# BMD Results for Table: Brain Weight Absolute

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 1.672 ± 0.144 | 1.797 ± 0.074 | 1.818 ± 0.029 | 1.784 ± 0.041 | 1.774 ± 0.072 | 1.772 ± 0.086 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 8.5E-04 | -97.079 | 8372.11 | 1037.59 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 2° | 8.5E-04 | -97.079 | 8372.35 | 1037.59 |
| Polynomial 3° | 8.5E-04 | -97.079 | 8369.54 | 1037.59 |
| Polynomial 4° | 8.5E-04 | -97.079 | 8386.37 | 1037.59 |
| Polynomial 5° | 8.5E-04 | -97.079 | 8368.36 | -999 |
| Power | 8.5E-04 | -97.079 | 8374.94 | 1061.68 |
| Hill | 0.145 | -109.063 | -999 | -999 |
| Exponential M2 | 8.5E-04 | -97.074 | 8454.15 | 1043.78 |
| Exponential M3 | 8.5E-04 | -97.074 | 8454.31 | 1043.78 |
| Exponential M4 | 0.077 | -107.063 | -999 | 0 |
| Exponential M5 | 0.033 | -105.063 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.025, BMDS Test 3 p-value = 0.812).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000851 < 0.1)  • BMD/high dose ratio is greater than threshold (8.1 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (8.07 > 5.0)  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!  • BMDL/high dose ratio is greater than threshold (1.0 > 1.0) |
| Polynomial 2° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000851 < 0.1)  • BMD/high dose ratio is greater than threshold (8.1 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (8.07 > 5.0)  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!  • BMDL/high dose ratio is greater than threshold (1.0 > 1.0) |
| Polynomial 3° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000851 < 0.1)  • BMD/high dose ratio is greater than threshold (8.1 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (8.07 > 5.0)  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!  • BMDL/high dose ratio is greater than threshold (1.0 > 1.0) |
| Polynomial 4° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000851 < 0.1)  • BMD/high dose ratio is greater than threshold (8.12 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (8.08 > 5.0)  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!  • BMDL/high dose ratio is greater than threshold (1.0 > 1.0) |
| Polynomial 5° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Goodness of fit p-value is less than threshold (0.000851 < 0.1)  • BMD/high dose ratio is greater than threshold (8.1 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMDL computation failed. |
| Power | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000851 < 0.1)  • BMD/high dose ratio is greater than threshold (8.11 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (7.89 > 5.0)  • BMDL/high dose ratio is greater than threshold (1.03 > 1.0) |
| Hill | Failure | **Failures**  • BMD does not exist  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMR value is not in the range of the mean function |
| Exponential M2 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00085 < 0.1)  • BMD/high dose ratio is greater than threshold (8.18 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (8.1 > 5.0)  • BMDL/high dose ratio is greater than threshold (1.01 > 1.0) |
| Exponential M3 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00085 < 0.1)  • BMD/high dose ratio is greater than threshold (8.18 > 1.0)  • Residual at lowest dose is greater than threshold (2.07 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (8.1 > 5.0)  • BMDL/high dose ratio is greater than threshold (1.01 > 1.0) |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0772 < 0.1) |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0327 < 0.1) |

## Recommended model

*No model was recommended as a best-fitting model.*

# BMD Results for Table: Brain Weight Relative

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 6.144 ± 0.525 | 6.986 ± 0.508 | 6.393 ± 0.18 | 6.497 ± 0.32 | 6.486 ± 0.315 | 6.765 ± 0.313 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power) | 0.034 | -17.747 | 1260.07 | 569.056 | Hill recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° | 0.016 | -15.792 | 1176.03 | 571.681 |
| Polynomial 3° | 0.016 | -15.859 | 1124.86 | 575.622 |
| Polynomial 4° | 0.016 | -15.888 | 1102.12 | 577.403 |
| Polynomial 5° | 0.017 | -15.901 | 1088.95 | 578.205 |
| Hillb | 0.104 | -20.476 | 4.8E-12 | 4.8E-12 |
| Exponential M2 (equivalent models include Exponential M3) | 0.034 | -17.751 | 1251.18 | 581.251 |
| Exponential M4 | 0.015 | -15.747 | 1260.7 | 3.546 |
| Exponential M5 | 0.015 | -15.747 | 1260.69 | 5.1E-04 |

a Constant variance case presented (BMDS Test 2 p-value = 0.378, BMDS Test 3 p-value = 0.378).

