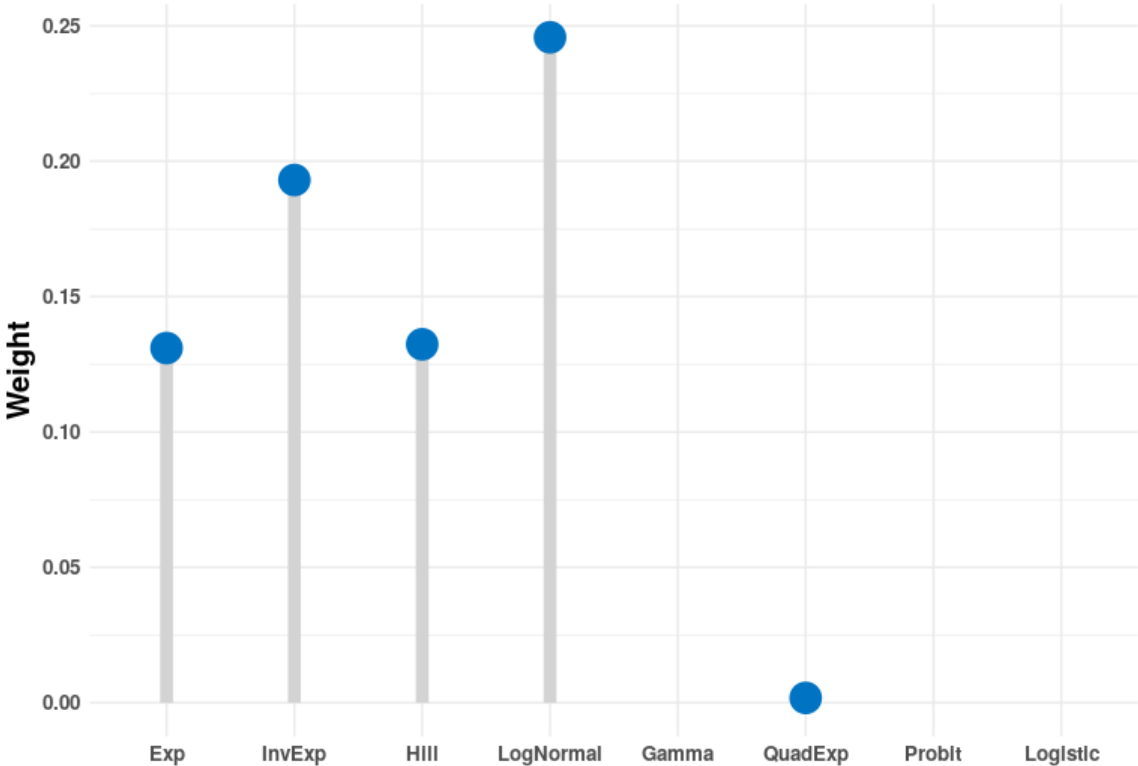
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.892	1.445	2.166

Estimated BMDs per model

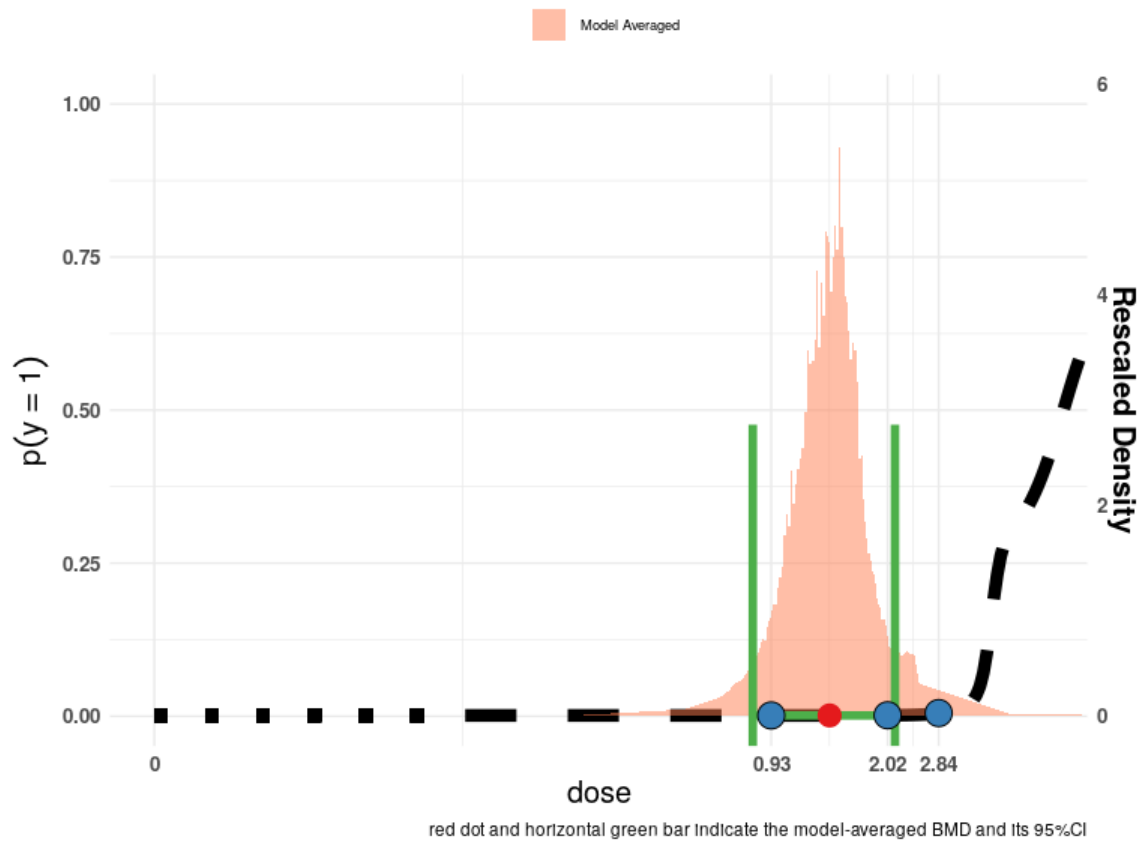
Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.846	1.301	1.820	0.131	0
IE4_Q	1.246	1.601	2.362	0.193	1
H4_Q	0.842	1.298	1.787	0.132	1
LN4_Q	1.114	1.489	2.189	0.246	1
QE4_Q	0.073	0.251	7.545	0.002	1

Plots of Fitted Models





red dot and horizontal green bar indicate the model-averaged BMD and its 95%CI



Wu et al. (2015) ischemic heart disease, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for ischemic heart disease

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
1.40	64	453
4.49	83	452
15.00	90	454

The 'Value for CES' is set to 0.00164524.

