# Female BMD Results for Table: Kidney-Left Absolute

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 0.644 ± 0.05 | 0.692 ± 0.049 | 0.66 ± 0.06 | 0.672 ± 0.031 | 0.676 ± 0.029 | 0.666 ± 0.029 | 0.688 ± 0.041 | 0.7 ± 0.031 | 0.724 ± 0.059 | 0.716 ± 0.038 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | 0.177 | -281.771 | 366.374 | 227.305 | Exponential-M4 recommended as best-fitting model on the basis of the lowest AIC. |
| Hill | 0.589 | -285.638 | 58.534 | 7.695 |
| Exponential M2 (equivalent models include Exponential M3) | 0.171 | -281.655 | 374.914 | 237.046 |
| Exponential M4b (equivalent models include Exponential M5) | 0.598 | -285.714 | 56.634 | 10.508 |

a Constant variance case presented (BMDS Test 2 p-value = 0.507, BMDS Test 3 p-value = 0.507).

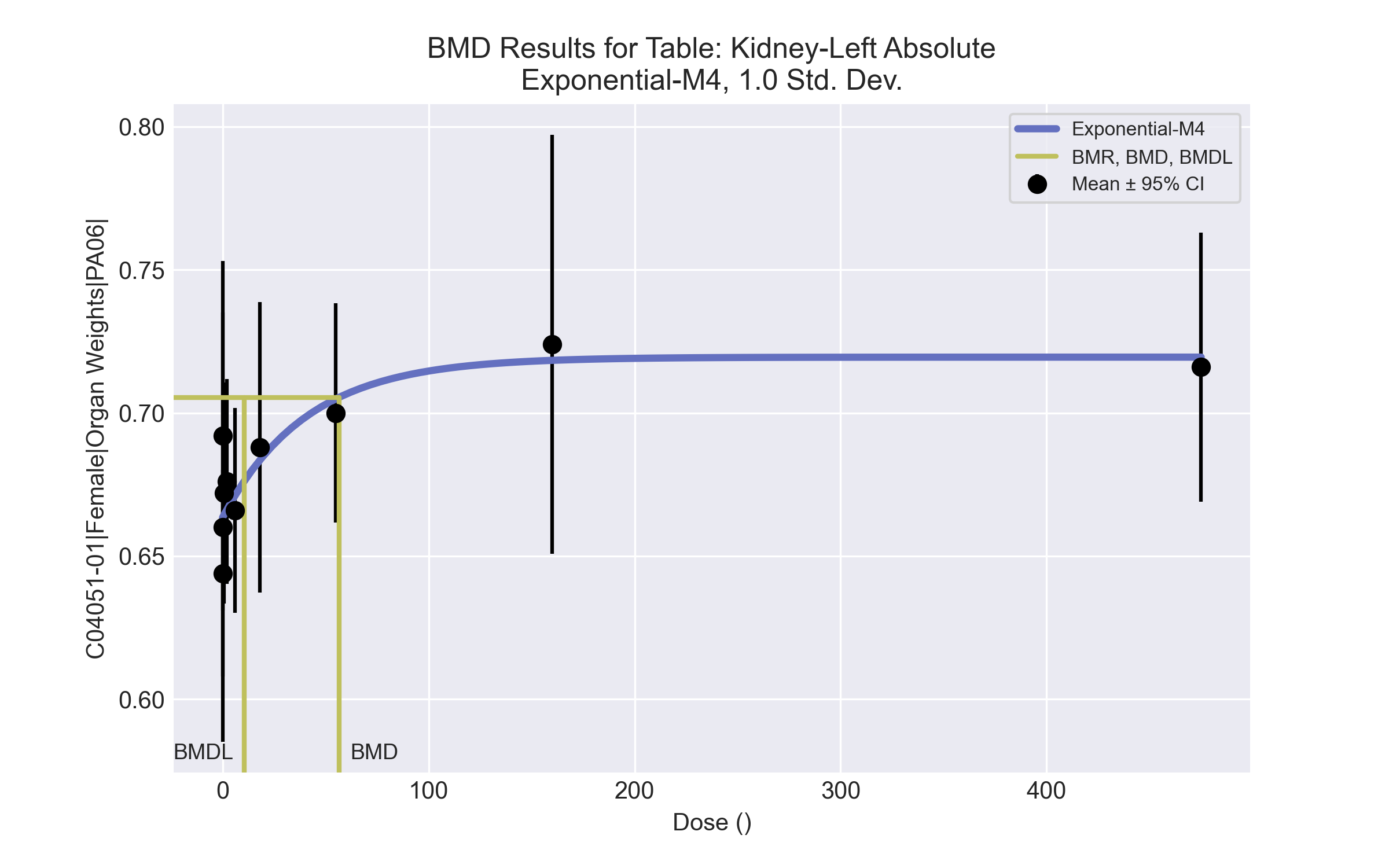
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | Warning | **Warnings**  • Residual at lowest dose is greater than threshold (2.02 > 2.0) |
| Hill | Valid | **Cautions**  • BMD/BMDL ratio is greater than threshold (7.61 > 5.0) |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Residual at lowest dose is greater than threshold (2.03 > 2.0) |
| Exponential M4a (equivalent models include Exponential M5) | Valid | **Cautions**  • BMD/BMDL ratio is greater than threshold (5.39 > 5.0) |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-p4\_u7hiu.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 09:56:27 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 = 10  
 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 4  
 -------- --------  
 lnalpha -6.44049   
 rho 0 Specified  
 a 0.6118   
 b 0.00340907   
 c 1.24256   
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 4 Std. Err.  
 -------- ------- ---------  
 lnalpha -6.34026 0.00033635  
 a 0.66346 0.00758079  
 b 0.0244564 0.0226753  
 c 1.08444 0.0239327  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 10 0.644 0.05038  
 0.07 5 0.692 0.04919  
 0.2 5 0.66 0.06042  
 0.7 5 0.672 0.03114  
 2 5 0.676 0.02881  
 6 5 0.666 0.02881  
 18 5 0.688 0.04087  
 55 5 0.7 0.03082  
 160 5 0.724 0.05899  
 475 5 0.716 0.03782  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 0.6635 0.042 -1.465  
 0.07 0.6636 0.042 1.514  
 0.2 0.6637 0.042 -0.1988  
 0.7 0.6644 0.042 0.404  
 2 0.6661 0.042 0.5253  
 6 0.6711 0.042 -0.2719  
 18 0.6834 0.042 0.2444  
 55 0.7049 0.042 -0.2602  
 160 0.7184 0.042 0.3002  
 475 0.7195 0.042 -0.1853  
  
  
  
 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 149.6133 11 -277.2267  
 A2 153.7503 20 -267.5006  
 A3 149.6133 11 -277.2267  
 R 140.2633 2 -276.5267  
 4 146.8573 4 -285.7145  
  
  
 Additive constant for all log-likelihoods = -50.54. 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 6a: Does Model 4 fit the data? (A3 vs 4)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 26.97 18 0.07949  
 Test 2 8.274 9 0.5068  
 Test 3 8.274 9 0.5068  
 Test 6a 5.512 7 0.5977  
  
  
 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 6a is greater than .1. Model 4 seems  
 to adequately describe the data.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 56.6339  
  
 BMDL = 10.5076  
  
 BMDU = 4.75e+006

# Female BMD Results for Table: Kidney-Left Relative

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 2.894 ± 0.202 | 3.096 ± 0.225 | 2.967 ± 0.231 | 3.008 ± 0.082 | 3.063 ± 0.15 | 2.924 ± 0.118 | 3.068 ± 0.147 | 3.085 ± 0.092 | 3.207 ± 0.203 | 3.166 ± 0.115 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | 0.105 | -131.973 | 385.142 | 234.684 | Exponential-M4 recommended as best-fitting model on the basis of the lowest AIC. |
| Hill | 0.192 | -132.497 | 87.571 | 15.481 |
| Exponential M2 (equivalent models include Exponential M3) | 0.102 | -131.885 | 392.086 | 242.982 |
| Exponential M4b | 0.286 | -134.626 | 85.629 | 17.286 |
| Exponential M5 | 0.2 | -132.627 | 85.314 | 17.294 |

a Constant variance case presented (BMDS Test 2 p-value = 0.194, BMDS Test 3 p-value = 0.194).

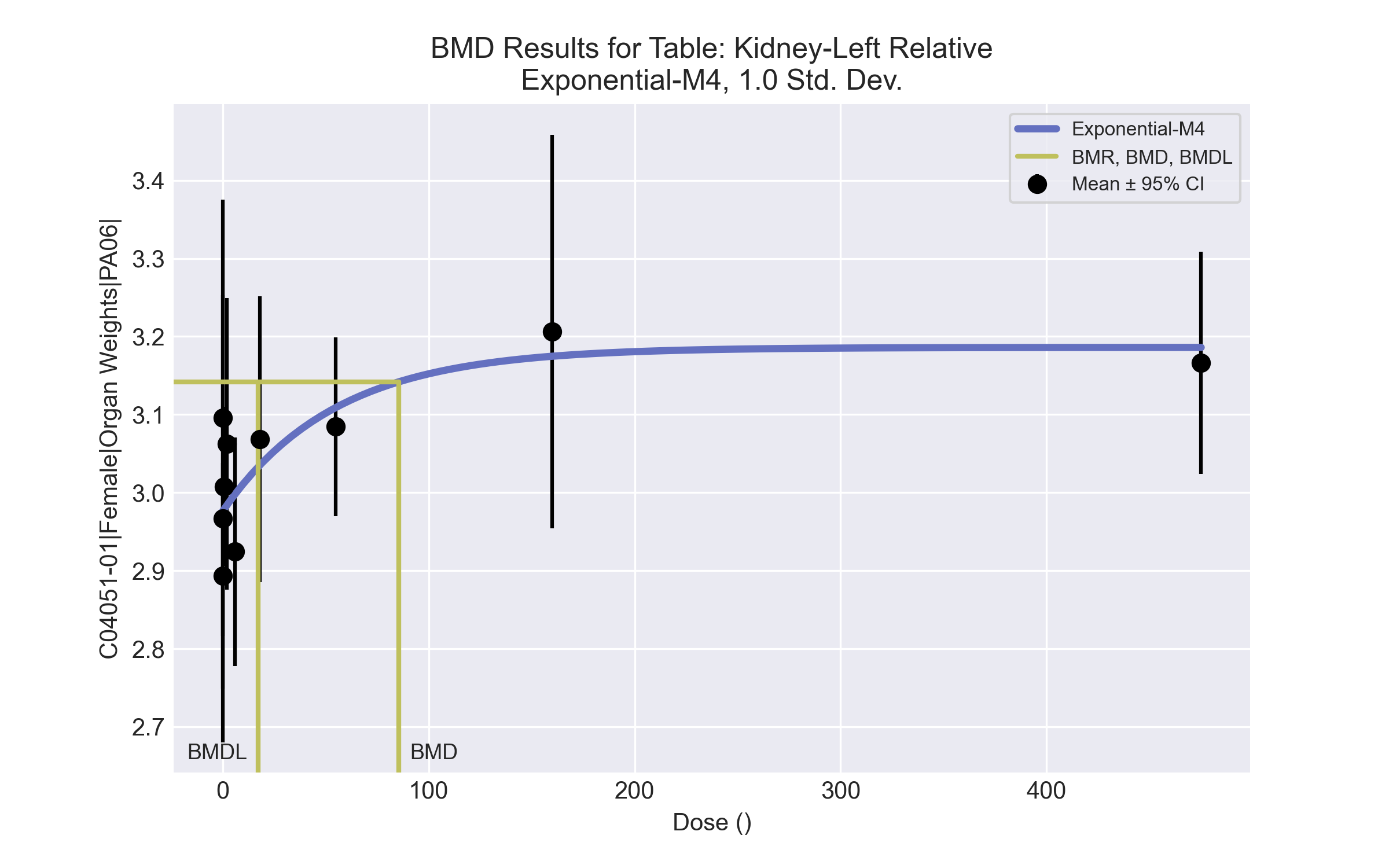
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | Warning | **Warnings**  • Residual at lowest dose is greater than threshold (2.03 > 2.0) |
| Hill | Valid | **Cautions**  • BMD/BMDL ratio is greater than threshold (5.66 > 5.0) |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Residual at lowest dose is greater than threshold (2.04 > 2.0) |
| Exponential M4a | Valid | - |
| Exponential M5 | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-49o9b\_o0.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 09:56:35 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 = 10  
 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 4  
 -------- --------  
 lnalpha -3.74888   
 rho 0 Specified  
 a 2.74884   
 b 0.00318188   
 c 1.22485   
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 4 Std. Err.  
 -------- ------- ---------  
 lnalpha -3.5932 0.00524598  
 a 2.97611 0.0289755  
 b 0.0182433 0.0162438  
 c 1.07052 0.0219726  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 10 2.894 0.2022  
 0.07 5 3.096 0.2252  
 0.2 5 2.967 0.2306  
 0.7 5 3.008 0.08211  
 2 5 3.063 0.1504  
 6 5 2.924 0.118  
 18 5 3.068 0.1472  
 55 5 3.085 0.09226  
 160 5 3.207 0.203  
 475 5 3.166 0.1148  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 2.976 0.1659 -1.575  
 0.07 2.976 0.1659 1.61  
 0.2 2.977 0.1659 -0.1363  
 0.7 2.979 0.1659 0.3928  
 2 2.984 0.1659 1.065  
 6 2.998 0.1659 -0.9904  
 18 3.035 0.1659 0.453  
 55 3.109 0.1659 -0.3299  
 160 3.175 0.1659 0.4304  
 475 3.186 0.1659 -0.2671  
  
  
  
 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 75.59426 11 -129.1885  
 A2 81.77062 20 -123.5412  
 A3 75.59426 11 -129.1885  
 R 65.68851 2 -127.377  
 4 71.31299 4 -134.626  
  
  
 Additive constant for all log-likelihoods = -50.54. 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 6a: Does Model 4 fit the data? (A3 vs 4)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 32.16 18 0.02102  
 Test 2 12.35 9 0.1941  
 Test 3 12.35 9 0.1941  
 Test 6a 8.563 7 0.2856  
  
  
 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 6a is greater than .1. Model 4 seems  
 to adequately describe the data.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 85.6285  
  
 BMDL = 17.2858  
  
 BMDU = 4.75e+006

# Female BMD Results for Table: Kidney-Right Absolute

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 0.661 ± 0.045 | 0.704 ± 0.021 | 0.676 ± 0.056 | 0.67 ± 0.035 | 0.68 ± 0.035 | 0.67 ± 0.023 | 0.698 ± 0.062 | 0.714 ± 0.032 | 0.724 ± 0.059 | 0.756 ± 0.046 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | 0.451 | -286.026 | 242.671 | 170.616 | Hill recommended as best-fitting model on the basis of the lowest BMDL. |
| Hillb | 0.689 | -287.089 | 72.145 | 18.001 |
| Exponential M2 (equivalent models include Exponential M3) | 0.435 | -285.863 | 251.543 | 180.135 |
| Exponential M4 (equivalent models include Exponential M5) | 0.649 | -286.757 | 84.051 | 19.608 |

a Constant variance case presented (BMDS Test 2 p-value = 0.245, BMDS Test 3 p-value = 0.245).