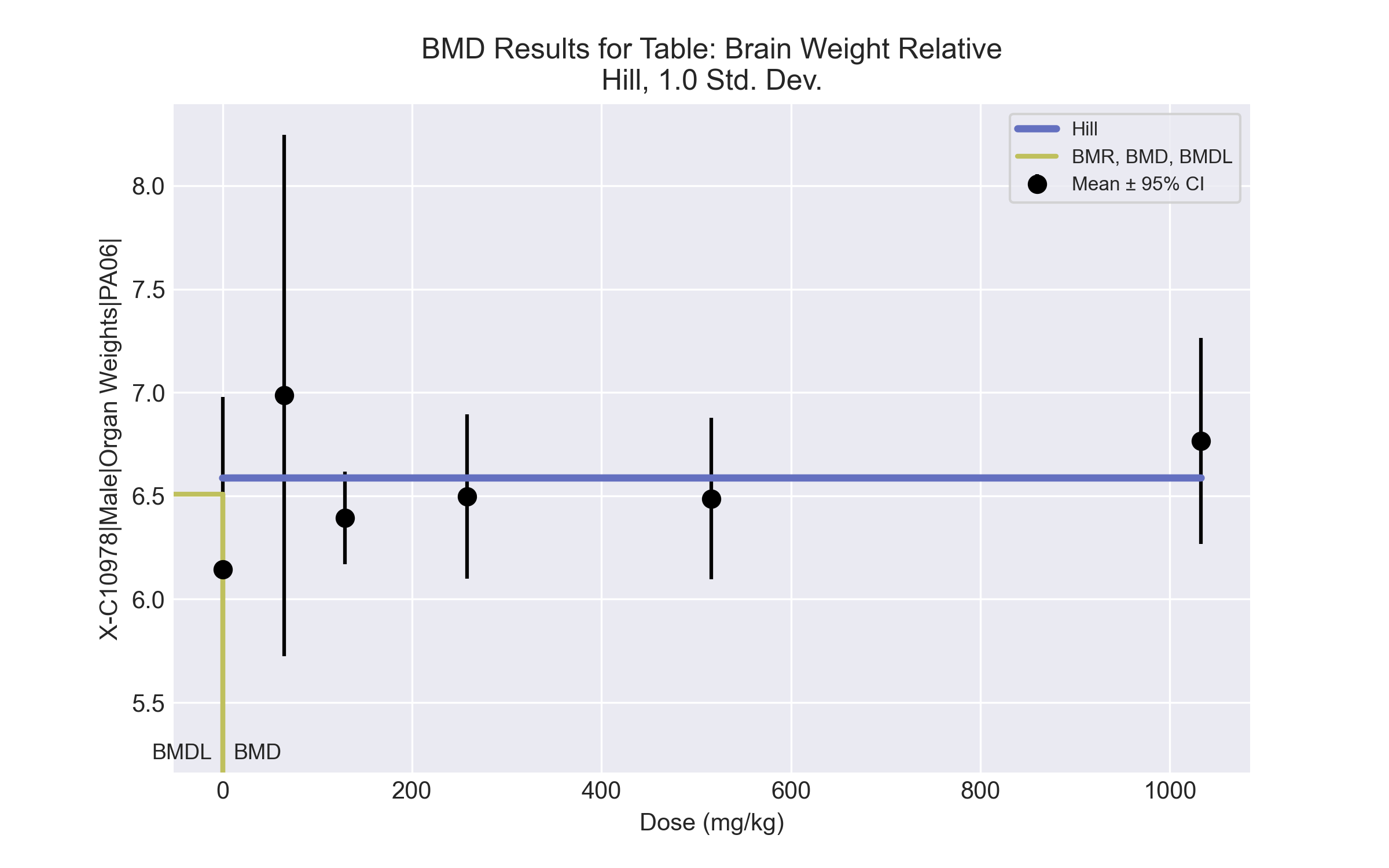
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0341 < 0.1)  • BMD/high dose ratio is greater than threshold (1.22 > 1.0) |
| Polynomial 2° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0157 < 0.1)  • BMD/high dose ratio is greater than threshold (1.14 > 1.0) |
| Polynomial 3° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0162 < 0.1)  • BMD/high dose ratio is greater than threshold (1.09 > 1.0) |
| Polynomial 4° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0164 < 0.1)  • BMD/high dose ratio is greater than threshold (1.07 > 1.0) |
| Polynomial 5° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0165 < 0.1)  • BMD/high dose ratio is greater than threshold (1.05 > 1.0) |
| Hilla | Valid | **Cautions**  • Minimum dose/BMD ratio is greater than threshold (1.35e+13 > 3.0) |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0341 < 0.1)  • BMD/high dose ratio is greater than threshold (1.21 > 1.0) |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0154 < 0.1)  • BMD/BMDL ratio is greater than threshold (3.56e+02 > 20.0)  • BMD/high dose ratio is greater than threshold (1.22 > 1.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (3.56e+02 > 5.0) |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0154 < 0.1)  • BMD/BMDL ratio is greater than threshold (2.47e+06 > 20.0)  • BMD/high dose ratio is greater than threshold (1.22 > 1.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (2.47e+06 > 5.0) |

a Recommended model

## Recommended model



====================================================================   
 Hill Model. (Version: 2.18; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-q2sal2ee.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-q2sal2ee.plt  
 Fri Jul 16 07:29:25 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = intercept + v\*dose^n/(k^n + dose^n)  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 rho is set to 0  
 Power parameter restricted to be greater than 1  
 A constant variance model is fit  
  
 Total number of dose groups = 6  
 Total number of records with missing values = 0  
 Maximum number of iterations = 500  
 Relative Function Convergence has been set to: 1e-008  
 Parameter Convergence has been set to: 1e-008  
  
  
  
 Default Initial Parameter Values   
 alpha = 0.128561  
 rho = 0 Specified  
 intercept = 6.14369  
 v = 0.841979  
 n = 0.109847  
 k = 97.5  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -rho -n -k   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 alpha intercept v  
  
 alpha 1 2.8e-008 7.4e-009  
  
 intercept 2.8e-008 1 -0.92  
  
 v 7.4e-009 -0.92 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 alpha 0.132881 0.0368545 0.0606472 0.205114  
 intercept 6.14369 0.182264 5.78646 6.50092  
 v 0.44263 0.198142 0.0542791 0.830981  
 n 1 NA  
 k 1.033e-012 NA  
  
NA - Indicates that this parameter has hit a bound  
 implied by some inequality constraint and thus  
 has no standard error.  
  
  
  
 Table of Data and Estimated Values of Interest  
  
 Dose N Obs Mean Est Mean Obs Std Dev Est Std Dev Scaled Res.  
------ --- -------- -------- ----------- ----------- ----------  
  
 0 4 6.14 6.14 0.525 0.365 -1.01e-007  
 65 3 6.99 6.59 0.508 0.365 1.9  
 129 5 6.39 6.59 0.18 0.365 -1.19  
 258 5 6.5 6.59 0.32 0.365 -0.546  
 516 5 6.49 6.59 0.315 0.365 -0.615  
 1033 4 6.77 6.59 0.313 0.365 0.982  
  
  
  
 Model Descriptions for likelihoods calculated  
  
  
 Model A1: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
  
 Model A2: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma(i)^2  
  
 Model A3: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
 Model A3 uses any fixed variance parameters that  
 were specified by the user  
  
 Model R: Yi = Mu + e(i)  
 Var{e(i)} = Sigma^2  
  
  
 Likelihoods of Interest  
  
 Model Log(likelihood) # Param's AIC  
 A1 17.078275 7 -20.156551  
 A2 19.739535 12 -15.479070  
 A3 17.078275 7 -20.156551  
 fitted 13.237954 3 -20.475908  
 R 10.955431 2 -17.910862  
  
  
 Explanation of Tests   
  
 Test 1: Do responses and/or variances differ among Dose levels?   
 (A2 vs. R)  
 Test 2: Are Variances Homogeneous? (A1 vs A2)  
 Test 3: Are variances adequately modeled? (A2 vs. A3)  
 Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)  
 (Note: When rho=0 the results of Test 3 and Test 2 will be the same.)  
  