Extended dose range is not applied.

Informative background prior: min: 0.13986755; the most likely: 0.14128035; max: 0.14269316. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 6.86e+00).

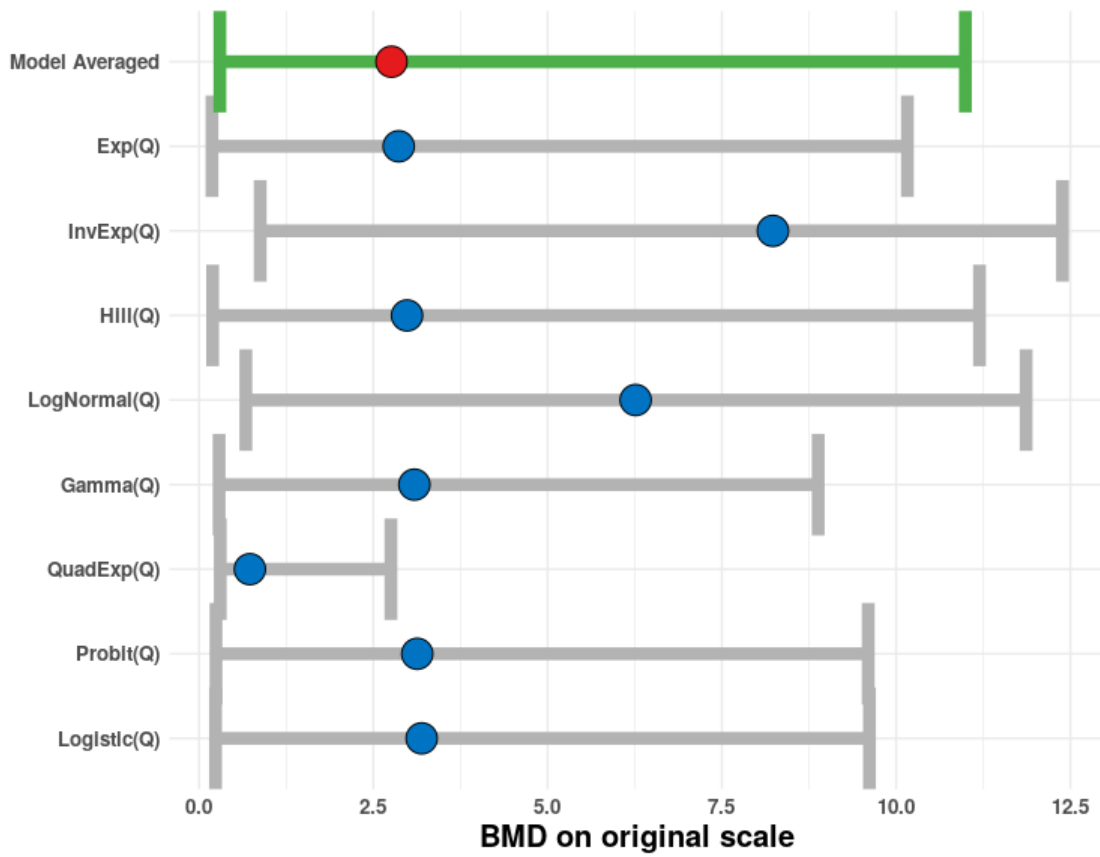
Model Averaged BMD

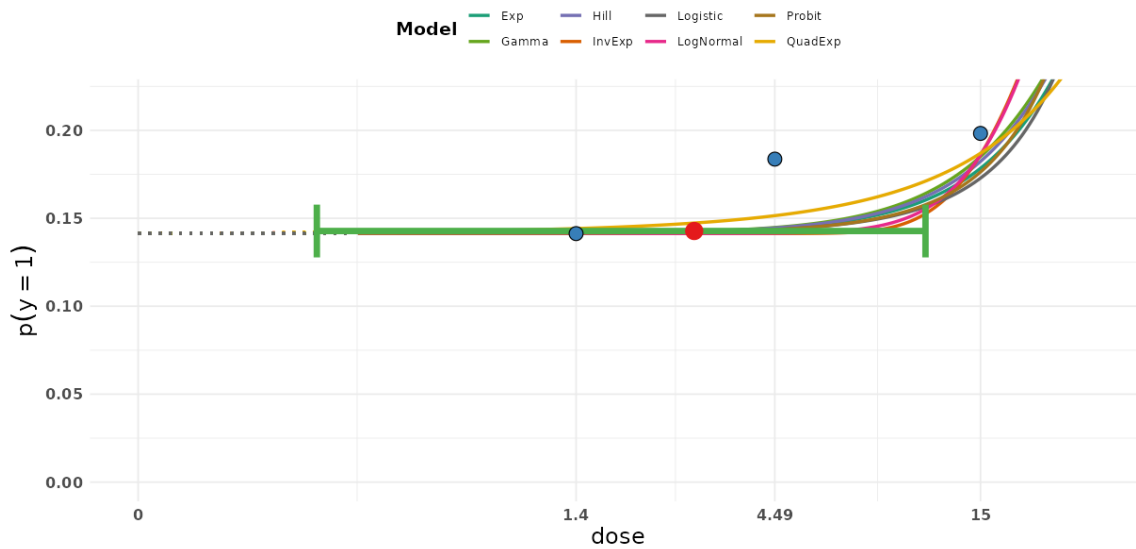
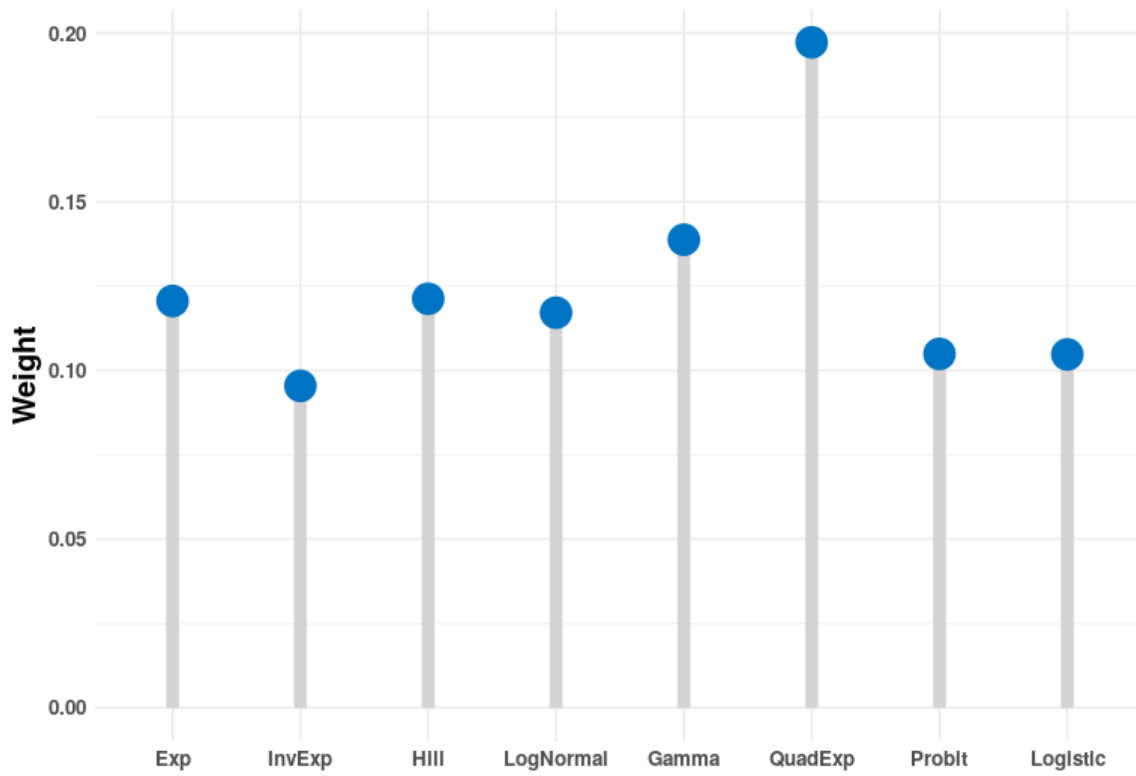
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.298	2.76	10.994