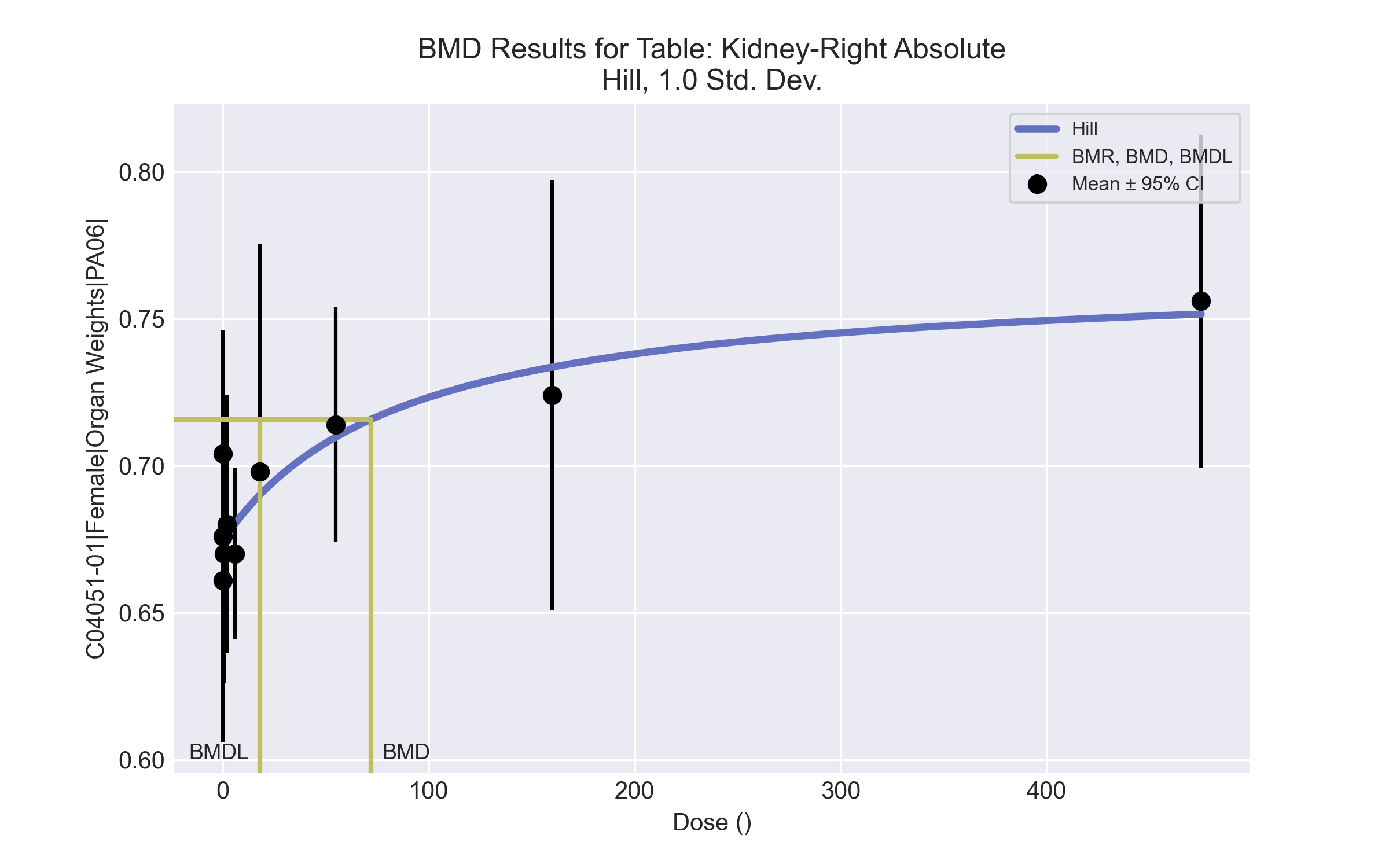
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | Valid | - |
| Hilla | Valid | - |
| Exponential M2 (equivalent models include Exponential M3) | Valid | - |
| Exponential M4 (equivalent models include Exponential M5) | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Hill Model. (Version: 2.18; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-klmp8hjn.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-klmp8hjn.plt  
 Tue Apr 13 09:56:38 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 = 10  
 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 = 0.00192821  
 rho = 0 Specified  
 intercept = 0.661  
 v = 0.095  
 n = 0.40759  
 k = 67.7187  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -rho -n   
 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 k  
  
 alpha 1 3e-009 5.7e-009 5.3e-009  
  
 intercept 3e-009 1 0.054 0.43  
  
 v 5.7e-009 0.054 1 0.81  
  
 k 5.3e-009 0.43 0.81 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 alpha 0.0017203 0.000328049 0.00107734 0.00236327  
 intercept 0.674309 0.00751048 0.659588 0.689029  
 v 0.0913551 0.0336258 0.0254496 0.15726  
 n 1 NA  
 k 86.7596 107.855 -124.633 298.152  
  
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 10 0.661 0.674 0.0451 0.0415 -1.01  
 0.07 5 0.704 0.674 0.0207 0.0415 1.6  
 0.2 5 0.676 0.675 0.0564 0.0415 0.0799  
 0.7 5 0.67 0.675 0.0354 0.0415 -0.272  
 2 5 0.68 0.676 0.0354 0.0415 0.196  
 6 5 0.67 0.68 0.0235 0.0415 -0.551  
 18 5 0.698 0.69 0.0622 0.0415 0.431  
 55 5 0.714 0.71 0.0321 0.0415 0.229  
 160 5 0.724 0.734 0.059 0.0415 -0.515  
 475 5 0.756 0.752 0.0456 0.0415 0.24  
  
  
  
 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 149.925411 11 -277.850822  
 A2 155.656445 20 -271.312890  
 A3 149.925411 11 -277.850822  
 fitted 147.544495 4 -287.088989  
 R 138.359208 2 -272.718417  
  
  
 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 34.5945 18 0.01063  
 Test 2 11.4621 9 0.2454  
 Test 3 11.4621 9 0.2454  
 Test 4 4.76183 7 0.689  
  
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 = 72.1451  
  
 BMDL = 18.0006  
  
 BMDU = 257.973

# Female BMD Results for Table: Kidney-Right Relative

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 2.971 ± 0.194 | 3.149 ± 0.069 | 3.039 ± 0.213 | 2.998 ± 0.086 | 3.082 ± 0.196 | 2.942 ± 0.098 | 3.108 ± 0.154 | 3.147 ± 0.126 | 3.208 ± 0.231 | 3.341 ± 0.086 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | 0.29 | -140.404 | 260.26 | 180.915 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Hill | 0.293 | -139.585 | 122.132 | 32.706 |
| Exponential M2 (equivalent models include Exponential M3) | 0.285 | -140.325 | 267.377 | 189.41 |
| Exponential M4 (equivalent models include Exponential M5) | 0.282 | -139.445 | 133.199 | 38.42 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.055, BMDS Test 3 p-value = 0.048).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0477) |
| Hill | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0477) |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0477) |
| Exponential M4 (equivalent models include Exponential M5) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0477) |

## Recommended model

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

# Female BMD Results for Table: Liver Weight Absolute

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 8.164 ± 0.768 | 8.314 ± 0.676 | 7.69 ± 0.702 | 8.16 ± 0.462 | 8.116 ± 0.442 | 9.1 ± 1.09 | 9.074 ± 0.869 | 9.86 ± 0.926 | 9.916 ± 1.074 | 10.022 ± 0.77 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | 5.0E-04 | 53.494 | 232.176 | 165.05 | Exponential-M4 recommended as best-fitting model on the basis of the lowest AIC. |
| Hill | 0.62 | 34.059 | 6.826 | 2.542 |
| Exponential M2 (equivalent models include Exponential M3) | 3.9E-04 | 54.147 | 252.301 | 184.166 |
| Exponential M4b (equivalent models include Exponential M5) | 0.675 | 32.52 | 8.801 | 3.465 |

a Constant variance case presented (BMDS Test 2 p-value = 0.576, BMDS Test 3 p-value = 0.576).

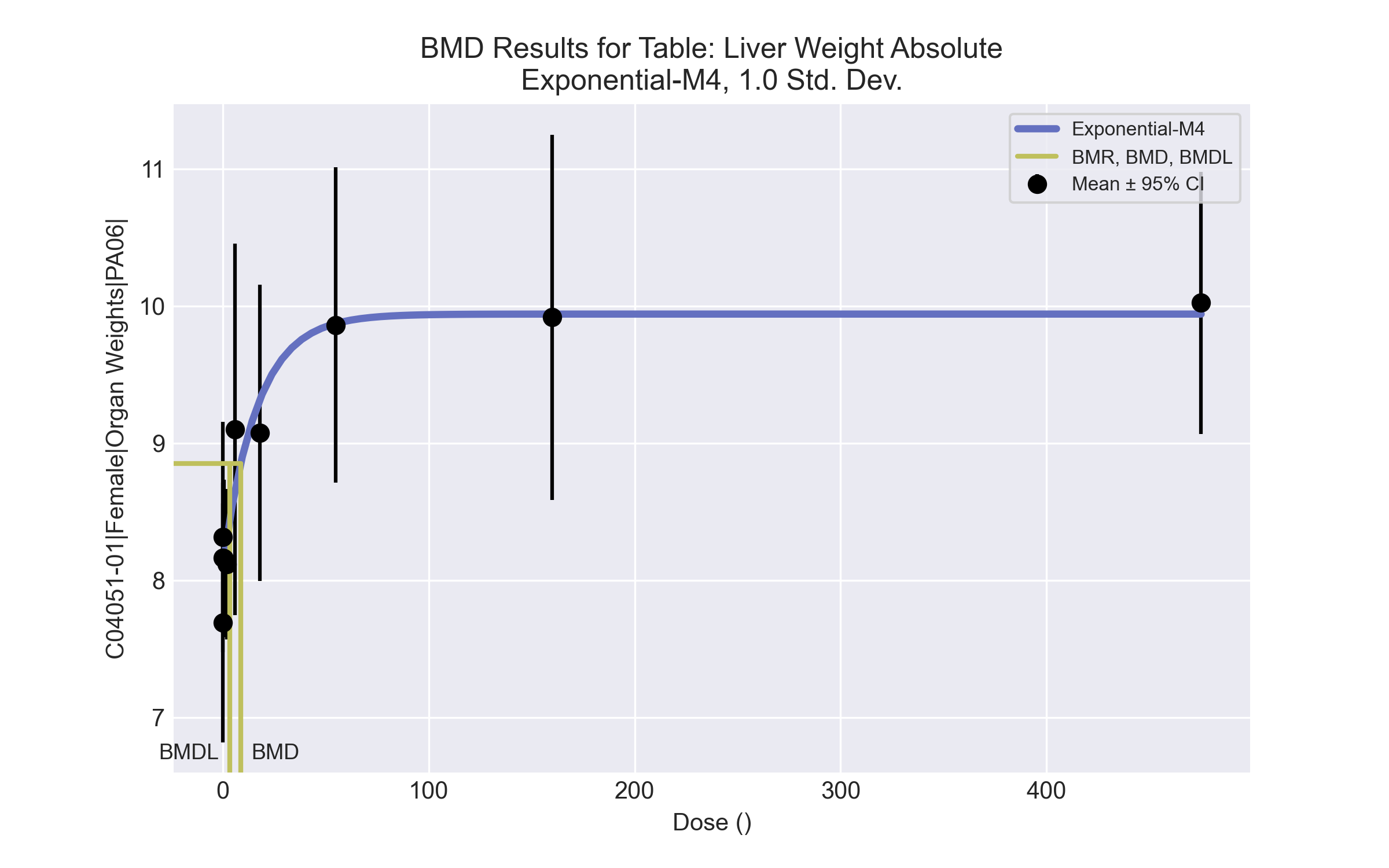
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000503 < 0.1) |
| Hill | Valid | - |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000387 < 0.1) |
| Exponential M4a (equivalent models include Exponential M5) | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-dtgl4q4o.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 09:57:20 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 = 10  
 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 4  
 -------- --------  
 lnalpha -0.642903   
 rho 0 Specified  
 a 7.3055   
 b 0.00493729   
 c 1.44044   
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 4 Std. Err.  
 -------- ------- ---------  
 lnalpha -0.554188 0.10956  
 a 8.09184 0.149609  
 b 0.0599768 0.0329075  
 c 1.2284 0.0332011  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 10 8.164 0.7676  
 0.07 5 8.314 0.6764  
 0.2 5 7.69 0.7017  
 0.7 5 8.16 0.4622  
 2 5 8.116 0.4417  
 6 5 9.1 1.09  
 18 5 9.074 0.8686  
 55 5 9.86 0.9258  
 160 5 9.916 1.074  
 475 5 10.02 0.77  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 8.092 0.758 0.301  
 0.07 8.1 0.758 0.6325  
 0.2 8.114 0.758 -1.25  
 0.7 8.168 0.758 -0.0231  
 2 8.301 0.758 -0.545  
 6 8.65 0.758 1.326  
 18 9.312 0.758 -0.7025  
 55 9.872 0.758 -0.03475  
 160 9.94 0.758 -0.07053  
 475 9.94 0.758 0.2418  
  
  
  
 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 -9.820155 11 41.64031  
 A2 -6.026058 20 52.05212  
 A3 -9.820155 11 41.64031  
 R -32.0117 2 68.02341  
 4 -12.25982 4 32.51964  
  
  
 Additive constant for all log-likelihoods = -50.54. 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 6a: Does Model 4 fit the data? (A3 vs 4)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 51.97 18 < 0.0001  
 Test 2 7.588 9 0.5761  
 Test 3 7.588 9 0.5761  
 Test 6a 4.879 7 0.6747  
  
  
 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 6a is greater than .1. Model 4 seems  
 to adequately describe the data.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 8.80071  
  
 BMDL = 3.46462  
  
 BMDU = 22.548

# Female BMD Results for Table: Liver Weight Relative

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475a |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 36.648 ± 2.675 | 37.159 ± 2.483 | 34.56 ± 2.511 | 36.519 ± 1.369 | 36.726 ± 0.844 | 39.902 ± 3.986 | 40.462 ± 3.606 | 43.484 ± 4.379 | 43.895 ± 3.908 | 44.265 ± 1.825 |

a Dose group removed in BMD modeling session

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 6°, 7°, 8°) | 0.002 | 174.497 | 42.344 | 21.145 | Exponential-M4 recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° (equivalent models include Polynomial 3°, 4°, 5°) | 0.002 | 174.497 | 42.344 | 21.145 |
| Hill | 0.276 | 162.754 | 4.62 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.002 | 175.67 | 50.468 | 26.401 |
| Exponential M4b | 0.325 | 161.38 | 5.372 | 2.294 |
| Exponential M5 | 0.224 | 163.379 | 5.383 | 2.294 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.034, BMDS Test 3 p-value = 0.193).