 Tests of Interest   
  
 Test -2\*log(Likelihood Ratio) Test df p-value   
  
 Test 1 17.5682 10 0.0627  
 Test 2 5.32252 5 0.3778  
 Test 3 5.32252 5 0.3778  
 Test 4 7.68064 4 0.104  
  
The p-value for Test 1 is greater than .05. There may not be a  
diffence between responses and/or variances among the dose levels  
Modelling the data with a dose/response curve may not be appropriate  
  
The p-value for Test 2 is greater than .1. A homogeneous variance   
model appears to be appropriate here  
  
  
The p-value for Test 3 is greater than .1. The modeled variance appears   
 to be appropriate here  
  
The p-value for Test 4 is greater than .1. The model chosen seems   
to adequately describe the data  
   
  
 Benchmark Dose Computation  
  
Specified effect = 1  
  
Risk Type = Estimated standard deviations from the control mean   
  
Confidence level = 0.95  
  
 BMD = 4.82135e-012  
  
 BMDL = 4.82135e-012  
  
 BMDU = 4.82137e-012

# BMD Results for Table: Liver Weight Absolute

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 10.4 ± 0.613 | 9.7 ± 0.165 | 12.626 ± 0.985 | 12.958 ± 0.556 | 15.002 ± 1.094 | 14.623 ± 0.944 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°) | <0.0001 | 49.268 | 189.459 | 82.086 | Exponential-M2 recommended as best-fitting model on the basis of the lowest AIC. |
| Hill | 1.3E-04 | 34.557 | 78.435 | 49.169 |
| Exponential M2b (equivalent models include Exponential M3) | <0.0001 | 51.612 | 313.013 | 121.543 |
| Exponential M4 | 1.3E-04 | 35.106 | 52.484 | 30.357 |
| Exponential M5 | 1.0E-04 | 34.974 | 81.742 | 39.523 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.059, BMDS Test 3 p-value = 0.216).

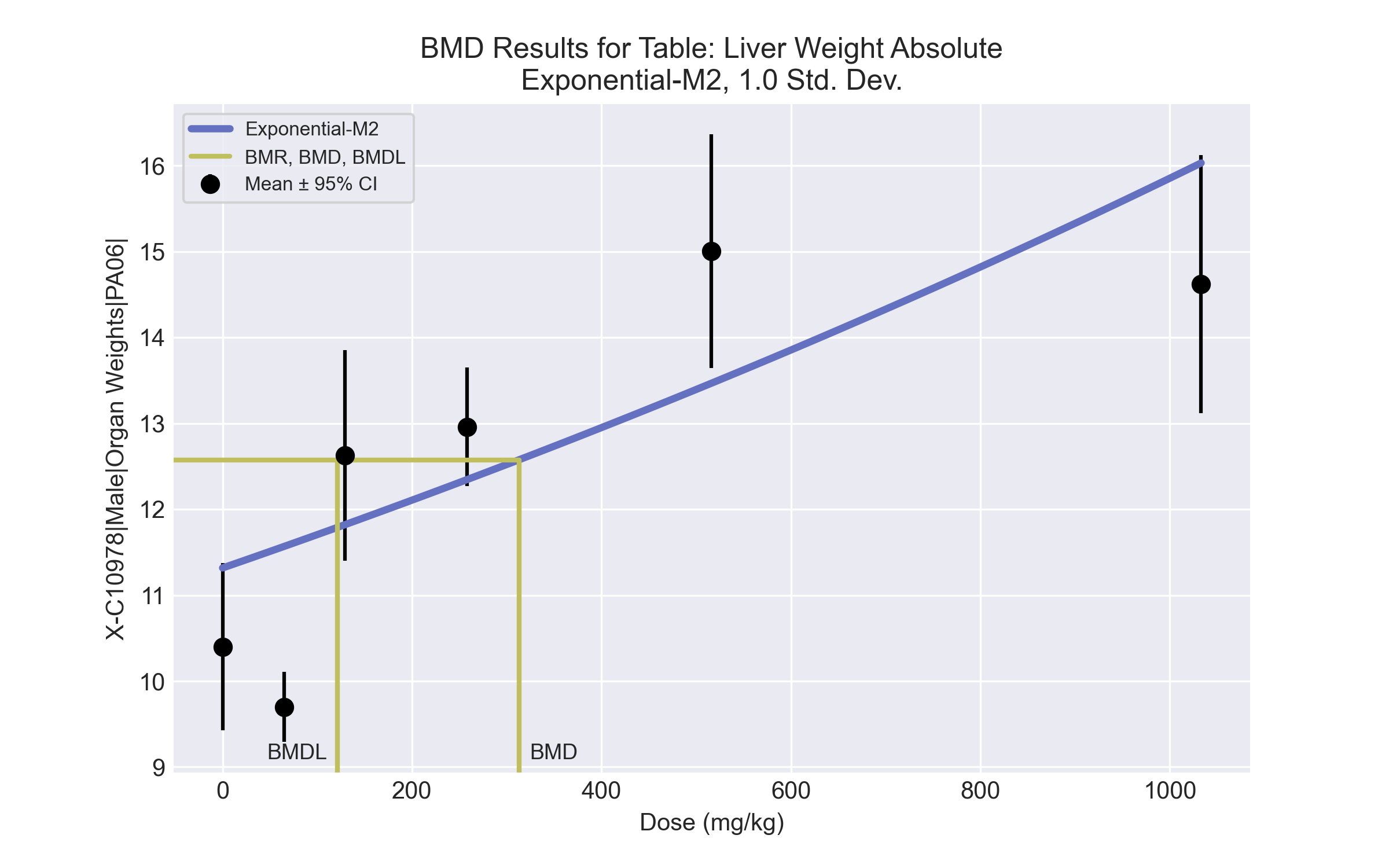
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°) | Warning | **Warnings**  • Ratio of modeled to actual stdev. at control is greater than threshold (1.71 > 1.5) |
| Hill | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000128 < 0.1) |
| Exponential M2a (equivalent models include Exponential M3) | Valid | - |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000135 < 0.1) |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000104 < 0.1) |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-y6lec25b.(d)   
 Gnuplot Plotting File:   
 Fri Jul 16 07:29:33 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function by Model:   
 Model 2: Y[dose] = a \* exp{sign \* b \* dose}  
 Model 3: Y[dose] = a \* exp{sign \* (b \* dose)^d}  
 Model 4: Y[dose] = a \* [c-(c-1) \* exp{-b \* dose}]  
 Model 5: Y[dose] = a \* [c-(c-1) \* exp{-(b \* dose)^d}]  
  
 Note: Y[dose] is the median response for exposure = dose;  
 sign = +1 for increasing trend in data;  
 sign = -1 for decreasing trend.  
  