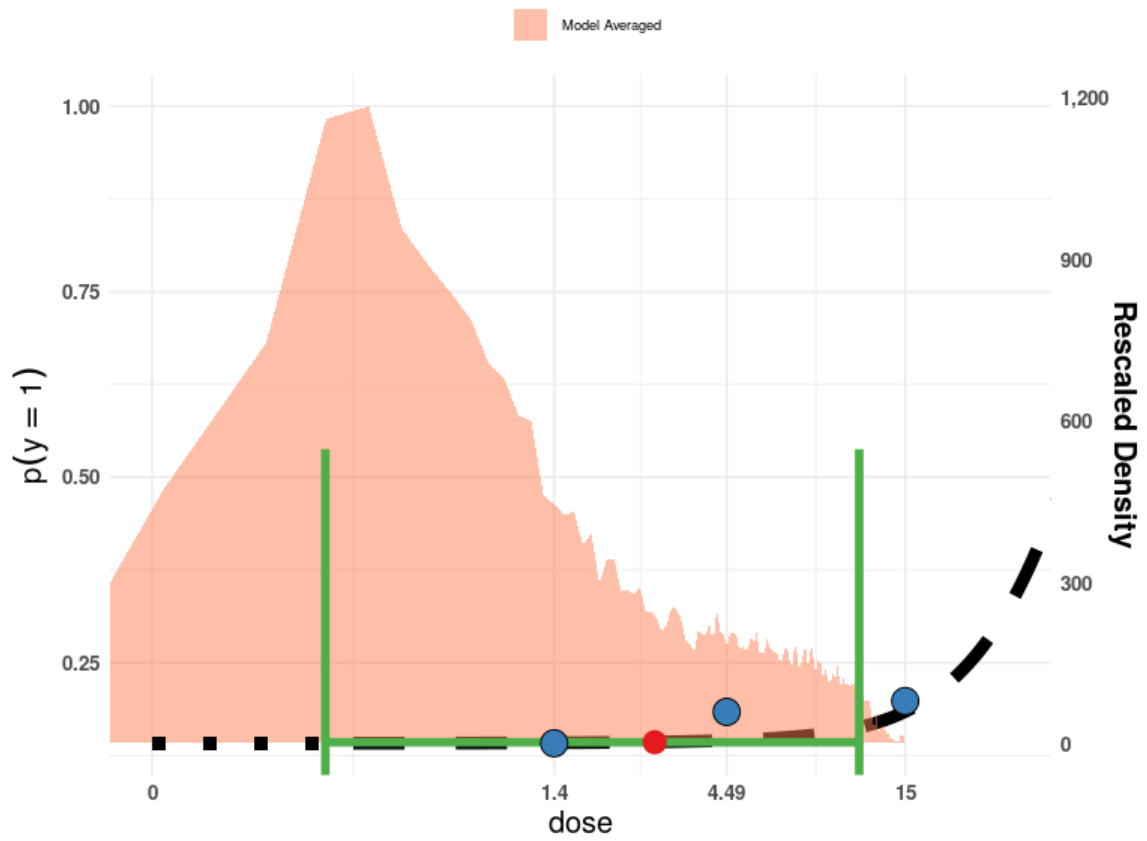
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.185	2.864	10.162	0.121	1
IE4_Q	0.877	8.232	12.387	0.095	1
H4_Q	0.194	2.983	11.196	0.121	1
LN4_Q	0.671	6.263	11.865	0.117	1
G4_Q	0.287	3.089	8.882	0.139	1
QE4_Q	0.304	0.729	2.752	0.197	1
P4_Q	0.243	3.130	9.600	0.105	1
L4_Q	0.236	3.193	9.618	0.105	1

Plots of Fitted Models







Xia et al. (2009) skin lesions, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for skin lesions

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.79	52	3215
1.07	33	845
1.48	56	1277
2.57	206	3429
4.75	137	1537
11.57	127	1021
17.02	10	92

The 'Value for CES' is set to 0.0001644.

Extended dose range is applied.

Informative background prior: min: 0.01536547; the most likely: 0.01617418; max: 0.01698289. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.04e-03).