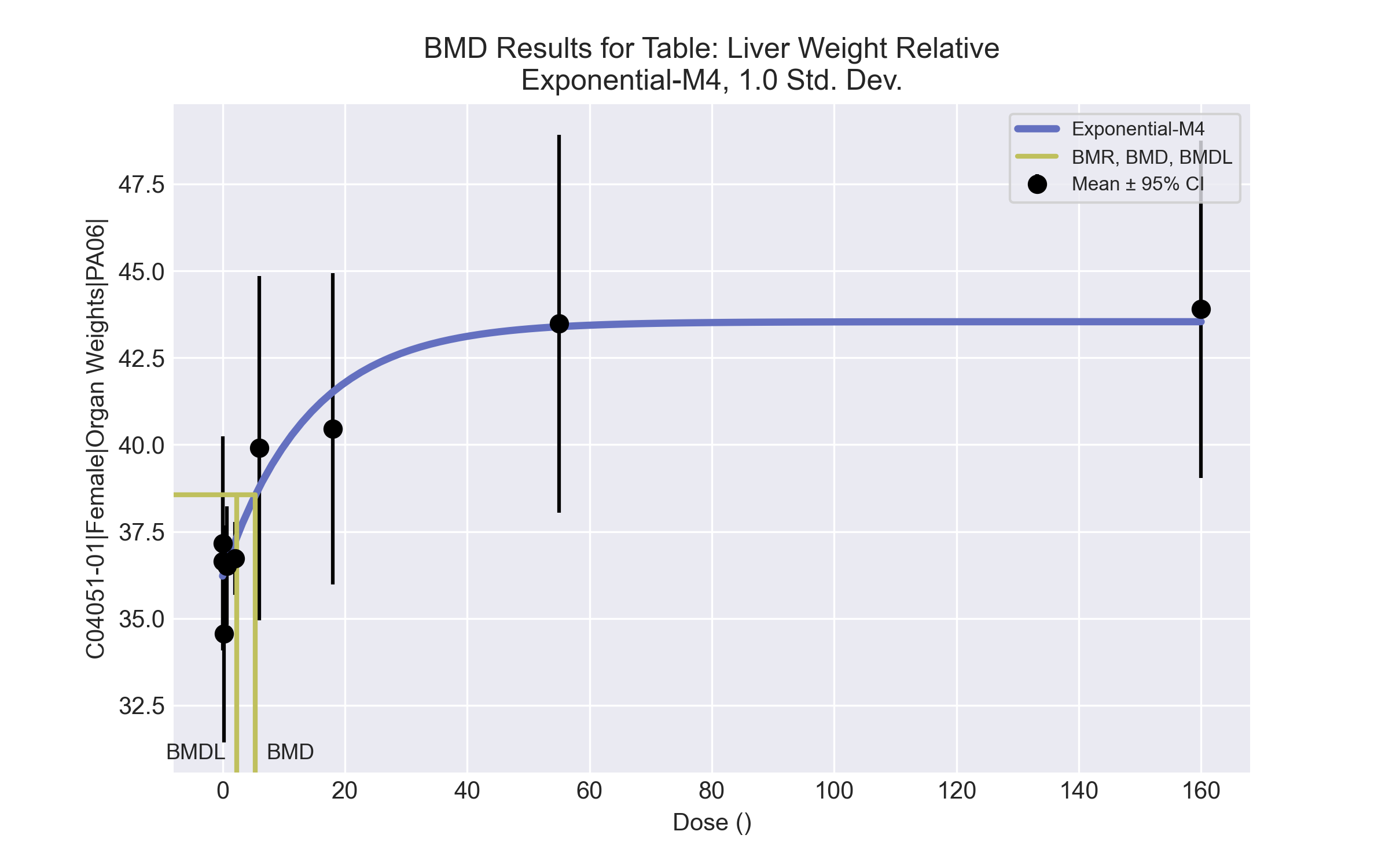
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 6°, 7°, 8°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00247 < 0.1) |
| Polynomial 2° (equivalent models include Polynomial 3°, 4°, 5°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00247 < 0.1) |
| Hill | Failure | **Failures**  • BMDL does not exist  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00155 < 0.1) |
| Exponential M4a | Valid | - |
| Exponential M5 | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-x8cnrp8l.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 09:57:28 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 = 9  
 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 4  
 -------- --------  
 lnalpha -29.5174   
 rho 8.58884   
 a 32.832   
 b 0.0137364   
 c 1.40382   
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 4 Std. Err.  
 -------- ------- ---------  
 lnalpha -18.0419 10.6827  
 rho 5.49765 2.92689  
 a 36.2205 0.471155  
 b 0.0714055 0.0393531  
 c 1.202 0.0378206  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 10 36.65 2.675  
 0.07 5 37.16 2.483  
 0.2 5 34.56 2.511  
 0.7 5 36.52 1.369  
 2 5 36.73 0.8443  
 6 5 39.9 3.986  
 18 5 40.46 3.606  
 55 5 43.48 4.379  
 160 5 43.9 3.908  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 36.22 2.331 0.5796  
 0.07 36.26 2.338 0.8625  
 0.2 36.32 2.349 -1.679  
 0.7 36.58 2.395 -0.05475  
 2 37.19 2.507 -0.4175  
 6 38.77 2.81 0.9006  
 18 41.51 3.391 -0.6935  
 55 43.39 3.83 0.05328  
 160 43.54 3.865 0.2074  
  
  
  
 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 -75.57336 10 171.1467  
 A2 -67.25425 18 170.5085  
 A3 -72.21398 11 166.428  
 R -95.31411 2 194.6282  
 4 -75.68975 5 161.3795  
  
  
 Additive constant for all log-likelihoods = -45.95. 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 6a: Does Model 4 fit the data? (A3 vs 4)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 56.12 16 < 0.0001  
 Test 2 16.64 8 0.0341  
 Test 3 9.919 7 0.1932  
 Test 6a 6.952 6 0.3254  
  
  
 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 6a is greater than .1. Model 4 seems  
 to adequately describe the data.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 5.37236  
  
 BMDL = 2.29362  
  
 BMDU = 13.7161

# Female BMD Results for Table: Alkaline phosphatase

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160a | 475a |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 200.1 ± 30.545 | 195.6 ± 23.512 | 176.8 ± 18.66 | 191.4 ± 30.303 | 207 ± 39.881 | 210.2 ± 21.487 | 235.4 ± 8.562 | 234.2 ± 14.307 | 235.6 ± 31.817 | 247.8 ± 17.964 |

a Dose group removed in BMD modeling session

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°, 6°) | 0.031 | 343.942 | 43.02 | 27.782 | Exponential-M5 recommended as best-fitting model on the basis of the lowest AIC. |
| Power (equivalent models include Polynomial 7°) | 0.031 | 343.942 | 43.02 | 27.782 |
| Polynomial 8° | 2.2E-04 | 356.095 | -9999 | -999 |
| Hill | 0.898 | 335.152 | 6.611 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.028 | 344.261 | 44.559 | 30.013 |
| Exponential M4 | 0.543 | 336.123 | 9.973 | 4.741 |
| Exponential M5b | 0.898 | 335.152 | 6.461 | 6.003 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.046, BMDS Test 3 p-value = 0.322).

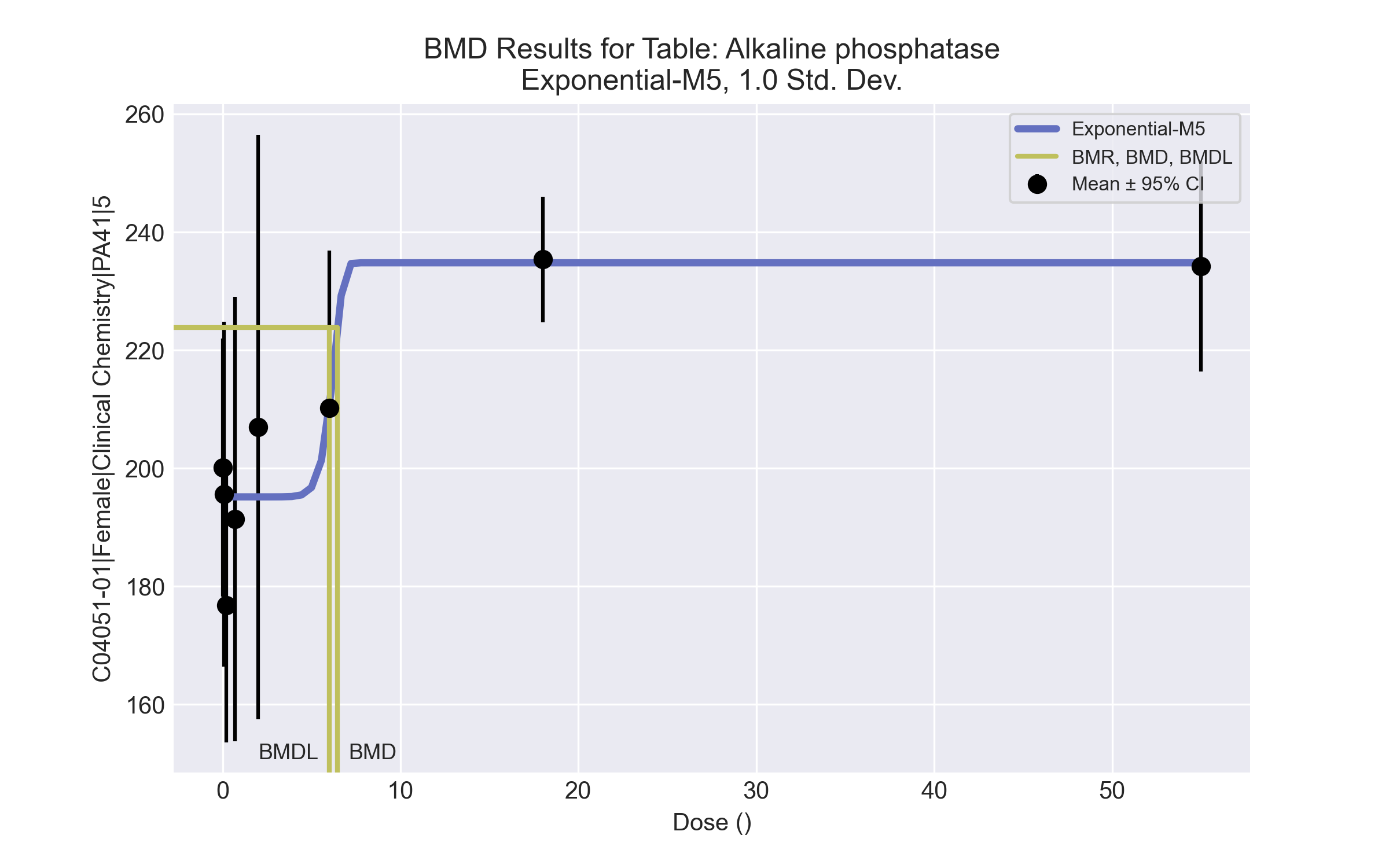
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°, 6°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0312 < 0.1) |
| Power (equivalent models include Polynomial 7°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0312 < 0.1) |
| Polynomial 8° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.000218 < 0.1)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMD = 100\*(maximum dose); BMDL computation failed. |
| Hill | Failure | **Failures**  • BMDL does not exist  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0276 < 0.1) |
| Exponential M4 | Valid | - |
| Exponential M5a | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-0ltil4st.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 10:13:49 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 = 8  
 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 5  
 -------- --------  
 lnalpha 36.4636   
 rho -5.69819   
 a 167.96   
 b 0.0413236   
 c 1.4716   
 d 1   
  
  
  
 Parameter Estimates  
  
 Variable Model 5 Std. Err.  
 -------- ------- ---------  
 lnalpha 63.7762 17.7129  
 rho -10.8197 3.31142  
 a 195.166 5.12577  
 b 0.157739 1.31378  
 c 1.20308 0.0361518  
 d 13.4456 2034.01  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 10 200.1 30.54  
 0.07 5 195.6 23.51  
 0.2 5 176.8 18.66  
 0.7 5 191.4 30.3  
 2 5 207 39.88  
 6 5 210.2 21.49  
 18 5 235.4 8.562  
 55 5 234.2 14.31  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 195.2 28.72 0.5433  
 0.07 195.2 28.72 0.03377  
 0.2 195.2 28.72 -1.43  
 0.7 195.2 28.72 -0.2933  
 2 195.2 28.72 0.9215  
 6 210.2 19.22 -0.0001639  
 18 234.8 10.56 0.127  
 55 234.8 10.56 -0.127  
  
  
  
 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 -164.6947 9 347.3894  
 A2 -157.543 16 347.0859  
 A3 -161.0383 10 342.0766  
 R -175.0473 2 354.0946  
 5 -161.5758 6 335.1516  
  
  
 Additive constant for all log-likelihoods = -41.35. 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 7a: Does Model 5 fit the data? (A3 vs 5)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 35.01 14 0.001466  
 Test 2 14.3 7 0.04604  
 Test 3 6.991 6 0.3217  
 Test 7a 1.075 4 0.8982  
  
  
 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 7a is greater than .1. Model 5 seems  
 to adequately describe the data.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 6.46054  
  