 Model 2 is nested within Models 3 and 4.  
 Model 3 is nested within Model 5.  
 Model 4 is nested within Model 5.  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 Data are assumed to be distributed: normally  
 Variance Model: exp(lnalpha +rho \*ln(Y[dose]))  
 The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) \* rho)  
  
 Total number of dose groups = 6  
 Total number of records with missing values = 0  
 Maximum number of iterations = 500  
 Relative Function Convergence has been set to: 1e-008  
 Parameter Convergence has been set to: 1e-008  
  
 MLE solution provided: Exact  
  
  
 Initial Parameter Values  
  
 Variable Model 2  
 -------- --------  
 lnalpha -17.2392   
 rho 6.47041   
 a 11.2501   
 b 0.000340673   
 c 0 Specified  
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 2 Std. Err.  
 -------- ------- ---------  
 lnalpha -4.11921 11.5744  
 rho 1.88775 4.55422  
 a 11.3168 0.55717  
 b 0.000337064 0.000128309  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 4 10.4 0.6131  
 65 3 9.7 0.1652  
 129 5 12.63 0.9853  
 258 5 12.96 0.5559  
 516 5 15 1.094  
 1033 4 14.62 0.944  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 11.32 1.259 -1.456  
 65 11.57 1.286 -2.516  
 129 11.82 1.312 1.374  
 258 12.34 1.367 1.003  
 516 13.47 1.484 2.314  
 1033 16.03 1.749 -1.61  
  
  
  
 Other models for which likelihoods are calculated:  
  
 Model A1: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
  
 Model A2: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma(i)^2  
  
 Model A3: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = exp(lalpha + log(mean(i)) \* rho)  
  
 Model R: Yij = Mu + e(i)  
 Var{e(ij)} = Sigma^2  
  
  
 Likelihoods of Interest  
  
 Model Log(likelihood) DF AIC  
 ------- ----------------- ---- ------------  
 A1 -4.733709 7 23.46742  
 A2 0.5794294 12 22.84114  
 A3 -2.311328 8 20.62266  
 R -30.94973 2 65.89946  
 2 -21.80625 4 51.61249  
  
  
 Additive constant for all log-likelihoods = -23.89. This constant added to the  
 above values gives the log-likelihood including the term that does not  
 depend on the model parameters.  
  
  
 Explanation of Tests  
  
 Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)  
 Test 2: Are Variances Homogeneous? (A2 vs. A1)  
 Test 3: Are variances adequately modeled? (A2 vs. A3)  
 Test 4: Does Model 2 fit the data? (A3 vs. 2)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 63.06 10 < 0.0001  
 Test 2 10.63 5 0.05931  
 Test 3 5.782 4 0.2161  
 Test 4 38.99 4 < 0.0001  
  
  
 The p-value for Test 1 is less than .05. There appears to be a  
 difference between response and/or variances among the dose  
 levels, it seems appropriate to model the data.  
  
 The p-value for Test 2 is less than .1. A non-homogeneous  
 variance model appears to be appropriate.  
  
 The p-value for Test 3 is greater than .1. The modeled  
 variance appears to be appropriate here.  
  
 The p-value for Test 4 is less than .1. Model 2 may not adequately  
 describe the data; you may want to consider another model.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 313.013  
  
 BMDL = 121.543  
  
 BMDU = 806.275

# BMD Results for Table: Liver Weight Relative

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 38.206 ± 2.298 | 37.703 ± 2.047 | 44.374 ± 3.292 | 47.134 ± 1.166 | 54.821 ± 3.716 | 55.79 ± 3.017 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°) | <0.0001 | 104.514 | 227.357 | 172.501 | Exponential-M2 recommended as best-fitting model on the basis of the lowest AIC. |
| Hill | 0.051 | 88.466 | 85.856 | 46.173 |
| Exponential M2b (equivalent models include Exponential M3) | <0.0001 | 107.353 | 288.723 | 223.524 |
| Exponential M4 | 0.048 | 88.42 | 48.938 | 33.791 |
| Exponential M5 | 0.067 | 87.918 | 82.675 | 42.905 |

a Constant variance case presented (BMDS Test 2 p-value = 0.22, BMDS Test 3 p-value = 0.22).

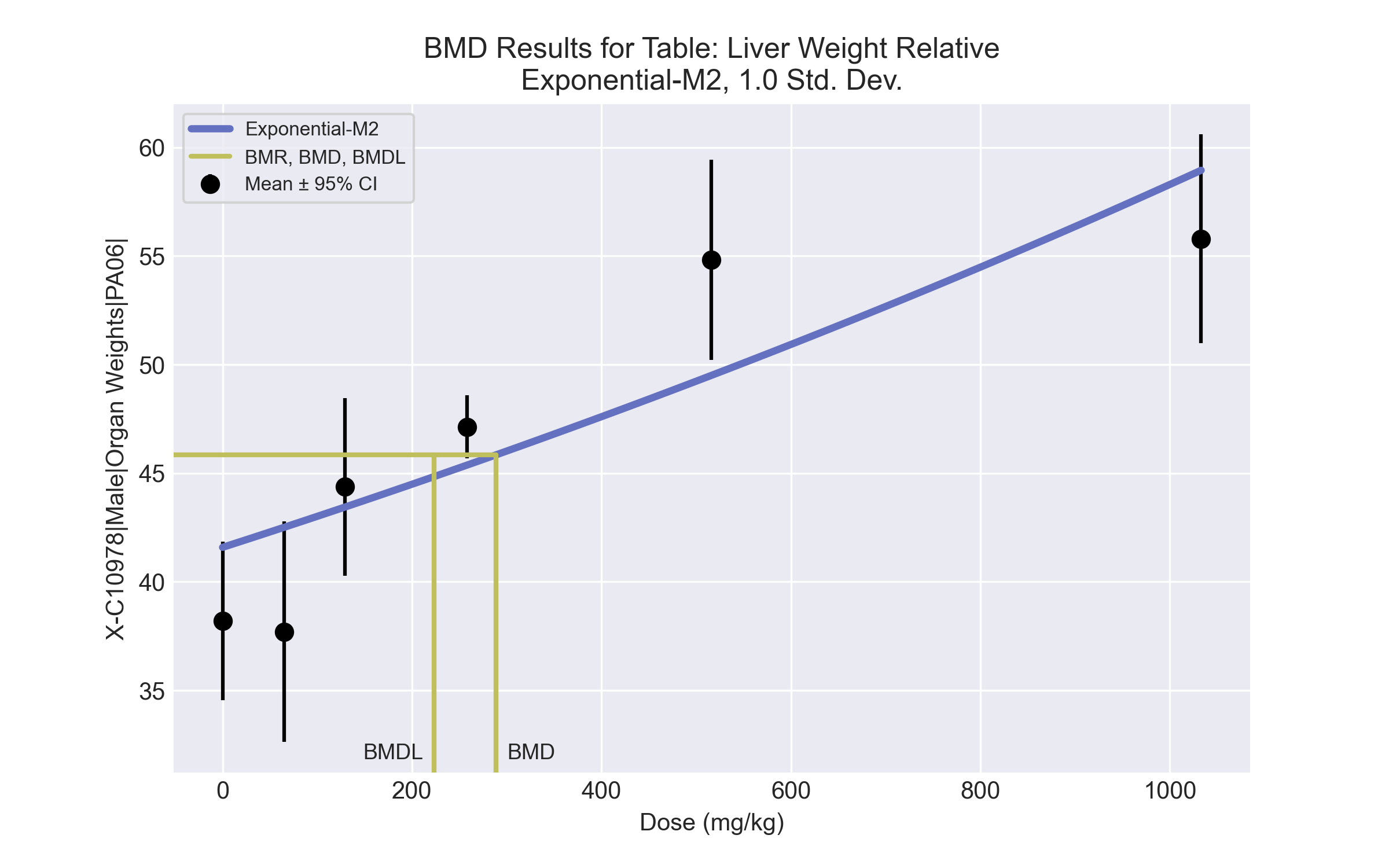
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°) | Warning | **Warnings**  • Ratio of modeled to actual stdev. at control is greater than threshold (1.75 > 1.5) |
| Hill | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0508 < 0.1) |
| Exponential M2a (equivalent models include Exponential M3) | Valid | - |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0478 < 0.1) |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0668 < 0.1) |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-pf31rf1n.(d)   
 Gnuplot Plotting File:   
 Fri Jul 16 07:29:36 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function by Model:   
 Model 2: Y[dose] = a \* exp{sign \* b \* dose}  
 Model 3: Y[dose] = a \* exp{sign \* (b \* dose)^d}  
 Model 4: Y[dose] = a \* [c-(c-1) \* exp{-b \* dose}]  
 Model 5: Y[dose] = a \* [c-(c-1) \* exp{-(b \* dose)^d}]  
  