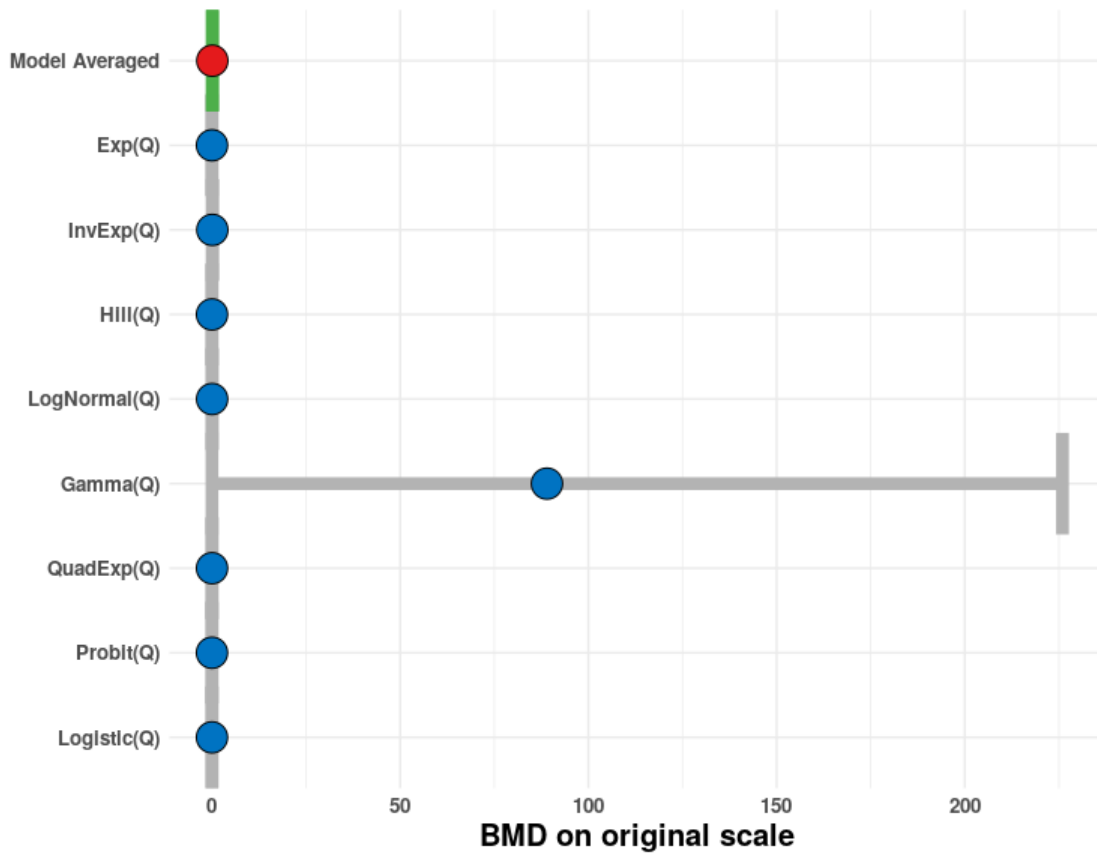
Model Averaged BMD

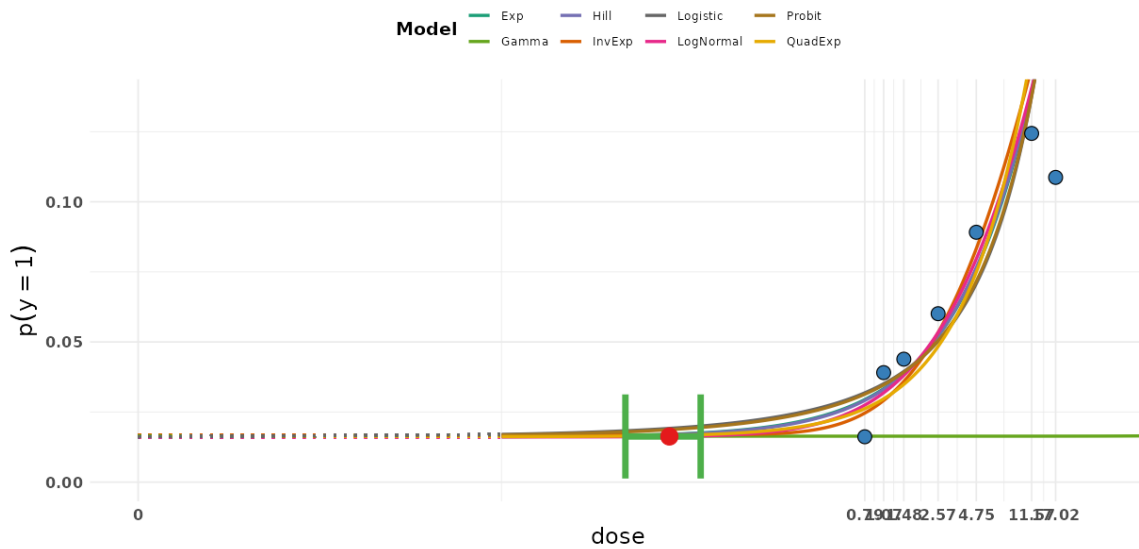
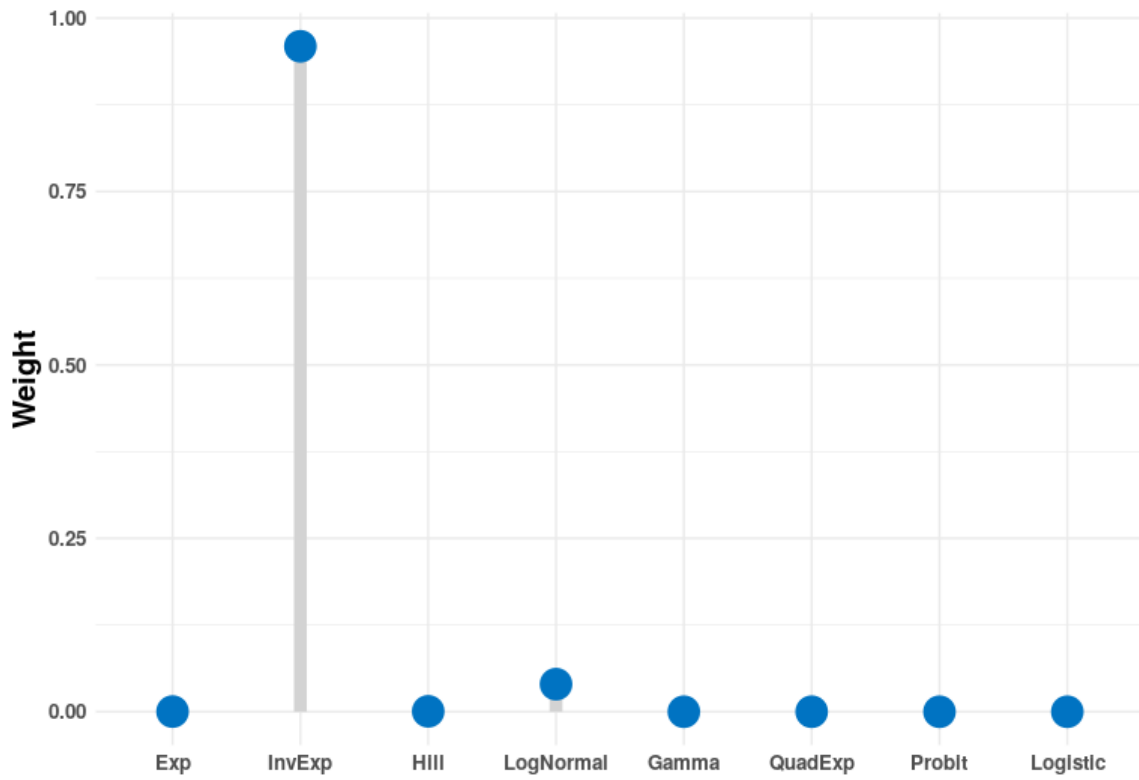
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.048	0.092	0.138