 BMDL = 6.00322  
  
 BMDU = 17.1972

# Female BMD Results for Table: Aspartate Aminotransferase

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 78.5 ± 6.721 | 81.4 ± 9.423 | 79.4 ± 5.03 | 84 ± 12.41 | 80.8 ± 3.701 | 75.8 ± 3.421 | 77.4 ± 3.715 | 92.8 ± 7.362 | 89.2 ± 7.05 | 82.6 ± 1.342 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 3.6E-04 | 283.894 | 6660.19 | -999 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 2° | 0.005 | 277.056 | 1840.29 | -999 |
| Polynomial 3° | 0.008 | 275.786 | 1062.94 | 675.398 |
| Polynomial 4° | 0.009 | 275.524 | 852.057 | -999 |
| Polynomial 5° | 0.009 | 275.455 | 754.827 | -999 |
| Polynomial 6° | 0.009 | 275.434 | 697.795 | 563.69 |
| Polynomial 7° | 0.009 | 275.427 | 660.307 | 550.015 |
| Polynomial 8° | 0.009 | 275.425 | 633.605 | 540.01 |
| Power | 0.009 | 275.423 | 539.857 | 502.863 |
| Hill | 0.008 | 276.102 | 33.025 | -999 |
| Exponential M2 | 3.6E-04 | 283.869 | 5806.98 | 778.106 |
| Exponential M3 | 0.005 | 277.423 | 545.73 | -999 |
| Exponential M4 | 9.7E-04 | 281.575 | 77.756 | 21.971 |
| Exponential M5 | 0.004 | 278.102 | 47.443 | 19.051 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.001, BMDS Test 3 p-value = 0.009).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.000357 < 0.1)  • BMD/high dose ratio is greater than threshold (14.0 > 1.0)  **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMDL computation failed. |
| Polynomial 2° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00517 < 0.1)  • BMD/high dose ratio is greater than threshold (3.87 > 1.0)  **Cautions**  • Warning(s): BMDL computation failed. |
| Polynomial 3° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00829 < 0.1)  • BMD/high dose ratio is greater than threshold (2.24 > 1.0)  **Cautions**  • BMDL/high dose ratio is greater than threshold (1.42 > 1.0) |
| Polynomial 4° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00914 < 0.1)  • BMD/high dose ratio is greater than threshold (1.79 > 1.0)  **Cautions**  • Warning(s): BMDL computation failed. |
| Polynomial 5° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00937 < 0.1)  • BMD/high dose ratio is greater than threshold (1.59 > 1.0)  **Cautions**  • Warning(s): BMDL computation failed. |
| Polynomial 6° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00944 < 0.1)  • BMD/high dose ratio is greater than threshold (1.47 > 1.0)  **Cautions**  • BMDL/high dose ratio is greater than threshold (1.19 > 1.0) |
| Polynomial 7° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00947 < 0.1)  • BMD/high dose ratio is greater than threshold (1.39 > 1.0)  **Cautions**  • BMDL/high dose ratio is greater than threshold (1.16 > 1.0) |
| Polynomial 8° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00948 < 0.1)  • BMD/high dose ratio is greater than threshold (1.33 > 1.0)  **Cautions**  • BMDL/high dose ratio is greater than threshold (1.14 > 1.0) |
| Power | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00948 < 0.1)  • BMD/high dose ratio is greater than threshold (1.14 > 1.0)  **Cautions**  • BMDL/high dose ratio is greater than threshold (1.06 > 1.0) |
| Hill | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00846 < 0.1)  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.000361 < 0.1)  • BMD/high dose ratio is greater than threshold (12.2 > 1.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (7.46 > 5.0)  • BMDL/high dose ratio is greater than threshold (1.64 > 1.0) |
| Exponential M3 | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00508 < 0.1)  • BMD/high dose ratio is greater than threshold (1.15 > 1.0) |
| Exponential M4 | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.000974 < 0.1)  • Residual of interest is greater than threshold (2.23 > 2.0) |
| Exponential M5 | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.008704)  • Goodness of fit p-value is less than threshold (0.00431 < 0.1) |

## Recommended model

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

# Female BMD Results for Table: Glucose

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 235.2 ± 46.576 | 218.6 ± 57.134 | 239.4 ± 33.65 | 236.8 ± 17.225 | 215.6 ± 19.139 | 211 ± 4.743 | 197 ± 38.743 | 199.6 ± 23.628 | 227.4 ± 49.339 | 203 ± 30.34 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.031 | 457.709 | 927.045 | 375.599 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 2° | 0.032 | 457.579 | 673.88 | 435.437 |
| Polynomial 3° | 0.034 | 457.445 | 598.808 | 439.463 |
| Polynomial 4° | 0.034 | 457.394 | 564.81 | 392.883 |
| Polynomial 5° | 0.034 | 457.377 | 545.497 | 456.504 |
| Polynomial 6° | <0.0001 | 985.106 | -9999 | -999 |
| Polynomial 7° | 0.035 | 457.368 | 524.322 | 456.627 |
| Polynomial 8° | <0.0001 | 974.903 | 17.024 | -999 |
| Power | 0.035 | 457.367 | 493.603 | 394.444 |
| Hill | 0.218 | 452.278 | -999 | -999 |
| Exponential M2 (equivalent models include Exponential M4) | 0.031 | 457.718 | 973.459 | 366.05 |
| Exponential M3 | 0.02 | 459.367 | 500.726 | 387.169 |
| Exponential M5 | 0.018 | 459.718 | 973.46 | 366.05 |

a Modeled variance case presented (BMDS Test 2 p-value = 4.6E-04, BMDS Test 3 p-value = 0.006).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0307 < 0.1)  • BMD/high dose ratio is greater than threshold (1.95 > 1.0) |
| Polynomial 2° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0321 < 0.1)  • BMD/high dose ratio is greater than threshold (1.42 > 1.0) |
| Polynomial 3° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0336 < 0.1)  • BMD/high dose ratio is greater than threshold (1.26 > 1.0) |
| Polynomial 4° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0342 < 0.1)  • BMD/high dose ratio is greater than threshold (1.19 > 1.0) |
| Polynomial 5° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0344 < 0.1)  • BMD/high dose ratio is greater than threshold (1.15 > 1.0) |
| Polynomial 6° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Residual at lowest dose is greater than threshold (3.56 > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (7.27 > 1.5)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMD = 100\*(maximum dose); BMDL computation failed. |
| Polynomial 7° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0345 < 0.1)  • BMD/high dose ratio is greater than threshold (1.1 > 1.0) |
| Polynomial 8° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Residual of interest is greater than threshold (2.36 > 2.0)  • Residual at lowest dose is greater than threshold (2.87 > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (9.03 > 1.5)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMDL computation failed. |
| Power | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0345 < 0.1)  • BMD/high dose ratio is greater than threshold (1.04 > 1.0) |
| Hill | Failure | **Failures**  • BMD does not exist  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.00578)  **Cautions**  • Warning(s): BMR value is not in the range of the mean function |
| Exponential M2 (equivalent models include Exponential M4) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0306 < 0.1)  • BMD/high dose ratio is greater than threshold (2.05 > 1.0) |
| Exponential M3 | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0201 < 0.1)  • BMD/high dose ratio is greater than threshold (1.05 > 1.0) |
| Exponential M5 | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.00578)  • Goodness of fit p-value is less than threshold (0.0177 < 0.1)  • BMD/high dose ratio is greater than threshold (2.05 > 1.0) |

## Recommended model

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

# Female BMD Results for Table: Sorbitol dehydrogenase

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 12.89 ± 2.868 | 17.28 ± 1.365 | 16.46 ± 0.658 | 15.2 ± 3.588 | 16.04 ± 0.832 | 14.54 ± 0.873 | 15.42 ± 1.862 | 19.04 ± 5.224 | 15.72 ± 1.91 | 19.12 ± 5.803 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 4°, 6°, 8°) | 0.008 | 186.209 | 317.692 | 150.172 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 3° (equivalent models include Polynomial 5°, 7°) | 0.008 | 186.209 | 317.693 | 150.172 |
| Hill | 0.044 | 181.871 | 34.488 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.007 | 186.351 | 338.03 | 176.472 |
| Exponential M4 | <0.0001 | 199 | -999 | 0 |
| Exponential M5 | <0.0001 | 199 | -999 | 0 |

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 Power, Polynomial 2°, 4°, 6°, 8°) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001)  • Goodness of fit p-value is less than threshold (0.00771 < 0.1)  • Residual at lowest dose is greater than threshold (2.73 > 2.0) |
| Polynomial 3° (equivalent models include Polynomial 5°, 7°) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001)  • Goodness of fit p-value is less than threshold (0.00771 < 0.1)  • Residual at lowest dose is greater than threshold (2.73 > 2.0) |
| Hill | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.0001)  • Goodness of fit p-value is less than threshold (0.0436 < 0.1)  • Residual at lowest dose is greater than threshold (2.82 > 2.0)  **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)  • Goodness of fit p-value is less than threshold (0.00732 < 0.1)  • Residual at lowest dose is greater than threshold (2.75 > 2.0) |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.0001)  • Residual at lowest dose is greater than threshold (2.79 > 2.0) |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.0001)  • Residual at lowest dose is greater than threshold (2.79 > 2.0) |

## Recommended model

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

# Female BMD Results for Table: Urea Nitrogen

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 16.6 ± 2.171 | 16.4 ± 1.14 | 15.2 ± 1.789 | 17.6 ± 2.074 | 16.6 ± 2.302 | 16.6 ± 0.548 | 15.6 ± 2.302 | 15.4 ± 1.517 | 14.6 ± 2.191 | 14.2 ± 1.789 |

## Summary table

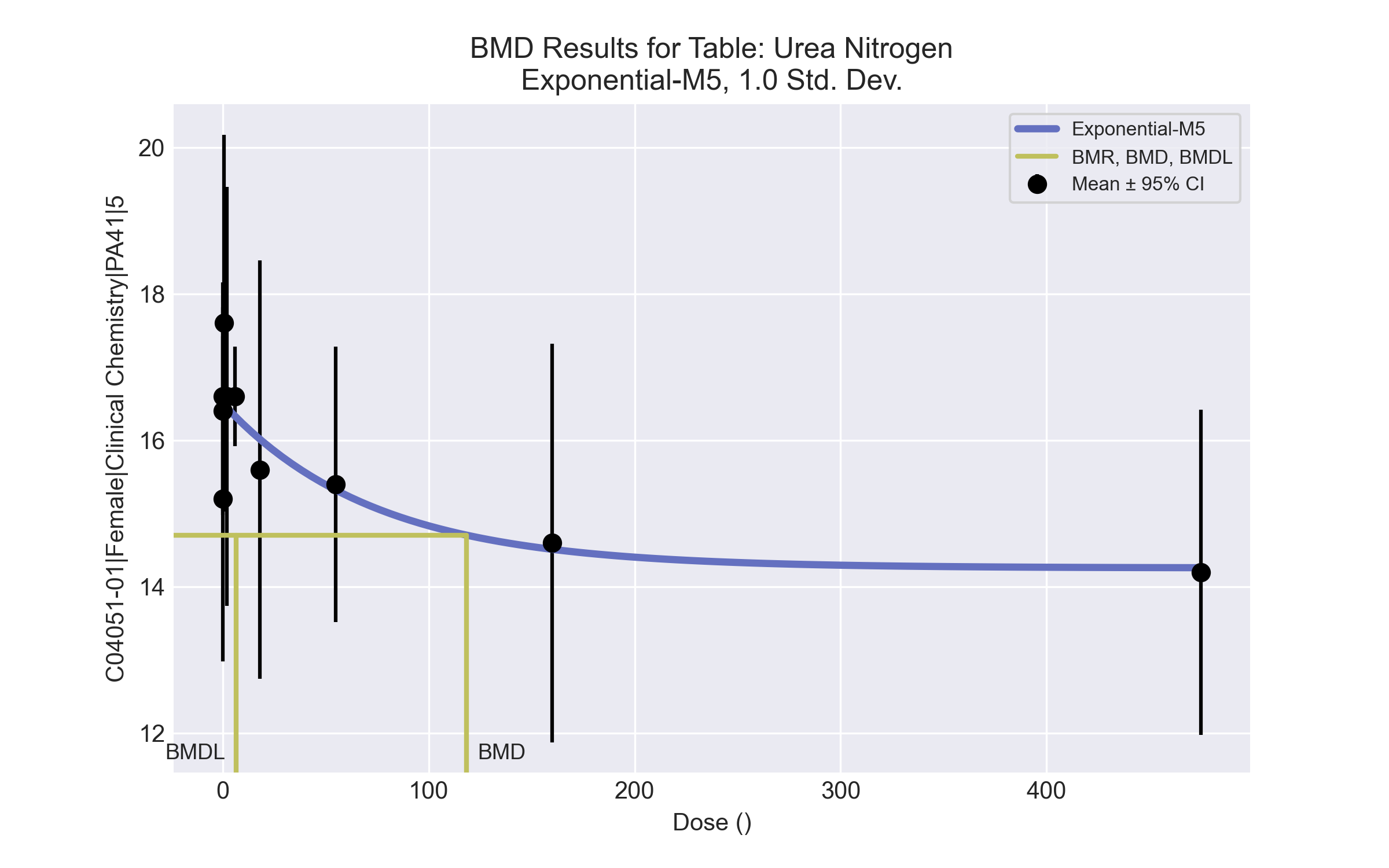
|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 7°, 8°) | 0.455 | 128.33 | 356.879 | 223.463 | Exponential-M5 recommended as best-fitting model on the basis of the lowest BMDL. |
| Polynomial 6° | 0.455 | 128.33 | 356.878 | 223.463 |
| Hill | 0.521 | 129.728 | 124.016 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.471 | 128.172 | 342.811 | 205.439 |
| Exponential M4 (equivalent models include Exponential M5) | 0.63 | 127.797 | 118.445 | 20.385 |

a Constant variance case presented (BMDS Test 2 p-value = 0.2, BMDS Test 3 p-value = 0.2).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 7°, 8°) | Valid | - |
| Polynomial 6° | Valid | - |
| Hill | Failure | **Failures**  • BMDL does not exist  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 (equivalent models include Exponential M3) | Valid | - |
| Exponential M4 (equivalent models include Exponential M5) | Valid | **Cautions**  • BMD/BMDL ratio is greater than threshold (5.81 > 5.0) |