 Note: Y[dose] is the median response for exposure = dose;  
 sign = +1 for increasing trend in data;  
 sign = -1 for decreasing trend.  
  
 Model 2 is nested within Models 3 and 4.  
 Model 3 is nested within Model 5.  
 Model 4 is nested within Model 5.  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 Data are assumed to be distributed: normally  
 Variance Model: exp(lnalpha +rho \*ln(Y[dose]))  
 rho is set to 0.  
 A constant variance model is fit.  
  
 Total number of dose groups = 6  
 Total number of records with missing values = 0  
 Maximum number of iterations = 500  
 Relative Function Convergence has been set to: 1e-008  
 Parameter Convergence has been set to: 1e-008  
  
 MLE solution provided: Exact  
  
  
 Initial Parameter Values  
  
 Variable Model 2  
 -------- --------  
 lnalpha 1.78873   
 rho 0 Specified  
 a 40.8823   
 b 0.00037526   
 c 0 Specified  
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 2 Std. Err.  
 -------- ------- ---------  
 lnalpha 2.89818 5.03141  
 a 41.586 1.09419  
 b 0.00033772 4.56093e-005  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 4 38.21 2.298  
 65 3 37.7 2.047  
 129 5 44.37 3.292  
 258 5 47.13 1.166  
 516 5 54.82 3.716  
 1033 4 55.79 3.017  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 41.59 4.259 -1.587  
 65 42.51 4.259 -1.954  
 129 43.44 4.259 0.4915  
 258 45.37 4.259 0.9249  
 516 49.5 4.259 2.792  
 1033 58.95 4.259 -1.482  
  
  
  
 Other models for which likelihoods are calculated:  
  
 Model A1: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
  
 Model A2: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma(i)^2  
  
 Model A3: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = exp(lalpha + log(mean(i)) \* rho)  
  
 Model R: Yij = Mu + e(i)  
 Var{e(ij)} = Sigma^2  
  
  
 Likelihoods of Interest  
  
 Model Log(likelihood) DF AIC  
 ------- ----------------- ---- ------------  
 A1 -36.25348 7 86.50696  
 A2 -32.7496 12 89.49919  
 A3 -36.25348 7 86.50696  
 R -64.57197 2 133.1439  
 2 -50.67629 3 107.3526  
  
  
 Additive constant for all log-likelihoods = -23.89. This constant added to the  
 above values gives the log-likelihood including the term that does not  
 depend on the model parameters.  
  
  
 Explanation of Tests  
  
 Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)  
 Test 2: Are Variances Homogeneous? (A2 vs. A1)  
 Test 3: Are variances adequately modeled? (A2 vs. A3)  
 Test 4: Does Model 2 fit the data? (A3 vs. 2)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 63.64 10 < 0.0001  
 Test 2 7.008 5 0.2201  
 Test 3 7.008 5 0.2201  
 Test 4 28.85 4 < 0.0001  
  
  
 The p-value for Test 1 is less than .05. There appears to be a  
 difference between response and/or variances among the dose  
 levels, it seems appropriate to model the data.  
  
 The p-value for Test 2 is greater than .1. A homogeneous  
 variance model appears to be appropriate here.  
  
 The p-value for Test 3 is greater than .1. The modeled  
 variance appears to be appropriate here.  
  
 The p-value for Test 4 is less than .1. Model 2 may not adequately  
 describe the data; you may want to consider another model.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 288.723  
  
 BMDL = 223.524  
  
 BMDU = 408.117

# BMD Results for Table: Bile salts/acids

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 52.15 ± 10.314 | 35.067 ± 3.953 | 41.86 ± 14.387 | 30.92 ± 20.234 | 41.46 ± 14.431 | 23.4 ± 11.558 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linearb (equivalent models include Power, Polynomial 2°) | 0.202 | 169.222 | 763.124 | 434.064 | Linear recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 3° | 0.116 | 171.164 | 832.321 | 436.088 |
| Polynomial 4° | 0.12 | 171.092 | 867.436 | 438.656 |
| Polynomial 5° | 0.122 | 171.046 | 889.801 | 440.331 |
| Hill | 0.149 | 170.586 | 127.806 | 0.003 |
| Exponential M2 | 0.201 | 169.227 | 704.783 | 320.489 |
| Exponential M3 (equivalent models include Exponential M4) | 0.201 | 169.227 | 704.782 | 320.489 |
| Exponential M5 | 0.113 | 171.227 | 704.783 | 6.061 |

a Constant variance case presented (BMDS Test 2 p-value = 0.146, BMDS Test 3 p-value = 0.146).