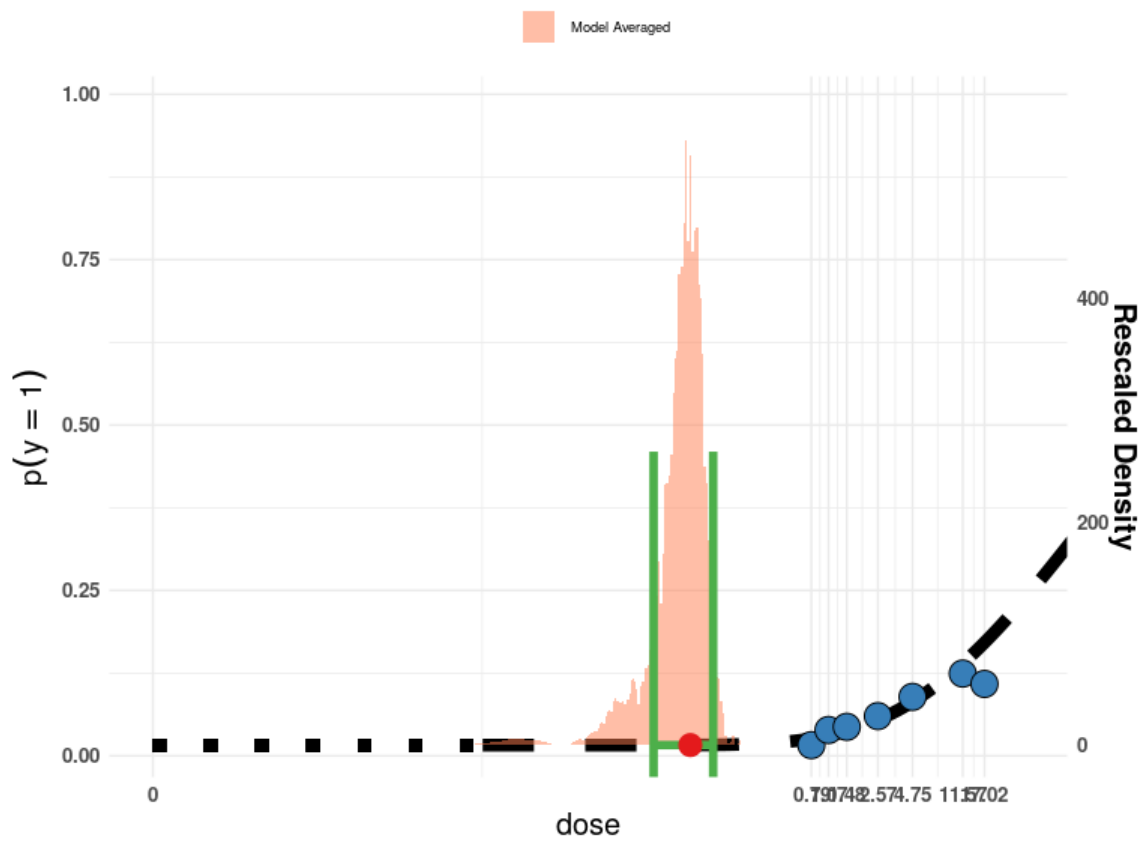
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.002	0.004	0.009	0.000	1
IE4_Q	0.057	0.094	0.139	0.959	1
H4_Q	0.002	0.005	0.011	0.001	1
LN4_Q	0.019	0.035	0.057	0.040	1
G4_Q	0.003	88.990	225.952	0.000	0
QE4_Q	0.012	0.013	0.014	0.000	1
P4_Q	0.000	0.000	0.000	0.000	1
L4_Q	0.000	0.000	0.000	0.000	1

Plots of Fitted Models







Zheng et al. (2015) chronic kidney disease, relative BMR 1%

Data Description

The endpoint to be analyzed is: Adj.cases for chronic kidney disease

Data used for analysis:

Exposure.µg.kg.bw.per.day	Adj.cases	N
0.061	101	772
0.160	113	781
0.260	124	784
0.310	164	782

The 'Value for CES' is set to 0.00150522.

Extended dose range is not applied.

Informative background prior: min: 0.12952073; the most likely: 0.13082902; max: 0.13213731. Shape parameter is applied.

The 'Sampling Method' is set to Bridge Sampling.

Results

Information pertaining to this endpoint.

Goodness of Fit

Best fitting model fits sufficiently well (Bayes factor is 2.40e-02).