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-kwfe2f6q.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 10:15:53 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 = 10  
 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 5  
 -------- --------  
 lnalpha 1.08273   
 rho 0 Specified  
 a 18.48   
 b 0.00496362   
 c 0.731808   
 d 1   
  
  
  
 Parameter Estimates  
  
 Variable Model 5 Std. Err.  
 -------- ------- ---------  
 lnalpha 1.17812 0.619419  
 a 16.5078 0.316054  
 b 0.0136288 0.015932  
 c 0.863691 0.0478851  
 d 1 NA  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 10 16.6 2.171  
 0.07 5 16.4 1.14  
 0.2 5 15.2 1.789  
 0.7 5 17.6 2.074  
 2 5 16.6 2.302  
 6 5 16.6 0.5477  
 18 5 15.6 2.302  
 55 5 15.4 1.517  
 160 5 14.6 2.191  
 475 5 14.2 1.789  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 16.51 1.802 0.1618  
 0.07 16.51 1.802 -0.1311  
 0.2 16.5 1.802 -1.615  
 0.7 16.49 1.802 1.382  
 2 16.45 1.802 0.1895  
 6 16.33 1.802 0.3336  
 18 16.02 1.802 -0.519  
 55 15.32 1.802 0.09804  
 160 14.51 1.802 0.1094  
 475 14.26 1.802 -0.07583  
  
  
  
 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 -57.27505 11 136.5501  
 A2 -51.1527 20 142.3054  
 A3 -57.27505 11 136.5501  
 R -64.96994 2 133.9399  
 5 -59.8983 4 127.7966  
  
  
 Additive constant for all log-likelihoods = -50.54. 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 7a: Does Model 5 fit the data? (A3 vs 5)  
  
  
 Tests of Interest  
  
 Test -2\*log(Likelihood Ratio) D. F. p-value  
 -------- ------------------------ ------ --------------  
 Test 1 27.63 18 0.06784  
 Test 2 12.24 9 0.1999  
 Test 3 12.24 9 0.1999  
 Test 7a 5.246 7 0.6299  
  
  
 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 7a is greater than .1. Model 5 seems  
 to adequately describe the data.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 118.445  
  
 BMDL = 6.61309  
  
 BMDU = 4.75e+006

# Female BMD Results for Table: Hematocrit

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 45.01 ± 2.443 | 46.94 ± 1.942 | 45.64 ± 1.534 | 45.8 ± 2.754 | 45.05 ± 2.024 | 44.12 ± 1.472 | 44.12 ± 2.383 | 44.52 ± 1.764 | 45.18 ± 1.415 | 43.96 ± 0.783 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.289 | 128.806 | -9999 | 1277.4 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 2° | 0.289 | 128.806 | -9999 | 764.731 |
| Polynomial 3° | 0.289 | 128.806 | -9999 | 653.425 |
| Polynomial 4° | 0.289 | 128.806 | -9999 | 607.874 |
| Polynomial 5° | 0.289 | 128.806 | -9999 | -999 |
| Polynomial 6° | 0.289 | 128.806 | -9999 | 557.511 |
| Polynomial 7° | 0.289 | 128.806 | -9999 | -999 |
| Polynomial 8° | 0.289 | 128.806 | -9999 | -999 |
| Power | 0.337 | 129.059 | 761.911 | 339.436 |
| Hill | 0.516 | 129.223 | -999 | -999 |
| Exponential M2 | 0.274 | 129.88 | -682.586 | -999 |
| Exponential M3 | 0.274 | 129.88 | -682.586 | -999 |
| Exponential M4 | 0.147 | 132.806 | -999 | 0 |
| Exponential M5 | 0.095 | 134.806 | -999 | 0 |

a Constant variance case presented (BMDS Test 2 p-value = 0.32, BMDS Test 3 p-value = 0.32).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (2.69 > 1.0) |
| Polynomial 2° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.61 > 1.0) |
| Polynomial 3° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.38 > 1.0) |
| Polynomial 4° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.28 > 1.0) |
| Polynomial 5° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Polynomial 6° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.17 > 1.0) |
| Polynomial 7° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Polynomial 8° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Power | Warning | **Warnings**  • BMD/high dose ratio is greater than threshold (1.6 > 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 | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M3 | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0946 < 0.1) |

## Recommended model

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

# Female BMD Results for Table: Hemoglobin

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 13.58 ± 0.811 | 14.28 ± 0.589 | 13.74 ± 0.65 | 13.875 ± 0.709 | 13.825 ± 0.709 | 13.34 ± 0.594 | 13.38 ± 0.726 | 13.46 ± 0.513 | 13.52 ± 0.415 | 13.36 ± 0.336 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.31 | 9.459 | -9999 | 1211.24 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 2° | 0.31 | 9.459 | -9999 | 721.906 |
| Polynomial 3° | 0.31 | 9.459 | -9999 | 624.265 |
| Polynomial 4° | 0.31 | 9.459 | -9999 | 582.404 |
| Polynomial 5° | 0.31 | 9.459 | -9999 | -999 |
| Polynomial 6° | 0.31 | 9.459 | -9999 | -999 |
| Polynomial 7° | 0.31 | 9.459 | -9999 | 534.059 |
| Polynomial 8° | 0.31 | 9.459 | -9999 | -999 |
| Power | 0.338 | 9.998 | 834.356 | 353.376 |
| Hill | 0.648 | 8.042 | -999 | -999 |
| Exponential M2 | 0.274 | 10.814 | -750.061 | -999 |
| Exponential M3 | 0.274 | 10.814 | -750.061 | -999 |
| Exponential M4 | 0.161 | 13.459 | -999 | 0 |
| Exponential M5 | 0.104 | 15.459 | -999 | 0 |

a Constant variance case presented (BMDS Test 2 p-value = 0.617, BMDS Test 3 p-value = 0.617).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (2.55 > 1.0) |
| Polynomial 2° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.52 > 1.0) |
| Polynomial 3° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.31 > 1.0) |
| Polynomial 4° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.23 > 1.0) |
| Polynomial 5° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Polynomial 6° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Polynomial 7° | Warning | **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.12 > 1.0) |
| Polynomial 8° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Power | Warning | **Warnings**  • BMD/high dose ratio is greater than threshold (1.76 > 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 | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M3 | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist |

## Recommended model

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

# Female BMD Results for Table: Large Unstained Cell count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 0.04 ± 0.014 | 0.05 ± 0.014 | 0.036 ± 0.013 | 0.035 ± 0.01 | 0.042 ± 0.013 | 0.05 ± 0.019 | 0.04 ± 0.012 | 0.052 ± 0.015 | 0.064 ± 0.021 | 0.07 ± 0.045 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°, 6°, 8°) | 0.427 | -377.651 | 157.679 | 87.184 | Hill recommended as best-fitting model on the basis of the lowest BMDL. |
| Polynomial 7° | <0.0001 | -350.94 | -9999 | -999 |
| Power | <0.0001 | 1.9E+07 | 1 | -999 |
| Hillb | 0.152 | -372.312 | 58.894 | 25.959 |
| Exponential M2 (equivalent models include Exponential M3) | 0.356 | -376.872 | 198.281 | 122.205 |
| Exponential M4 (equivalent models include Exponential M5) | 0.368 | -376.106 | 120.138 | 43.813 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.007, BMDS Test 3 p-value = 0.947).

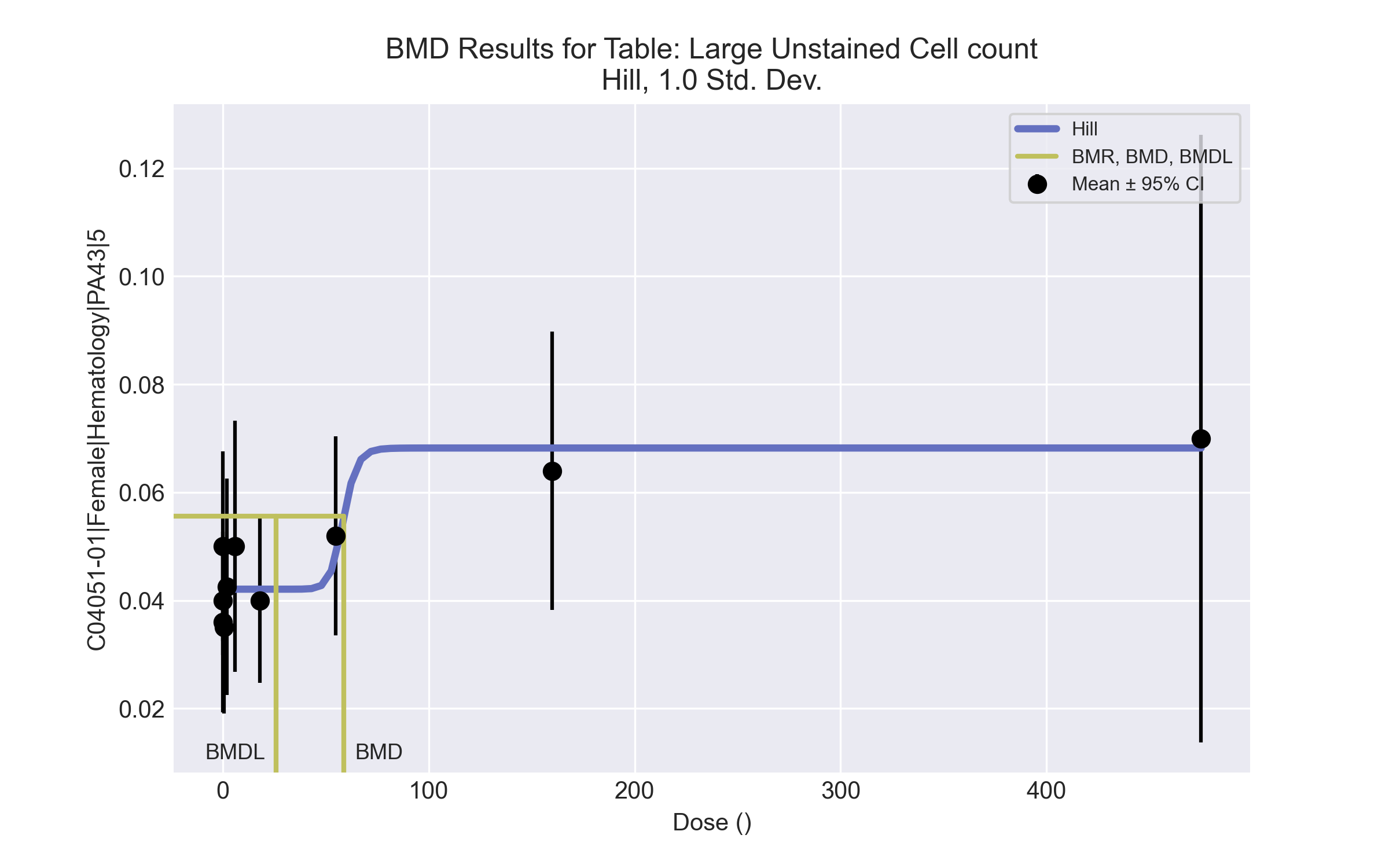
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°, 6°, 8°) | Valid | - |
| Polynomial 7° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Power | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Residual at lowest dose is greater than threshold (nan > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (nan > 1.5)  **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMDL computation failed. |
| Hilla | Valid | **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED! |
| Exponential M2 (equivalent models include Exponential M3) | Valid | - |
| Exponential M4 (equivalent models include Exponential M5) | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Hill Model. (Version: 2.18; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-xmqiqihu.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-xmqiqihu.plt  
 Tue Apr 13 11:21:18 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  
 Power parameter restricted to be greater than 1  
 The variance is to be modeled as Var(i) = exp(lalpha + rho \* ln(mean(i)))  
  
 Total number of dose groups = 10  
 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   
 lalpha = -7.84195  
 rho = 0  
 intercept = 0.04  
 v = 0.03  
 n = 18  
 k = 238.75  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 lalpha rho intercept v n k  
  
 lalpha 1 1 0.25 -0.7 NA NA   
  
 rho 1 1 0.29 -0.69 NA NA   
  
 intercept 0.25 0.29 1 -0.25 NA NA   
  
 v -0.7 -0.69 -0.25 1 NA NA   
  
 n NA NA NA NA NA NA   
  
 k NA NA NA NA NA NA   
  
  
NA - This parameter's variance has been estimated as zero or less.  
THE MODEL HAS PROBABLY NOT CONVERGED!!!  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 lalpha 2.23799 NA NA NA  
 rho 3.42354 NA NA NA  
 intercept 0.042089 NA NA NA  
 v 0.026123 NA NA NA  
 n 17.9707 NA NA NA  
 k 58.6658 NA NA NA  
  
At least some variance estimates are negative.  
THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!  
Try again from another starting point.  
  