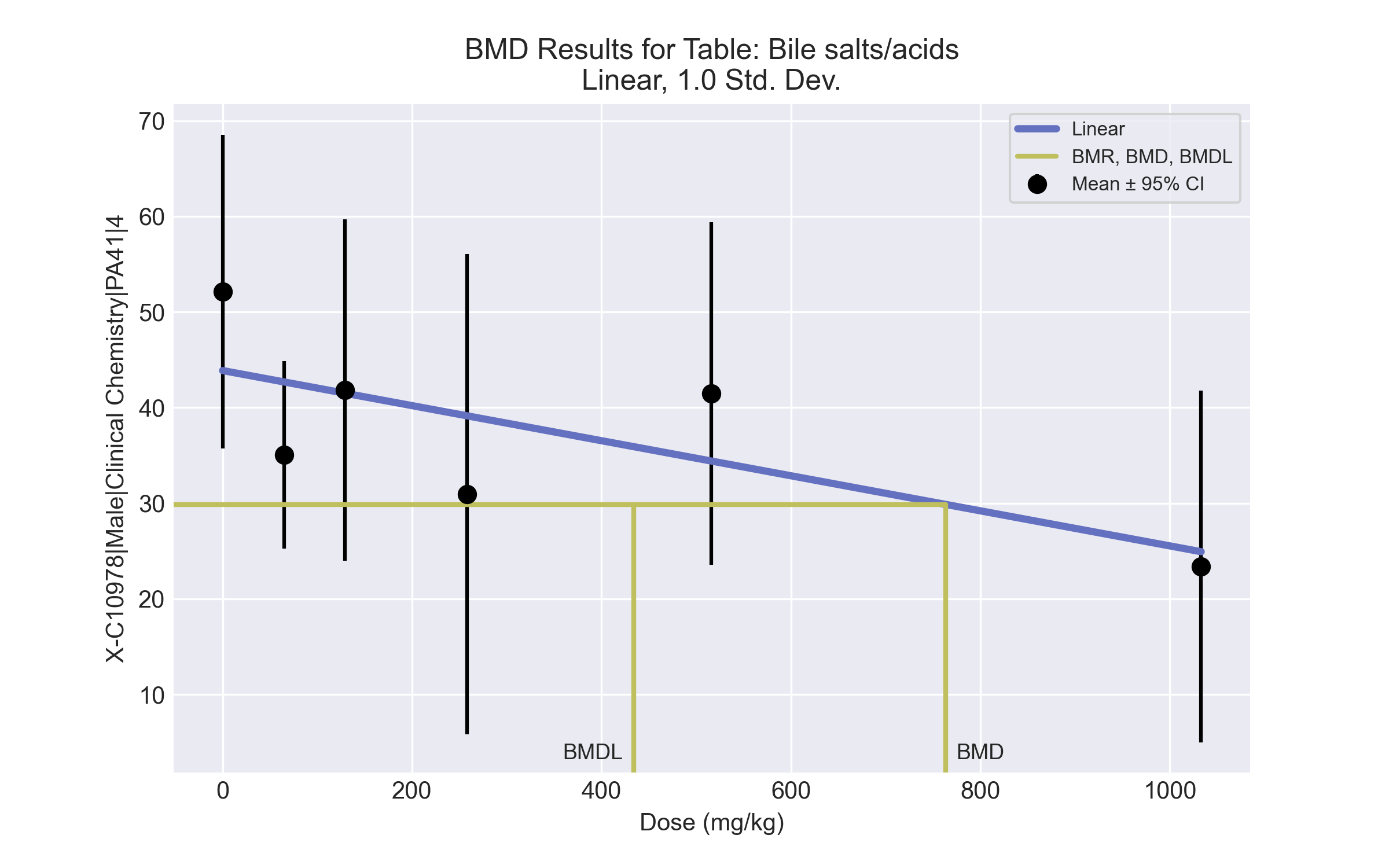
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Lineara (equivalent models include Power, Polynomial 2°) | Valid | - |
| Polynomial 3° | Valid | - |
| Polynomial 4° | Valid | - |
| Polynomial 5° | Valid | - |
| Hill | Warning | **Warnings**  • BMD/BMDL ratio is greater than threshold (4.23e+04 > 20.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (4.23e+04 > 5.0) |
| Exponential M2 | Valid | - |
| Exponential M3 (equivalent models include Exponential M4) | Valid | - |
| Exponential M5 | Warning | **Warnings**  • BMD/BMDL ratio is greater than threshold (1.16e+02 > 20.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (1.16e+02 > 5.0) |

a Recommended model

## Recommended model



====================================================================   
 Polynomial Model. (Version: 2.21; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-ysvu\_yka.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-ysvu\_yka.plt  
 Fri Jul 16 07:36:04 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = beta\_0 + beta\_1\*dose + beta\_2\*dose^2 + ...  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 rho is set to 0  
 The polynomial coefficients are restricted to be negative  
 A constant variance model is fit  
  
 Total number of dose groups = 6  
 Total number of records with missing values = 0  
 Maximum number of iterations = 500  
 Relative Function Convergence has been set to: 1e-008  
 Parameter Convergence has been set to: 1e-008  
  
  
  
 Default Initial Parameter Values   
 alpha = 202.488  
 rho = 0 Specified  
 beta\_0 = 43.5701  
 beta\_1 = -0.0182728  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -rho   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 alpha beta\_0 beta\_1  
  
 alpha 1 4.1e-008 7.2e-011  
  
 beta\_0 4.1e-008 1 -0.71  
  
 beta\_1 7.2e-011 -0.71 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 alpha 195.93 54.3412 89.4232 302.437  
 beta\_0 43.8763 3.87758 36.2764 51.4762  
 beta\_1 -0.0183424 0.00805282 -0.0341256 -0.00255912  
  
  
  
 Table of Data and Estimated Values of Interest  
  
 Dose N Obs Mean Est Mean Obs Std Dev Est Std Dev Scaled Res.  
------ --- -------- -------- ----------- ----------- ----------  
  
 0 4 52.1 43.9 10.3 14 1.18  
 65 3 35.1 42.7 3.95 14 -0.943  
 129 5 41.9 41.5 14.4 14 0.0559  
 258 5 30.9 39.1 20.2 14 -1.31  
 516 5 41.5 34.4 14.4 14 1.13  
 1033 4 23.4 24.9 11.6 14 -0.218  
  
  
  
 Model Descriptions for likelihoods calculated  
  
  
 Model A1: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
  
 Model A2: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma(i)^2  
  
 Model A3: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
 Model A3 uses any fixed variance parameters that  
 were specified by the user  
  
 Model R: Yi = Mu + e(i)  
 Var{e(i)} = Sigma^2  
  
  
 Likelihoods of Interest  
  
 Model Log(likelihood) # Param's AIC  
 A1 -78.628141 7 171.256281  
 A2 -74.529605 12 173.059211  
 A3 -78.628141 7 171.256281  
 fitted -81.610854 3 169.221708  
 R -83.976104 2 171.952209  
  
  
 Explanation of Tests   
  
 Test 1: Do responses and/or variances differ among Dose levels?   
 (A2 vs. R)  
 Test 2: Are Variances Homogeneous? (A1 vs A2)  
 Test 3: Are variances adequately modeled? (A2 vs. A3)  
 Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)  
 (Note: When rho=0 the results of Test 3 and Test 2 will be the same.)  
  