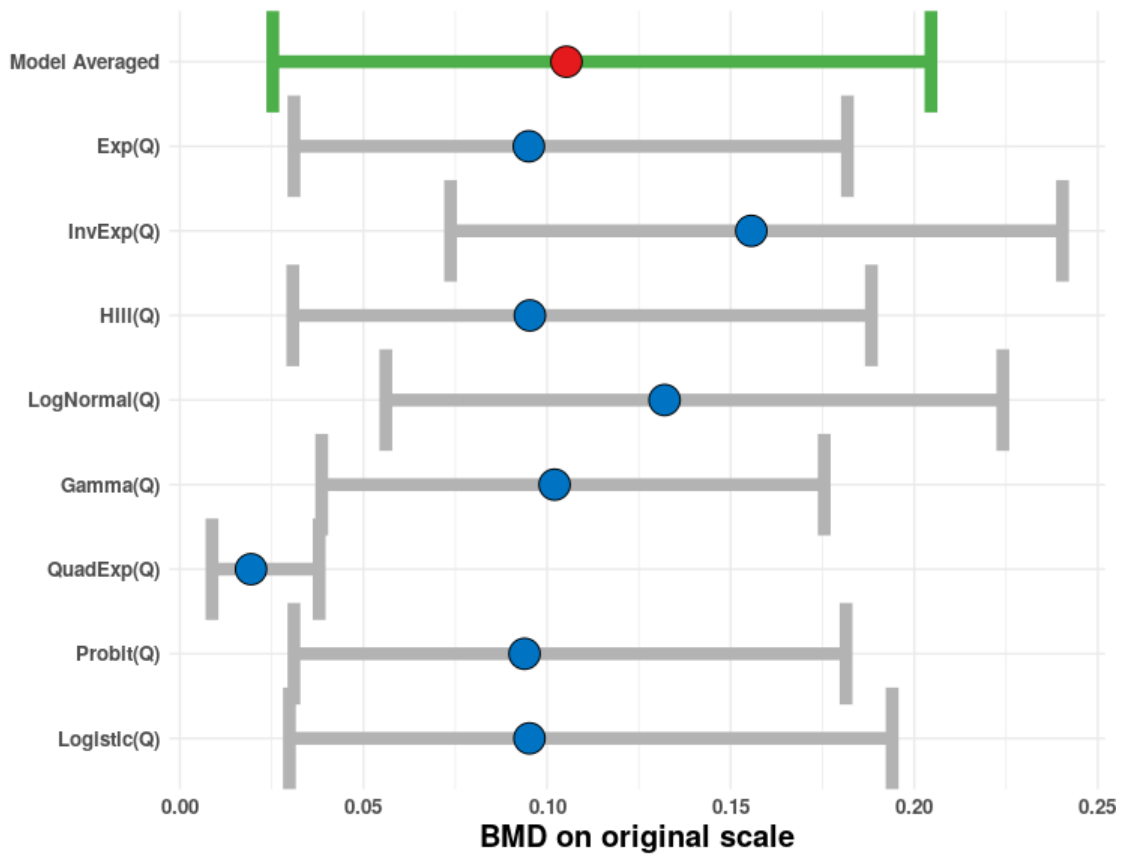
Model Averaged BMD

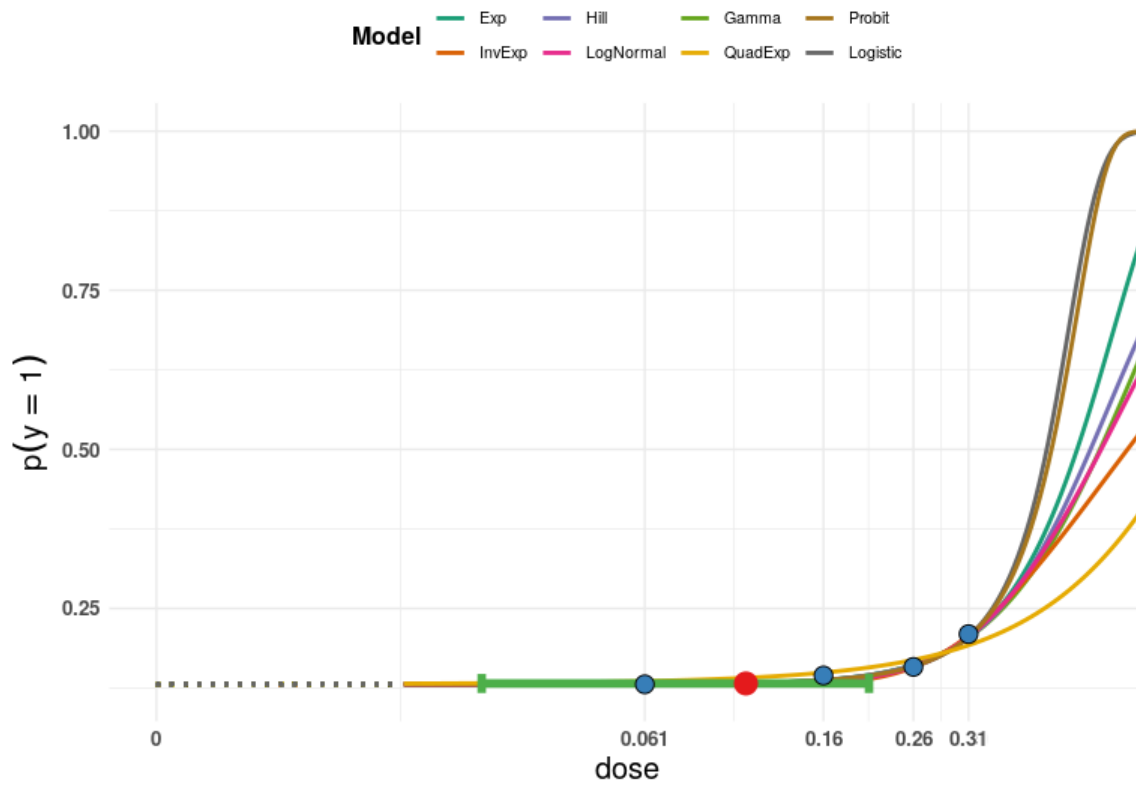
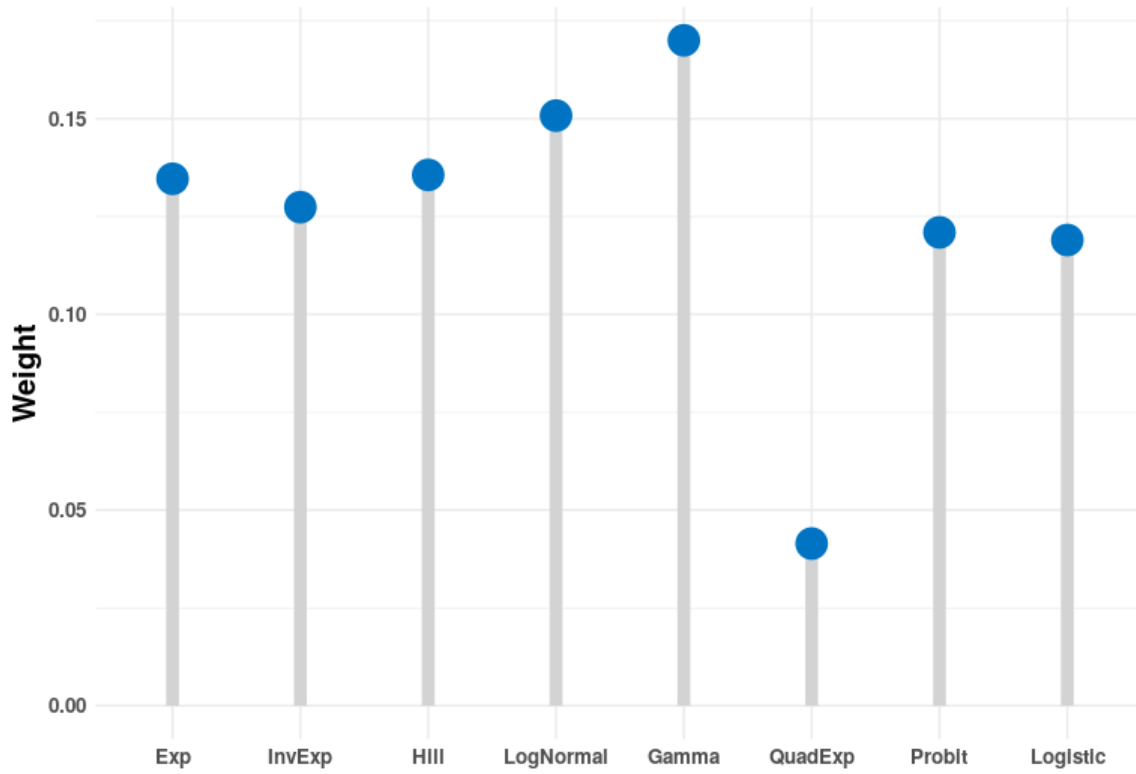
Model	Type	BMDL	BMD	BMDU
Model Averaged	BS	0.025	0.105	0.205