  
  
 Table of Data and Estimated Values of Interest  
  
 Dose N Obs Mean Est Mean Obs Std Dev Est Std Dev Scaled Res.  
------ --- -------- -------- ----------- ----------- ----------  
  
 0 10 0.04 0.0421 0.0141 0.0135 -0.489  
 0.07 5 0.05 0.0421 0.0141 0.0135 1.31  
 0.2 5 0.036 0.0421 0.0134 0.0135 -1.01  
 0.7 4 0.035 0.0421 0.01 0.0135 -1.05  
 2 4 0.0425 0.0421 0.0126 0.0135 0.0608  
 6 5 0.05 0.0421 0.0187 0.0135 1.31  
 18 5 0.04 0.0421 0.0122 0.0135 -0.346  
 55 5 0.052 0.0483 0.0148 0.0171 0.48  
 160 5 0.064 0.0682 0.0207 0.0309 -0.305  
 475 5 0.07 0.0682 0.0453 0.0309 0.129  
  
  
  
 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)} = exp(lalpha + rho\*ln(Mu(i)))  
 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 186.852718 11 -351.705435  
 A2 198.255920 20 -356.511841  
 A3 196.857705 12 -369.715409  
 fitted 192.155750 6 -372.311500  
 R 178.470094 2 -352.940188  
  
  
 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 39.5717 18 0.002386  
 Test 2 22.8064 9 0.006646  
 Test 3 2.79643 8 0.9465  
 Test 4 9.40391 6 0.1521  
  
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 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 = 58.8938  
  
 BMDL = 25.9591  
  
 BMDU = 2.25625e+009

# Female BMD Results for Table: Leukocyte Count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 5.941 ± 1.323 | 7.708 ± 1.541 | 6.858 ± 2.263 | 6.33 ± 0.219 | 5.737 ± 0.615 | 7.538 ± 1.765 | 6.86 ± 1.822 | 7.234 ± 1.557 | 7.876 ± 2.117 | 7.558 ± 1.76 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°) | 0.043 | 110.721 | 630.723 | 250.584 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 5° (equivalent models include Polynomial 6°, 8°) | 0.043 | 110.721 | 630.724 | 250.584 |
| Polynomial 7° | 0.043 | 110.721 | 630.726 | 250.584 |
| Hill | 0.076 | 109.59 | -999 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.042 | 110.805 | 637.403 | 277.005 |
| Exponential M4 | 0.052 | 110.691 | -999 | 0 |
| Exponential M5 | 0.052 | 110.691 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.019, BMDS Test 3 p-value = 0.093).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.09304)  • Goodness of fit p-value is less than threshold (0.0429 < 0.1)  • BMD/high dose ratio is greater than threshold (1.33 > 1.0) |
| Polynomial 5° (equivalent models include Polynomial 6°, 8°) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.09304)  • Goodness of fit p-value is less than threshold (0.0429 < 0.1)  • BMD/high dose ratio is greater than threshold (1.33 > 1.0) |
| Polynomial 7° | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.09304)  • Goodness of fit p-value is less than threshold (0.0429 < 0.1)  • BMD/high dose ratio is greater than threshold (1.33 > 1.0) |
| Hill | Failure | **Failures**  • BMD does not exist  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.09304)  • Goodness of fit p-value is less than threshold (0.0762 < 0.1)  **Cautions**  • Warning(s): BMR value is not in the range of the mean function |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.09304)  • Goodness of fit p-value is less than threshold (0.0417 < 0.1)  • BMD/high dose ratio is greater than threshold (1.34 > 1.0) |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.09304)  • Goodness of fit p-value is less than threshold (0.0523 < 0.1) |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.09304)  • Goodness of fit p-value is less than threshold (0.0523 < 0.1) |

## Recommended model

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

# Female BMD Results for Table: Monocyte count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 0.18 ± 0.068 | 0.196 ± 0.067 | 0.216 ± 0.105 | 0.17 ± 0.048 | 0.19 ± 0.076 | 0.288 ± 0.085 | 0.244 ± 0.067 | 0.278 ± 0.095 | 0.384 ± 0.159 | 0.302 ± 0.198 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 3°, 4°, 5°, 6°, 7°, 8°) | 0.058 | -189.138 | 133.546 | 68.109 | Hill recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° | 0.058 | -189.138 | 133.545 | 68.109 |
| Hillb | 0.273 | -193.479 | 20.731 | 4.642 |
| Exponential M2 (equivalent models include Exponential M3) | 0.023 | -186.474 | 204.747 | 112.137 |
| Exponential M4 (equivalent models include Exponential M5) | 0.25 | -193.165 | 36.274 | 4.837 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.028, BMDS Test 3 p-value = 0.847).

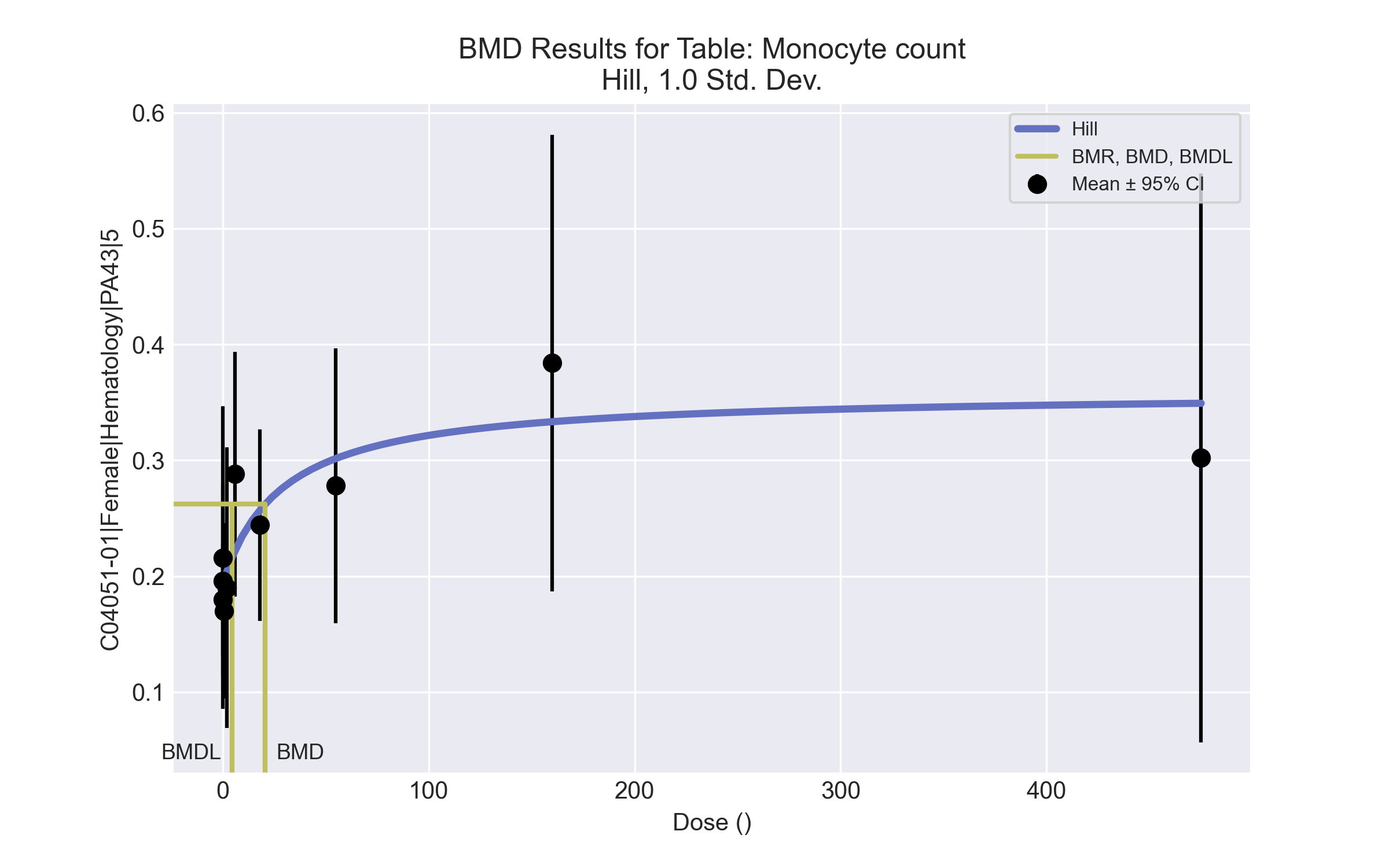
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 3°, 4°, 5°, 6°, 7°, 8°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0578 < 0.1) |
| Polynomial 2° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0578 < 0.1) |
| Hilla | Valid | - |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0233 < 0.1) |
| Exponential M4 (equivalent models include Exponential M5) | Valid | **Cautions**  • BMD/BMDL ratio is greater than threshold (7.5 > 5.0) |

a Recommended model

## Recommended model



====================================================================   
 Hill Model. (Version: 2.18; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-og9sohbc.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-og9sohbc.plt  
 Tue Apr 13 11:22:26 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  
 Power parameter restricted to be greater than 1  
 The variance is to be modeled as Var(i) = exp(lalpha + rho \* ln(mean(i)))  
  
 Total number of dose groups = 10  
 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   
 lalpha = -4.52066  
 rho = 0  
 intercept = 0.18  
 v = 0.204  
 n = 0.527466  
 k = 6.2449  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -n   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 lalpha rho intercept v k  
  
 lalpha 1 0.99 0.28 -0.41 0.061  
  
 rho 0.99 1 0.34 -0.39 0.068  
  
 intercept 0.28 0.34 1 0.074 0.57  
  
 v -0.41 -0.39 0.074 1 0.65  
  
 k 0.061 0.068 0.57 0.65 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 lalpha -0.939548 1.49958 -3.87867 1.99957  
 rho 2.69453 1.01469 0.705771 4.68329  
 intercept 0.193736 0.0155845 0.163191 0.224281  
 v 0.164954 0.0609344 0.0455244 0.284383  
 n 1 NA  
 k 29.1947 42.4017 -53.9111 112.3  
  
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 10 0.18 0.194 0.0682 0.0685 -0.634  
 0.07 5 0.196 0.194 0.0666 0.0687 0.0609  
 0.2 5 0.216 0.195 0.105 0.069 0.685  
 0.7 4 0.17 0.198 0.0476 0.0703 -0.785  
 2 4 0.19 0.204 0.0762 0.0736 -0.389  
 6 5 0.288 0.222 0.085 0.0822 1.8  
 18 5 0.244 0.257 0.0666 0.1 -0.283  
 55 5 0.278 0.301 0.0955 0.124 -0.423  
 160 5 0.384 0.333 0.159 0.142 0.798  
 475 5 0.302 0.349 0.198 0.151 -0.696  
  
  
  
 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)} = exp(lalpha + rho\*ln(Mu(i)))  
 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 98.838321 11 -175.676642  
 A2 108.158831 20 -176.317661  
 A3 106.102926 12 -188.205853  
 fitted 101.739445 5 -193.478890  
 R 88.633134 2 -173.266268  
  
  
 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 39.0514 18 0.002805  
 Test 2 18.641 9 0.02842  
 Test 3 4.11181 8 0.8469  
 Test 4 8.72696 7 0.2729  
  
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 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 = 20.7313  
  
 BMDL = 4.64196  
  
 BMDU = 128.137

# Female BMD Results for Table: Neutrophil Count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 0.419 ± 0.083 | 0.526 ± 0.066 | 0.616 ± 0.14 | 0.492 ± 0.067 | 0.525 ± 0.152 | 0.57 ± 0.202 | 0.534 ± 0.181 | 0.614 ± 0.108 | 0.604 ± 0.278 | 0.718 ± 0.251 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 5°, 7°, 8°) | 0.02 | -139.094 | 265.284 | 129.413 | Hill recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 3° (equivalent models include Polynomial 4°, 6°) | 0.02 | -139.094 | 265.283 | 129.413 |
| Hillb | 0.134 | -144.212 | 0.071 | 0.013 |
| Exponential M2 (equivalent models include Exponential M3) | 0.017 | -138.623 | 302.453 | 165.474 |
| Exponential M4 | 0.026 | -139.385 | 98.068 | 0.239 |
| Exponential M5 | 0.026 | -139.385 | 98.069 | 2.0E-04 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.006, BMDS Test 3 p-value = 0.414).

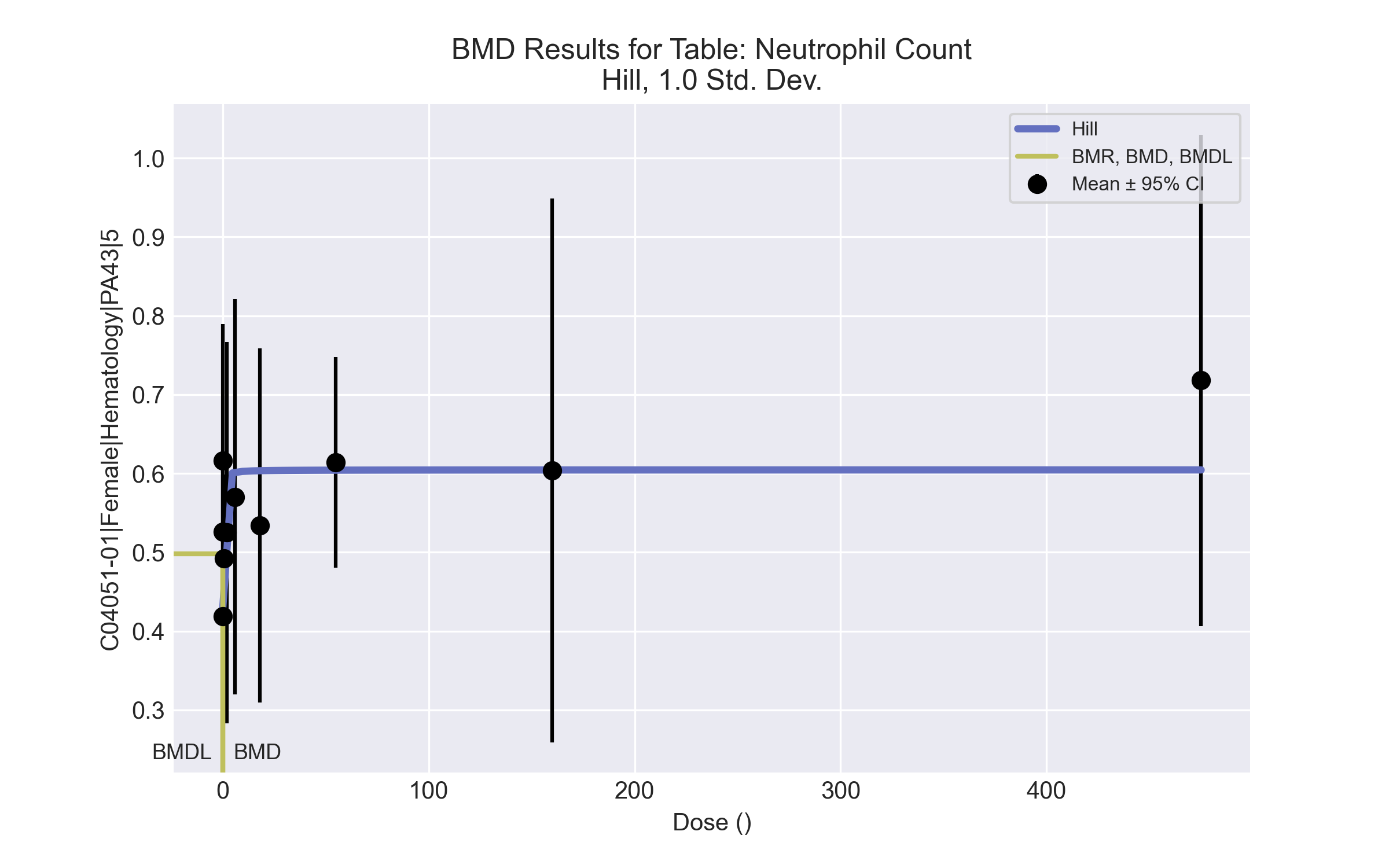
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 5°, 7°, 8°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0196 < 0.1)  • Residual at lowest dose is greater than threshold (2.28 > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.64 > 1.5) |
| Polynomial 3° (equivalent models include Polynomial 4°, 6°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0196 < 0.1)  • Residual at lowest dose is greater than threshold (2.28 > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.64 > 1.5) |
| Hilla | Valid | **Cautions**  • BMD/BMDL ratio is greater than threshold (5.43 > 5.0) |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0166 < 0.1)  • Residual at lowest dose is greater than threshold (2.31 > 2.0) |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0257 < 0.1)  • BMD/BMDL ratio is greater than threshold (4.11e+02 > 20.0)  • Residual at lowest dose is greater than threshold (2.17 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (4.11e+02 > 5.0) |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0257 < 0.1)  • BMD/BMDL ratio is greater than threshold (4.8e+05 > 20.0)  • Residual at lowest dose is greater than threshold (2.17 > 2.0)  **Cautions**  • BMD/BMDL ratio is greater than threshold (4.8e+05 > 5.0) |

a Recommended model

## Recommended model



====================================================================   
 Hill Model. (Version: 2.18; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-7z9n551h.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-7z9n551h.plt  
 Tue Apr 13 11:22:31 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  
 Power parameter restricted to be greater than 1  
 The variance is to be modeled as Var(i) = exp(lalpha + rho \* ln(mean(i)))  
  