 Tests of Interest   
  
 Test -2\*log(Likelihood Ratio) Test df p-value   
  
 Test 1 18.893 10 0.04164  
 Test 2 8.19707 5 0.1457  
 Test 3 8.19707 5 0.1457  
 Test 4 5.96543 4 0.2017  
  
The p-value for Test 1 is less than .05. There appears to be a  
difference between response and/or variances among the dose levels  
It seems appropriate to model the data  
  
The p-value for Test 2 is greater than .1. A homogeneous variance   
model appears to be appropriate here  
  
  
The p-value for Test 3 is greater than .1. The modeled variance appears   
 to be appropriate here  
  
The p-value for Test 4 is greater than .1. The model chosen seems   
to adequately describe the data  
   
  
 Benchmark Dose Computation  
  
Specified effect = 1  
  
Risk Type = Estimated standard deviations from the control mean  
  
Confidence level = 0.95  
  
 BMD = 763.124  
  
  
 BMDL = 434.064  
  
  
 BMDU = 3134.22

# BMD Results for Table: Creatinine

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 0.35 ± 0.058 | 0.33 ± 0 | 0.332 ± 0.033 | 0.31 ± 0.039 | 0.302 ± 0.04 | 0.275 ± 0.04 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°) | <0.0001 | -139.397 | 558.244 | 313.597 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Power | <0.0001 | -139.397 | 558.245 | 313.597 |
| Hill | <0.0001 | -138.12 | 298.435 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | -999 | -139.542 | 520.134 | 276.409 |
| Exponential M4 | -999 | -129.145 | 170163 | 149.024 |
| Exponential M5 | -999 | -138.056 | 322.362 | 82.438 |

a Modeled variance case presented (BMDS Test 2 p-value = <0.0001, BMDS Test 3 p-value = <0.0001).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001)  **Cautions**  • Warning(s): Warning: Likelihood for fitted model larger than the Likelihood for model A3. |
| Power | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001)  **Cautions**  • Warning(s): Warning: Likelihood for fitted model larger than the Likelihood for model A3. |
| Hill | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001)  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001) |
| Exponential M4 | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001)  • BMD/BMDL ratio is greater than threshold (1.14e+03 > 20.0)  • BMD/high dose ratio is greater than threshold (1.65e+02 > 1.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (1.14e+03 > 5.0) |
| Exponential M5 | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001) |

## Recommended model

*No model was recommended as a best-fitting model.*

# BMD Results for Table: Cholinesterase

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 291.25 ± 18.768 | 209 ± 24 | 236 ± 15.017 | 183.4 ± 19.578 | 152.4 ± 44.797 | 129 ± 29.698 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°) | 2.7E-04 | 219.218 | 275.574 | 204.11 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Hill | 0.046 | 207.846 | 41.286 | 21.42 |
| Exponential M2 (equivalent models include Exponential M3) | 0.002 | 214.524 | 160.655 | 111.684 |
| Exponential M4 (equivalent models include Exponential M5) | 0.036 | 208.39 | 54.864 | 32.977 |

a Constant variance case presented (BMDS Test 2 p-value = 0.146, BMDS Test 3 p-value = 0.146).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000267 < 0.1)  • Residual at lowest dose is greater than threshold (2.59 > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.95 > 1.5) |
| Hill | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.046 < 0.1)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.51 > 1.5) |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00223 < 0.1)  • Residual at lowest dose is greater than threshold (2.1 > 2.0) |
| Exponential M4 (equivalent models include Exponential M5) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.036 < 0.1) |

## Recommended model

*No model was recommended as a best-fitting model.*

# BMD Results for Table: Total Thyroxine

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 65 | 129 | 258 | 516 | 1033 |
| N | 4 | 3 | 5 | 5 | 5 | 4 |
| Mean ± SD | 3.973 ± 0.469 | 4.157 ± 0.938 | 4.692 ± 0.494 | 4.108 ± 0.632 | 3.31 ± 0.523 | 2.768 ± 0.508 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.093 | 5.291 | 369.717 | 260.327 | Hill recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° (equivalent models include Polynomial 3°, 4°, 5°) | 0.048 | 7.247 | 408.337 | 260.962 |
| Power | 0.056 | 6.907 | 452.938 | 266.176 |
| Hillb | 0.104 | 5.879 | 391.168 | 256.902 |
| Exponential M2 (equivalent models include Exponential M4) | 0.084 | 5.564 | 324.719 | 211.965 |
| Exponential M3 | 0.066 | 6.532 | 437.613 | 229.709 |
| Exponential M5 | 0.101 | 5.929 | 411.175 | 264.783 |

a Constant variance case presented (BMDS Test 2 p-value = 0.819, BMDS Test 3 p-value = 0.819).