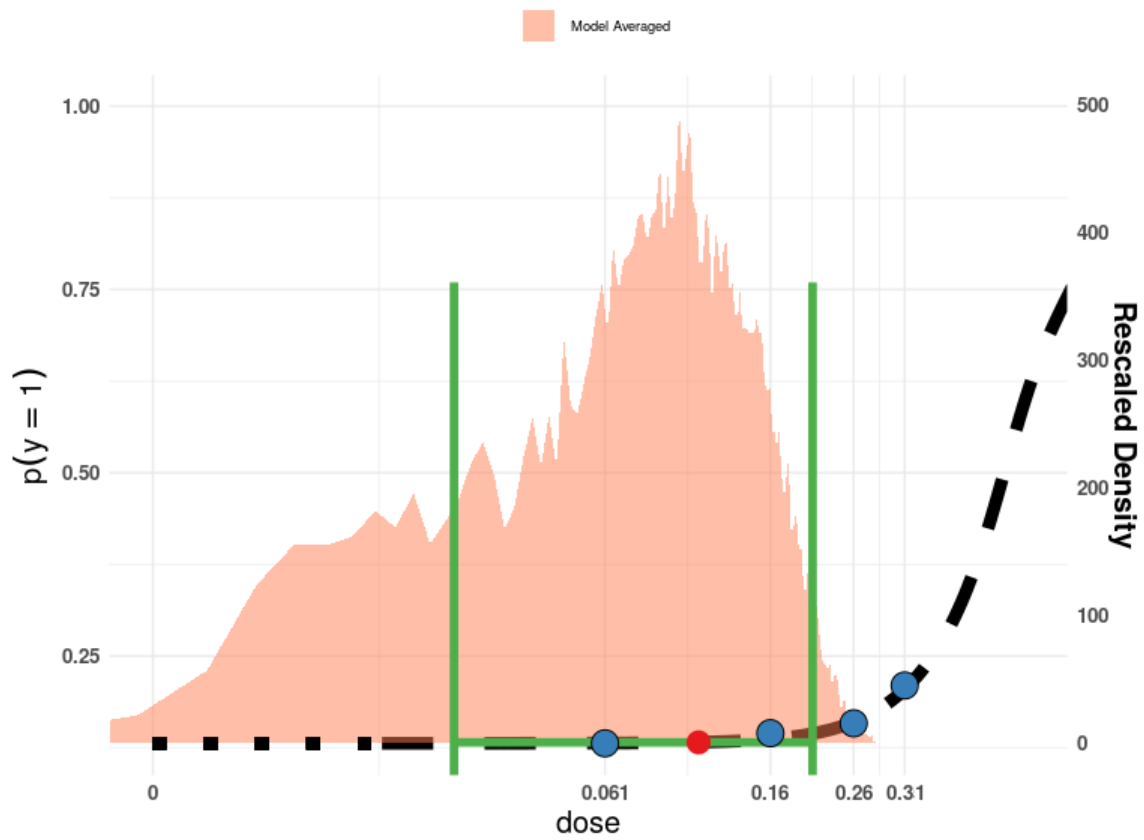
Estimated BMDs per model

Model	BMDL	BMD	BMDU	Model Weights	Converged
E4_Q	0.031	0.095	0.182	0.135	1
IE4_Q	0.074	0.156	0.240	0.127	1
H4_Q	0.031	0.095	0.188	0.136	1
LN4_Q	0.056	0.132	0.224	0.151	1
G4_Q	0.039	0.102	0.175	0.170	1
QE4_Q	0.009	0.019	0.038	0.041	1
P4_Q	0.031	0.094	0.181	0.121	1
L4_Q	0.030	0.095	0.194	0.119	1

Plots of Fitted Models







References

- Ahsan H, Chen Y, Parvez F, Zablotska L, Argos M, Hussain I, Momotaj H, Levy D, Cheng Z, Slavkovich V, van Geen A, Howe GR, Graziano JH, 2006. Arsenic exposure from drinking water and risk of premalignant skin lesions in Bangladesh: baseline results from the Health Effects of Arsenic Longitudinal Study. *Am J Epidemiol*, 163(12):1138-48. doi: 10.1093/aje/kwj154.
- Chen CL, Chiou HY, Hsu LI, Hsueh YM, Wu MM and Chen CJ, 2010a. Ingested arsenic, characteristics of well water consumption and risk of different histological types of lung cancer in northeastern Taiwan. *Environ Res*, 110:455-462. doi: 10.1016/j.envres.2009.08.010
- Chen CL, Chiou HY, Hsu LI, Hsueh YM, Wu MM, Wang YH and Chen CJ, 2010b. Arsenic in drinking water and risk of urinary tract cancer: a follow-up study from northeastern Taiwan. *Cancer Epidemiol Biomarkers Prev*, 19:101-110. doi: 10.1158/1055-9965.Epi-09-0333
- Cherry N, Shaikh K, McDonald C, Chowdhury Z, 2008. Stillbirth in rural Bangladesh: arsenic exposure and other etiological factors: a report from Gonoshasthaya Kendra. *Bulletin of the World Health Organization* 86, 172-177.
- EFSA Scientific Committee, More SJ, Bampidis V, Benford D, Bragard C, Halldorsson TI, Hernandez-Jerez AF, Bennekou SH, Koutsoumanis K, Lambré C, Machera K, Mennes W, Mullins E, Nielsen SS, Schrenk D, Turck D, Younes M, Aerts M, Edler L, Sand S, Wright M, Binaglia M, Bottex B, Cortinas Abrahantes J and Schlatter J, 2022. Guidance on the use of the benchmark dose approach in risk assessment. *EFSA Journal* 2022;20(10):7584, 67 pp. <https://doi.org/10.2903/j.efsa.2022.7584>
- Gilbert-Diamond D, Li Z, Perry AE, Spencer SK, Gandolfi AJ, Karagas MR, 2013. A population-based case-control study of urinary arsenic species and squamous cell carcinoma in New Hampshire, USA. *Environ Health Perspect*, 121(10):1154.
- Hsueh YM, Chung CJ, Shiue HS, Chen JB, Chiang SS, Yang MH, Tai CW and Su CT, 2009. Urinary arsenic species and CKD in a Taiwanese population: a case-control study. *Am J Kidney Dis*, 54:859-870. doi: 10.1053/j.ajkd.2009.06.016 Epub 2009 Aug 14.
- James KA, Byers T, Hokanson JE, Meliker JR, Zerbe GO and Marshall JA, 2015. Association between lifetime exposure to inorganic arsenic in drinking water and coronary heart disease in Colorado residents. *Environ Health Perspect*, 123:128-134. doi: 10.1289/ehp.1307839
- Leonardi G, Vahter M, Clemens F, Goessler W, Gurzau E, Hemminki K, Hough R, Koppova K, Kumar R, Rudnai P, Surdu S and Fletcher T, 2012. Inorganic arsenic and basal cell carcinoma in areas of Hungary, Romania, and Slovakia: a case-control study. *Environ Health Perspect*, 120:721-726. doi: 10.1289/ehp.1103534
- Milton AH, Smith W, Rahman B, Hasan Z, Kulsum U, Dear K, Rakibuddin M, Ali A, 2005. Chronic arsenic exposure and adverse pregnancy outcomes in Bangladesh. *Epidemiology* 16 (1), 82-86.
- Moon KA, Guallar E, Umans JG, Devereux RB, Best LG, Francesconi KA, Goessler W, Pollak J, Silbergeld EK, Howard BV and Navas-Acien A, 2013. Association between exposure to low to moderate arsenic levels and incident cardiovascular disease. A prospective cohort study. *Ann Intern Med*, 159:649-659. doi: 10.7326/0003-4819-159-10-201311190-00719
- Parvez F, Chen Y, Yunus M, Olopade C, Segers S, Slavkovich V, Argos M, Hasan R, Ahmed A, Islam T, Akter MM, Graziano JH and Ahsan H, 2013. Arsenic exposure and impaired lung function. Findings from a large population-based prospective cohort study. *Am J Respir Crit Care Med*, 188:813-819. doi: 10.1164/rccm.201212-2282OC
- Pierce BL, Argos M, Chen Y, Melkonian S, Parvez F, Islam T, Ahmed A, Hasan R, Rathouz PJ, Ahsan H, 2011. Arsenic exposure, dietary patterns, and skin lesion risk in Bangladesh: a prospective study. *Am J Epidemiol*, 173(3):345-54. doi: 10.1093/aje/kwq366.