 Total number of dose groups = 10  
 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   
 lalpha = -3.62899  
 rho = 0  
 intercept = 0.419  
 v = 0.299  
 n = 0.0793903  
 k = 0.268611  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -n   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 lalpha rho intercept v k  
  
 lalpha 1 0.97 0.37 -0.65 0.042  
  
 rho 0.97 1 0.46 -0.59 0.062  
  
 intercept 0.37 0.46 1 -0.59 0.33  
  
 v -0.65 -0.59 -0.59 1 0.073  
  
 k 0.042 0.062 0.33 0.073 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 lalpha -0.686358 1.11452 -2.87077 1.49805  
 rho 5.34583 1.71058 1.99315 8.69851  
 intercept 0.425528 0.0233968 0.379671 0.471385  
 v 0.178941 0.0394247 0.10167 0.256212  
 n 1 NA  
 k 0.104564 0.0771162 -0.0465806 0.255709  
  
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 10 0.419 0.426 0.0831 0.0723 -0.286  
 0.07 5 0.526 0.497 0.0662 0.11 0.586  
 0.2 5 0.616 0.543 0.14 0.139 1.18  
 0.7 4 0.492 0.581 0.0665 0.166 -1.07  
 2 4 0.525 0.596 0.152 0.178 -0.795  
 6 5 0.57 0.601 0.202 0.182 -0.385  
 18 5 0.534 0.603 0.181 0.184 -0.844  
 55 5 0.614 0.604 0.108 0.184 0.12  
 160 5 0.604 0.604 0.278 0.185 -0.00427  
 475 5 0.718 0.604 0.251 0.185 1.37  
  
  
  
 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)} = exp(lalpha + rho\*ln(Mu(i)))  
 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 75.209227 11 -128.418453  
 A2 86.758026 20 -133.516051  
 A3 82.659540 12 -141.319080  
 fitted 77.106192 5 -144.212384  
 R 67.394809 2 -130.789618  
  
  
 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 38.7264 18 0.003101  
 Test 2 23.0976 9 0.005981  
 Test 3 8.19697 8 0.4145  
 Test 4 11.1067 7 0.134  
  
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 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 = 0.0708856  
  
 BMDL = 0.0130537  
  
  
BMDU computation failed.

# Female BMD Results for Table: Platelet count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55a | 160a | 475a |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 1041.2 ± 116.812 | 1067.2 ± 115.912 | 996.6 ± 76.356 | 970.5 ± 52.221 | 996.5 ± 37.811 | 965.6 ± 63.528 | 925.6 ± 69.694 | 1011.2 ± 47.061 | 916.4 ± 76.291 | 823.4 ± 122.382 |

a Dose group removed in BMD modeling session

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°) | 0.121 | 382.182 | 16.536 | 9.974 | Exponential-M2 recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 8° | <0.0001 | 872.478 | 0.308 | -999 |
| Hill | 0.674 | 379.013 | -999 | -999 |
| Exponential M2b (equivalent models include Exponential M3) | 0.126 | 382.085 | 16.335 | 9.571 |
| Exponential M4 | 0.66 | 377.89 | -999 | 0 |
| Exponential M5 | 0.674 | 379.013 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.094, BMDS Test 3 p-value = 0.474).

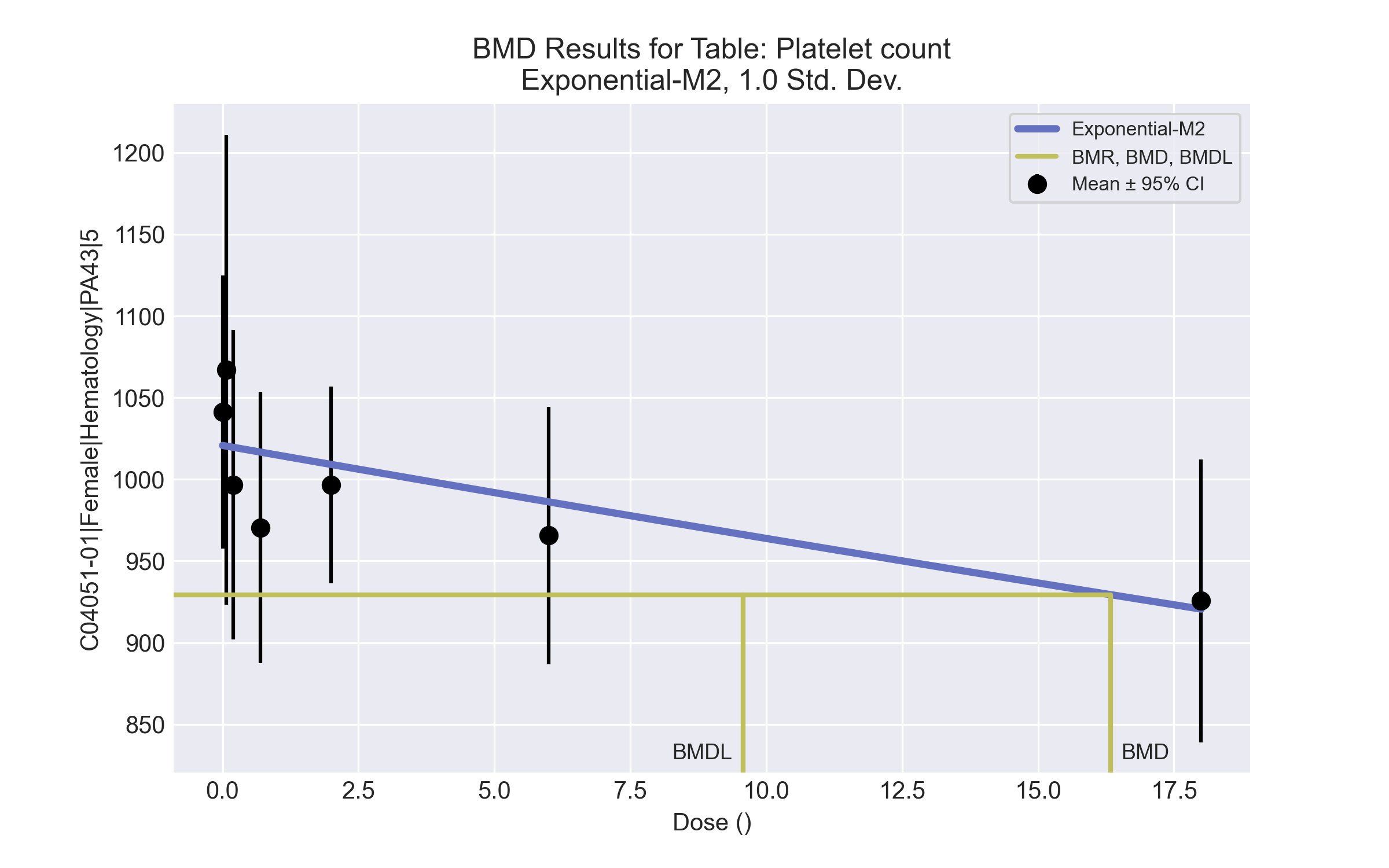
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 6°, 7°) | Valid | - |
| Polynomial 8° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Ratio of modeled to actual stdev. at control is greater than threshold (3.13 > 1.5)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMDL computation failed. |
| 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 M2a (equivalent models include Exponential M3) | Valid | - |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-p\_ty5kab.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 11:22:57 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 = 7  
 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 -60.3714   
 rho 9.98261   
 a 979.759   
 b 0.00600486   
 c 0 Specified  
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 2 Std. Err.  
 -------- ------- ---------  
 lnalpha -55.3411 48.9507  
 rho 9.29103 7.08797  
 a 1020.75 16.7812  
 b 0.00574065 0.00182515  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 10 1041 116.8  
 0.07 5 1067 115.9  
 0.2 5 996.6 76.36  
 0.7 4 970.5 52.22  
 2 4 996.5 37.81  
 6 5 965.6 63.53  
 18 5 925.6 69.69  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 1021 91.37 0.7079  
 0.07 1020 91.2 1.149  
 0.2 1020 90.88 -0.5653  
 0.7 1017 89.68 -1.029  
 2 1009 86.62 -0.2908  
 6 986.2 77.86 -0.5913  
 18 920.5 56.54 0.2002  
  
  
  
 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 -185.8816 8 387.7632  
 A2 -180.4682 14 388.9365  
 A3 -182.7387 9 383.4775  
 R -191.0006 2 386.0012  
 2 -187.0425 4 382.0849  
  
  
 Additive constant for all log-likelihoods = -34.92. 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 21.06 12 0.04944  
 Test 2 10.83 6 0.09388  
 Test 3 4.541 5 0.4744  
 Test 4 8.607 5 0.1258  
  
  
 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 greater than .1. Model 2 seems  
 to adequately describe the data.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 16.3353  
  
 BMDL = 9.5714  
  
 BMDU = 37.2712

# Female BMD Results for Table: Reticulocyte count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160a | 475a |
| N | 10 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 223.21 ± 39.358 | 243.74 ± 50.624 | 225.06 ± 28.057 | 211.225 ± 34.914 | 218.4 ± 32.006 | 207.94 ± 18.031 | 223.48 ± 40.939 | 182.22 ± 11.666 | 192.8 ± 24.218 | 201.64 ± 17.641 |

a Dose group removed in BMD modeling session

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.144 | 345.871 | 47.868 | 33.921 | Power recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° | 0.226 | 344.467 | 51.226 | 37.518 |
| Polynomial 3° | 0.161 | 346.223 | 52.096 | 38.382 |
| Polynomial 4° | 0.165 | 346.142 | 52.678 | 38.698 |
| Polynomial 5° | 0.167 | 346.115 | 53.084 | 38.806 |
| Polynomial 6° | 0.167 | 346.106 | 53.375 | 38.841 |
| Polynomial 7° | 0.167 | 346.103 | 53.591 | 38.853 |
| Polynomial 8° | 0.168 | 346.102 | 53.758 | 38.857 |
| Powerb | 0.244 | 344.214 | 54.561 | 38.414 |
| Hill | 0.095 | 348.214 | 52.406 | -999 |
| Exponential M2 (equivalent models include Exponential M4) | 0.129 | 346.195 | 47.612 | 32.226 |
| Exponential M3 | 0.161 | 346.214 | 54.354 | 38.408 |
| Exponential M5 | 0.095 | 348.214 | 52.114 | 19.53 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.077, BMDS Test 3 p-value = 0.964).

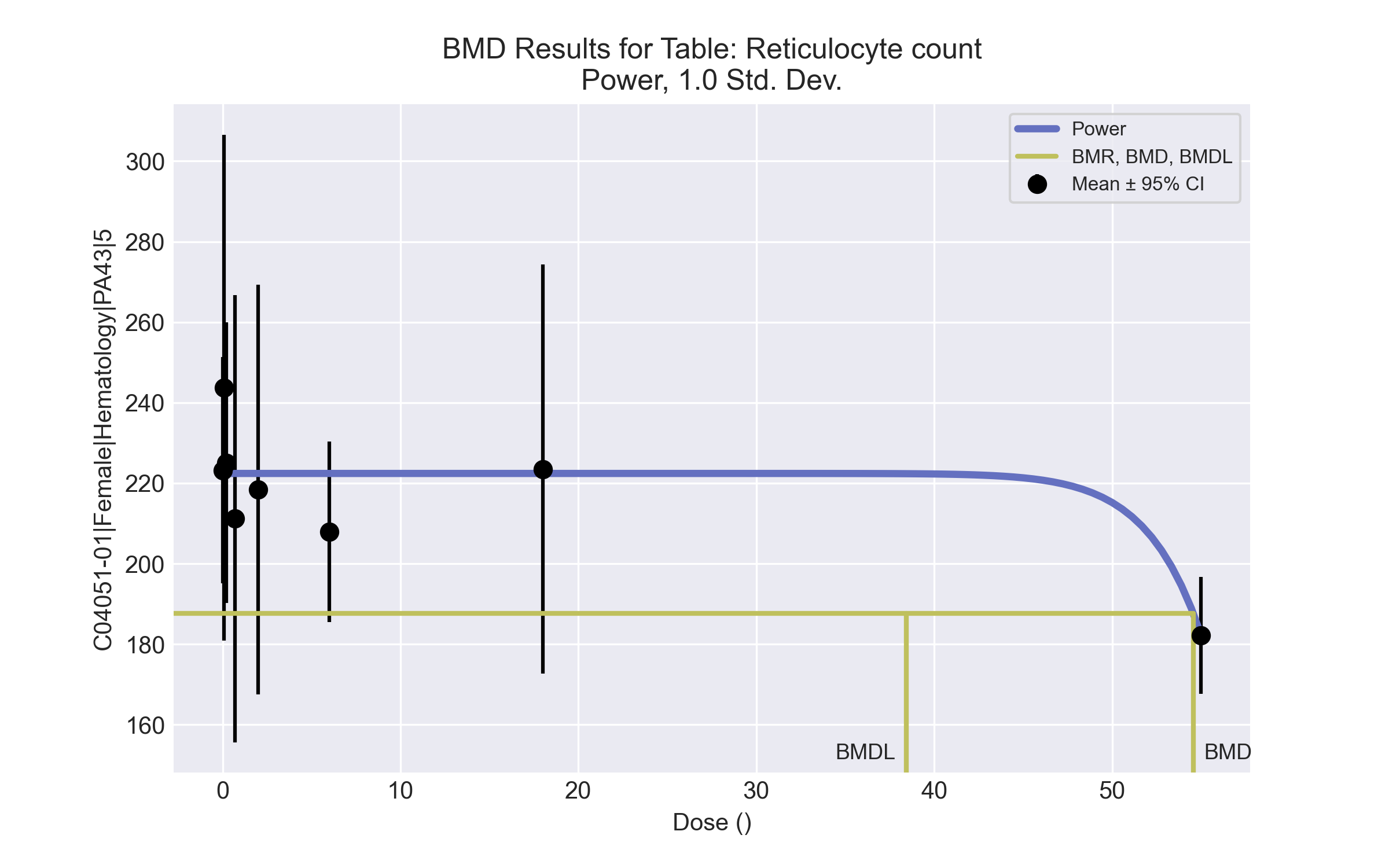
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Valid | - |
| Polynomial 2° | Valid | - |
| Polynomial 3° | Valid | - |
| Polynomial 4° | Valid | - |
| Polynomial 5° | Valid | - |
| Polynomial 6° | Valid | - |
| Polynomial 7° | Valid | - |
| Polynomial 8° | Valid | - |
| Powera | Valid | - |
| Hill | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Goodness of fit p-value is less than threshold (0.0948 < 0.1)  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 (equivalent models include Exponential M4) | Valid | - |
| Exponential M3 | Valid | - |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0948 < 0.1) |

a Recommended model

## Recommended model



====================================================================   
 Power Model. (Version: 2.19; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-2g3ug6wq.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-2g3ug6wq.plt  
 Tue Apr 13 11:23:11 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = control + slope \* dose^power  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 The power is restricted to be greater than or equal to 1  
 The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) \* rho)  
  