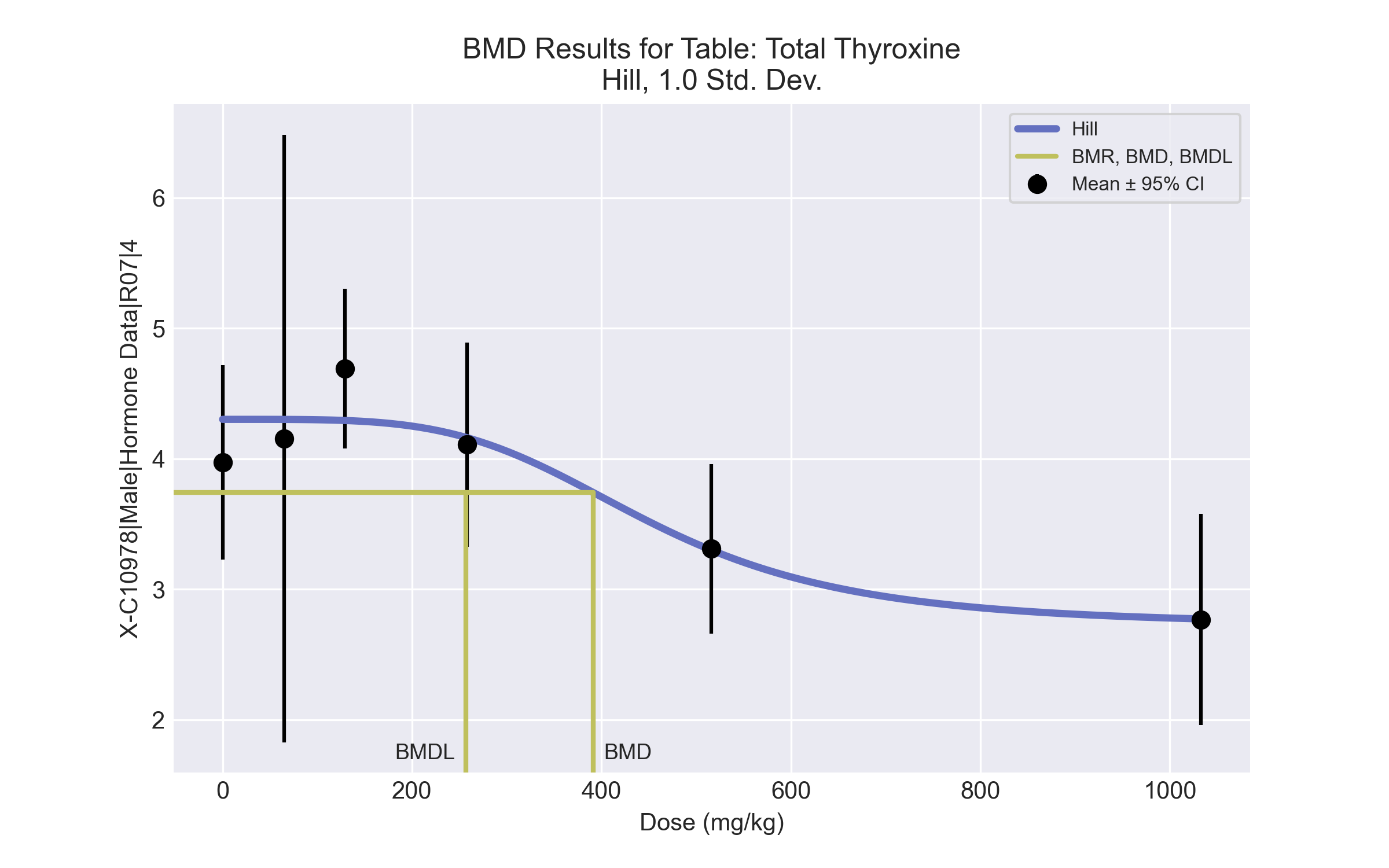
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0935 < 0.1) |
| Polynomial 2° (equivalent models include Polynomial 3°, 4°, 5°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.048 < 0.1) |
| Power | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.056 < 0.1) |
| Hilla | Valid | - |
| Exponential M2 (equivalent models include Exponential M4) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0838 < 0.1) |
| Exponential M3 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0661 < 0.1) |
| Exponential M5 | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Hill Model. (Version: 2.18; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-ugof5124.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-ugof5124.plt  
 Fri Jul 16 07:37:03 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = intercept + v\*dose^n/(k^n + dose^n)  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 rho is set to 0  
 Power parameter restricted to be greater than 1  
 A constant variance model is fit  
  
 Total number of dose groups = 6  
 Total number of records with missing values = 0  
 Maximum number of iterations = 500  
 Relative Function Convergence has been set to: 1e-008  
 Parameter Convergence has been set to: 1e-008  
  
  
  
 Default Initial Parameter Values   
 alpha = 0.342809  
 rho = 0 Specified  
 intercept = 3.9725  
 v = -1.205  
 n = 5.21499  
 k = 496.602  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -rho   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 alpha intercept v n k  
  
 alpha 1 -4.9e-009 3.2e-008 -2.7e-008 -3.5e-008  
  
 intercept -4.9e-009 1 -0.48 -0.39 -0.31  
  
 v 3.2e-008 -0.48 1 0.54 -0.41  
  
 n -2.7e-008 -0.39 0.54 1 -0.0068  
  
 k -3.5e-008 -0.31 -0.41 -0.0068 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 alpha 0.313954 0.0870751 0.14329 0.484618  
 intercept 4.30223 0.161014 3.98665 4.61781  
 v -1.57912 0.398407 -2.35998 -0.798254  
 n 4.15383 2.79474 -1.32376 9.63141  
 k 451.724 101.843 252.116 651.333  
  
  
  
 Table of Data and Estimated Values of Interest  
  
 Dose N Obs Mean Est Mean Obs Std Dev Est Std Dev Scaled Res.  
------ --- -------- -------- ----------- ----------- ----------  
  
 0 4 3.97 4.3 0.469 0.56 -1.18  
 65 3 4.16 4.3 0.938 0.56 -0.448  
 129 5 4.69 4.29 0.494 0.56 1.59  
 258 5 4.11 4.16 0.632 0.56 -0.215  
 516 5 3.31 3.3 0.523 0.56 0.0403  
 1033 4 2.77 2.77 0.508 0.56 -0.0174  
  
  
  
 Model Descriptions for likelihoods calculated  
  
  
 Model A1: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
  
 Model A2: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma(i)^2  
  
 Model A3: Yij = Mu(i) + e(ij)  
 Var{e(ij)} = Sigma^2  
 Model A3 uses any fixed variance parameters that  
 were specified by the user  
  
 Model R: Yi = Mu + e(i)  
 Var{e(i)} = Sigma^2  
  
  
 Likelihoods of Interest  
  
 Model Log(likelihood) # Param's AIC  
 A1 4.328317 7 5.343366  
 A2 5.434700 12 13.130601  
 A3 4.328317 7 5.343366  
 fitted 2.060623 5 5.878754  
 R -7.644158 2 19.288316  
  
  
 Explanation of Tests   
  
 Test 1: Do responses and/or variances differ among Dose levels?   
 (A2 vs. R)  
 Test 2: Are Variances Homogeneous? (A1 vs A2)  
 Test 3: Are variances adequately modeled? (A2 vs. A3)  
 Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)  
 (Note: When rho=0 the results of Test 3 and Test 2 will be the same.)  
  
 Tests of Interest   
  
 Test -2\*log(Likelihood Ratio) Test df p-value   
  
 Test 1 26.1577 10 0.003534  
 Test 2 2.21277 5 0.819  
 Test 3 2.21277 5 0.819  
 Test 4 4.53539 2 0.1036  
  
The p-value for Test 1 is less than .05. There appears to be a  
difference between response and/or variances among the dose levels  
It seems appropriate to model the data  
  
The p-value for Test 2 is greater than .1. A homogeneous variance   
model appears to be appropriate here  
  
  
The p-value for Test 3 is greater than .1. The modeled variance appears   
 to be appropriate here  
  
The p-value for Test 4 is greater than .1. The model chosen seems   
to adequately describe the data  
   
  
 Benchmark Dose Computation  
  
Specified effect = 1  
  
Risk Type = Estimated standard deviations from the control mean   
  
Confidence level = 0.95  
  
 BMD = 391.168  
  
 BMDL = 256.902  
  
 BMDU = 561.507