Powers M, Sanchez TR, Grau-Perez M, Yeh F, Francesconi KA, Goessler W, George CM, Heaney C, Best LG, Umans JG, Brown RH and Navas-Acien A, 2019. Low-moderate arsenic exposure and respiratory in American Indian communities in the Strong Heart Study. *Environ Health*, 18:104. doi: 10.1186/s12940-019-0539-6

Rahman A, Vahter M, Ekstrom EC, Rahman M, Mustafa AMG, Wahed MA, Yunus M, Persson LA, 2007. Association of arsenic exposure during pregnancy with foetal loss and infant death: a cohort study in Bangladesh. *American Journal of Epidemiology* 165 (12), 1389-1396.

Rahman A, Persson L, Nermell B, El Arifeen S, Ekström EC, Smith AH and Vahter M, 2010. Arsenic exposure and risk of spontaneous abortion, stillbirth, and infant mortality. *Epidemiology*, 21:797-804. doi: 10.1097/EDE.0b013e3181f56a0d

Richter F, Kloster S, Wodschow K, Hansen B, Schullehner J, Kristiansen SM, Petersen MM, Strandberg-Larsen K and Ersbøll AK, 2022. Maternal exposure to arsenic in drinking water and risk of congenital heart disease in the offspring. *Environment International*, 160:107051. doi: <https://doi.org/10.1016/j.envint.2021.107051>

Siddique AE, Rahman M, Hossain MI, Karim Y, Hasibuzzaman MM, Biswas S, Islam MS, Rahman A, Hossen F, Mondal V and Banna HU, 2020. Association between chronic arsenic exposure and the characteristic features of asthma. *Chemosphere*, 246:125790.

Steinmaus CM, Ferreccio C, Romo JA, Yuan Y, Cortes S, Marshall G, Moore LE, Balmes JR, Liaw J, Golden T, Smith AH, 2013. Drinking water arsenic in northern Chile: high cancer risks 40 years after exposure cessation. *Cancer Epidemiol Biomarkers Prev*, 22(4):623-30.

Steinmaus C, Ferreccio C, Yuan Y, Acevedo J, González F, Perez L, Cortés S, Balmes JR, Liaw J, Smith AH, 2014a. Elevated lung cancer in younger adults and low concentrations of arsenic in water. *Am J Epidemiol*, 180(11):1082-7. doi: 10.1093/aje/kwu238

Vahter M, Skröder H, Rahman SM, Levi M, Derakhshani Hamadani J, Kippler M, 2020. Prenatal and childhood arsenic exposure through drinking water and food and cognitive abilities at 10 years of age: A prospective cohort study. *Environ Int*, 139:105723. doi: 10.1016/j.envint.2020.105723

Wade TJ, Xia Y, Mumford J, Wu K, Le XC, Sams E and Sanders WE, 2015. Cardiovascular disease and arsenic exposure in Inner Mongolia, China: a case control study. *Environ Health*, 14:35. doi: 10.1186/s12940-015-0022-y

Wu F, Jasmine F, Kibriya MG, Liu M, Cheng X, Parvez F, Islam T, Ahmed A, Rakibuz-Zaman M, Jiang J, Roy S, Paul-Brutus R, Slavkovich V, Islam T, Levy D, VanderWeele TJ, Pierce BL, Graziano JH, Ahsan H and Chen Y, 2015. Interaction between arsenic exposure from drinking water and genetic polymorphisms on cardiovascular disease in Bangladesh: a prospective case-cohort study. *Environ Health Perspect*, 123:451-457. doi: 10.1289/ehp.1307883

Xia Y, Wade TJ, Wu K, Li Y, Ning Z, Le XC, He X, Chen B, Feng Y, Mumford JL, 2009. Well water arsenic exposure, arsenic induced skin-lesions and self-reported morbidity in Inner Mongolia. *Int J Environ Res Public Health*, 6(3):1010-25. doi: 10.3390/ijerph6031010

Zheng LY, Umans JG, Yeh F, Francesconi KA, Goessler W, Silbergeld EK, Bandeen-Roche K, Guallar E, Howard BV, Weaver VM and Navas-Acien A, 2015. The association of urine arsenic with prevalent and incident chronic kidney disease: evidence from the Strong Heart Study. *Epidemiology*, 26:601-612. doi: 10.1097/ede.0000000000000313