 Total number of dose groups = 8  
 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   
 lalpha = 7.10474  
 rho = 0  
 control = 182.22  
 slope = 38.2475  
 power = -9999  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -power   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 lalpha rho control slope  
  
 lalpha 1 -1 0.37 -0.53  
  
 rho -1 1 -0.38 0.54  
  
 control 0.37 -0.38 1 -0.77  
  
 slope -0.53 0.54 -0.77 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 lalpha -58.2126 21.5532 -100.456 -15.9691  
 rho 12.0846 4.02136 4.20287 19.9663  
 control 222.413 5.64471 211.35 233.477  
 slope -1.89506e-030 3.45315e-031 -2.57187e-030 -1.21826e-030  
 power 18 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 10 223 222 39.4 34.8 0.0724  
 0.07 5 244 222 50.6 34.8 1.37  
 0.2 5 225 222 28.1 34.8 0.17  
 0.7 4 211 222 34.9 34.8 -0.643  
 2 4 218 222 32 34.8 -0.231  
 6 5 208 222 18 34.8 -0.93  
 18 5 223 222 40.9 34.8 0.0686  
 55 5 182 182 11.7 10.4 -1e-008  
  
  
  
 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)} = exp(lalpha + rho\*ln(Mu(i)))  
 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 -169.826130 9 357.652261  
 A2 -163.433180 16 358.866360  
 A3 -164.149823 10 348.299646  
 fitted -168.107176 4 344.214353  
 R -174.791274 2 353.582547  
  
  
 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 22.7162 14 0.06505  
 Test 2 12.7859 7 0.0775  
 Test 3 1.43329 6 0.9638  
 Test 4 7.91471 6 0.2444  
  
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 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 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 = 54.5612   
  
  
 BMDL = 38.4142   
  
  
 BMDU = 64.4371

# Female BMD Results for Table: Free Thyroxine

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 3 | 4 | 5 | 5 | 5 | 4 | 3 |
| Mean ± SD | 7.023 ± 2.407 | 6.89 ± 1.574 | 8.894 ± 7.083 | 7.277 ± 1.349 | 7.995 ± 1.441 | 8.554 ± 1.178 | 10.044 ± 2.696 | 9.84 ± 1.58 | 8.908 ± 0.986 | 8.807 ± 2.675 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | 6.9E-04 | 157.337 | 1601.19 | 435.925 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Power | 6.9E-04 | 157.337 | 1601.2 | 435.925 |
| Hill | 0.051 | 146.822 | -999 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 6.7E-04 | 157.404 | 1539.59 | 449.133 |
| Exponential M4 | 0.049 | 146.373 | -999 | 0 |
| Exponential M5 | 0.04 | 147.454 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = <0.0001, BMDS Test 3 p-value = 0.038).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.03806)  • Goodness of fit p-value is less than threshold (0.000689 < 0.1)  • BMD/high dose ratio is greater than threshold (3.37 > 1.0) |
| Power | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.03806)  • Goodness of fit p-value is less than threshold (0.000689 < 0.1)  • BMD/high dose ratio is greater than threshold (3.37 > 1.0) |
| Hill | Failure | **Failures**  • BMD does not exist  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.03806)  • Goodness of fit p-value is less than threshold (0.0508 < 0.1)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.52 > 1.5)  **Cautions**  • Warning(s): BMR value is not in the range of the mean function |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.03806)  • Goodness of fit p-value is less than threshold (0.000671 < 0.1)  • BMD/high dose ratio is greater than threshold (3.24 > 1.0) |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.03806)  • Goodness of fit p-value is less than threshold (0.0494 < 0.1) |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.03806)  • Goodness of fit p-value is less than threshold (0.0403 < 0.1) |

## Recommended model

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

# Female BMD Results for Table: Triiodothyronine

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.07 | 0.2 | 0.7 | 2 | 6 | 18 | 55 | 160 | 475 |
| N | 10 | 5 | 5 | 3 | 4 | 5 | 5 | 5 | 4 | 3 |
| Mean ± SD | 60.03 ± 11.713 | 67.18 ± 10.445 | 69.92 ± 14.716 | 70.5 ± 17.84 | 57.2 ± 14.166 | 62.22 ± 3.759 | 59.36 ± 10.114 | 58.32 ± 6.276 | 57.85 ± 4.034 | 45.333 ± 6.789 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.013 | 292.964 | -9999 | 1781.48 | Power recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° | 0.013 | 292.964 | -9999 | 883.499 |
| Polynomial 3° | 0.013 | 292.964 | -9999 | 422.902 |
| Polynomial 4° | 0.013 | 292.964 | -9999 | 423.244 |
| Polynomial 5° | 0.013 | 292.964 | -9999 | -999 |
| Polynomial 6° | 0.013 | 292.964 | -9999 | -999 |
| Polynomial 7° | 0.015 | 292.624 | -9999 | 440.836 |
| Polynomial 8° | 0.013 | 292.964 | -9999 | -999 |
| Powerb | 0.349 | 282.979 | 296.488 | 213.03 |
| Hill | 0.364 | 283.714 | 198.09 | -999 |
| Exponential M2 | 0.226 | 284.65 | -205.54 | -999 |
| Exponential M3 | 0.226 | 284.65 | -205.54 | -999 |
| Exponential M4 | 0.017 | 293.181 | -999 | 0 |
| Exponential M5 | 0.016 | 293.749 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.037, BMDS Test 3 p-value = 0.113).

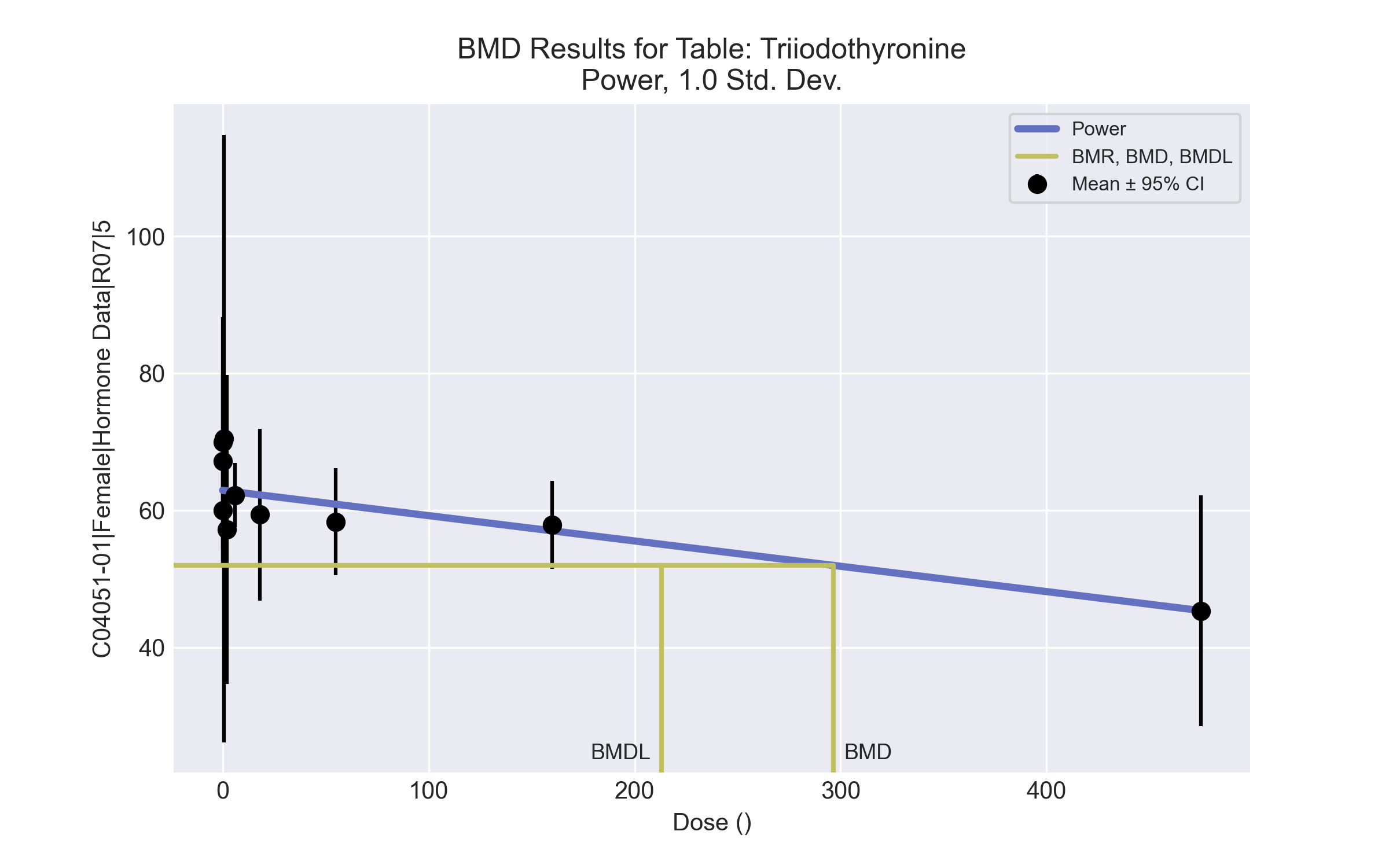
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0131 < 0.1)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (3.75 > 1.0) |
| Polynomial 2° | Warning | **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0131 < 0.1)  **Cautions**  • Warning(s): BMD = 100\*(maximum dose)  • BMDL/high dose ratio is greater than threshold (1.86 > 1.0) |
| Polynomial 3° | Warning | **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0131 < 0.1)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMD = 100\*(maximum dose) |
| Polynomial 4° | Warning | **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0131 < 0.1)  **Cautions**  • Warning(s): BMD = 100\*(maximum dose) |
| Polynomial 5° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0131 < 0.1)  **Cautions**  • Warning(s): BMD = 100\*(maximum dose); BMDL computation failed. |
| Polynomial 6° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0131 < 0.1)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMD = 100\*(maximum dose); BMDL computation failed. |
| Polynomial 7° | Warning | **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0147 < 0.1)  **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMD = 100\*(maximum dose) |
| Polynomial 8° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0131 < 0.1)  **Cautions**  • Warning(s): THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMD = 100\*(maximum dose); BMDL computation failed. |
| Powera | Valid | - |
| Hill | Failure | **Failures**  • BMDL does not exist  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M3 | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Goodness of fit p-value is less than threshold (0.0166 < 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 (0.0155 < 0.1) |

a Recommended model

## Recommended model



====================================================================   
 Power Model. (Version: 2.19; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-mriivf32.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-mriivf32.plt  
 Tue Apr 13 11:27:18 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = control + slope \* dose^power  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 The power is restricted to be greater than or equal to 1  
 The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) \* rho)  
  
 Total number of dose groups = 10  
 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   
 lalpha = 4.7572  
 rho = 0  
 control = 45.3333  
 slope = 18.7284  
 power = -9999  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -power   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 lalpha rho control slope  
  
 lalpha 1 -1 0.21 -0.44  
  
 rho -1 1 -0.22 0.44  
  
 control 0.21 -0.22 1 -0.59  
  
 slope -0.44 0.44 -0.59 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 lalpha -17.2236 9.97026 -36.765 2.31774  
 rho 5.31426 2.42972 0.552102 10.0764  
 control 62.9187 1.64937 59.6859 66.1514  
 slope -0.0369419 0.00672555 -0.0501238 -0.0237601  
 power 1 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 10 60 62.9 11.7 11 -0.834  
 0.07 5 67.2 62.9 10.4 11 0.871  
 0.2 5 69.9 62.9 14.7 10.9 1.43  
 0.7 3 70.5 62.9 17.8 10.9 1.2  
 2 4 57.2 62.8 14.2 10.9 -1.03  
 6 5 62.2 62.7 3.76 10.9 -0.0983  
 18 5 59.4 62.3 10.1 10.6 -0.608  
 55 5 58.3 60.9 6.28 10 -0.572  
 160 4 57.9 57 4.03 8.43 0.2  
 475 3 45.3 45.4 6.79 4.59 -0.0143  
  
  
  
 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)} = exp(lalpha + rho\*ln(Mu(i)))  
 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 -135.458963 11 292.917925  
 A2 -126.546532 20 293.093063  
 A3 -133.029849 12 290.059699  
 fitted -137.489468 4 282.978937  
 R -143.482137 2 290.964273  
  
  
 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 33.8712 18 0.01306  
 Test 2 17.8249 9 0.03726  
 Test 3 12.9666 8 0.113  
 Test 4 8.91924 8 0.3492  
  
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 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 = 296.488   
  
  
 BMDL = 213.03   
  
  
 BMDU = 454.833