# Male BMD Results for Table: Liver Weight Absolute

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4a | 12a | 37a | 111a | 333a | 1000a |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 12.679 ± 1.208 | 12.46 ± 0.962 | 12.142 ± 0.733 | 14.416 ± 0.871 | 13.164 ± 1.022 | 12.84 ± 1.629 | 12.816 ± 1.3 | 13.194 ± 0.51 | 15.484 ± 1.13 | 14.89 ± 1.482 |

a Dose group removed in BMD modeling session

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.075 | 33.015 | 0.839 | 0.533 | Polynomial-8 recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° | 0.327 | 30.064 | 1.005 | 0.822 |
| Polynomial 3° | 0.487 | 29.266 | 1.113 | 0.976 |
| Polynomial 4° | 0.55 | 29.026 | 1.177 | 0.853 |
| Polynomial 5° | 0.572 | 28.946 | 1.218 | 0.851 |
| Polynomial 6° | 0.58 | 28.918 | 1.246 | 0.854 |
| Polynomial 7° | 0.583 | 28.908 | 1.267 | 0.855 |
| Polynomial 8°b | 0.584 | 28.905 | 1.283 | 0.821 |
| Power | 0.3 | 30.903 | 1.341 | 0.805 |
| Hill | -999 | 32.903 | 1.336 | 0.53 |
| Exponential M2 | 0.083 | 32.8 | 0.841 | 0.554 |
| Exponential M3 | 0.3 | 30.903 | 1.347 | 0.811 |
| Exponential M4 | 0.023 | 35.015 | 0.839 | 0.533 |
| Exponential M5 | -999 | 32.903 | 1.342 | 0.805 |

a Constant variance case presented (BMDS Test 2 p-value = 0.508, BMDS Test 3 p-value = 0.508).

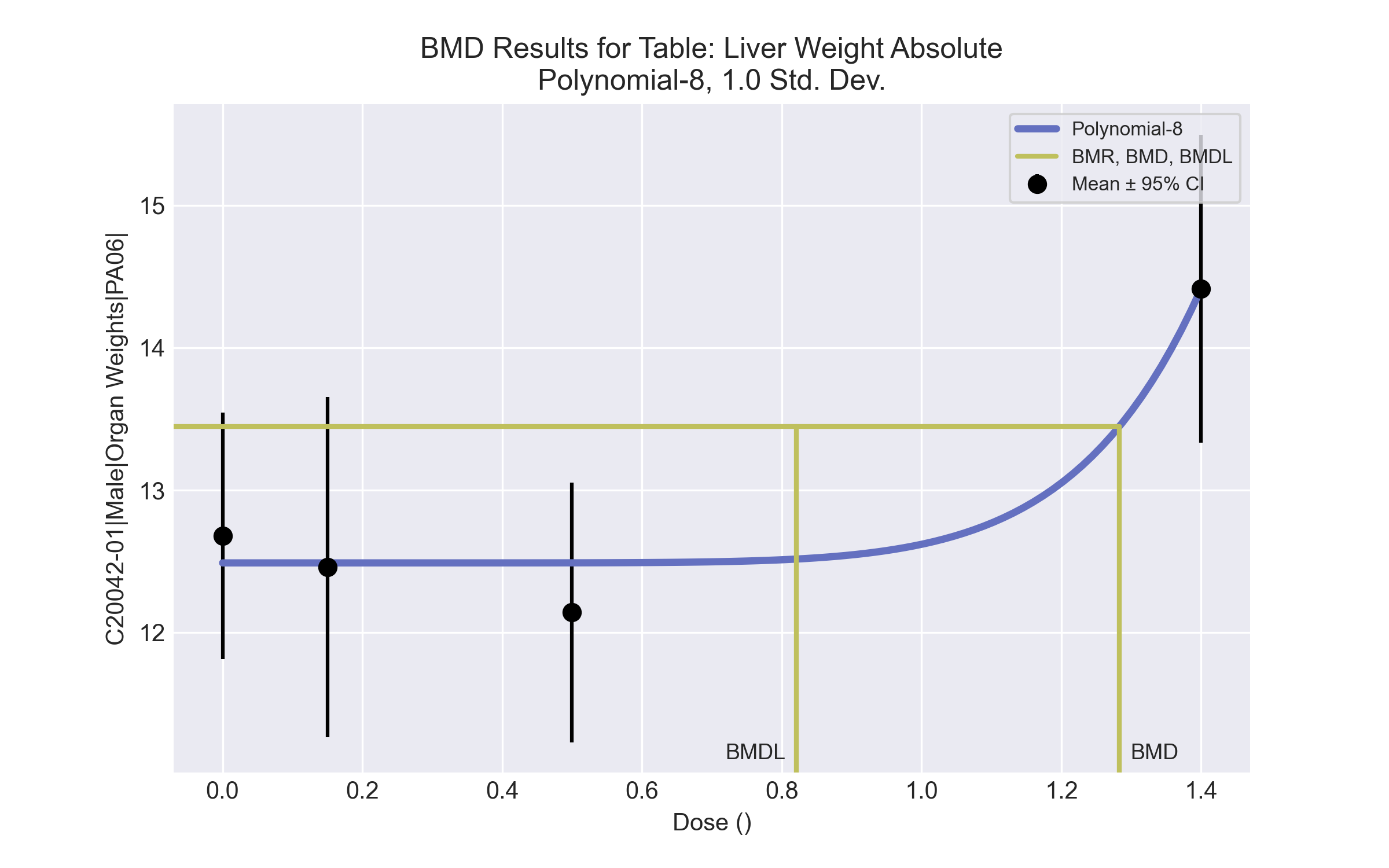
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0748 < 0.1) |
| Polynomial 2° | Valid | - |
| Polynomial 3° | Valid | - |
| Polynomial 4° | Valid | - |
| Polynomial 5° | Valid | - |
| Polynomial 6° | Valid | - |
| Polynomial 7° | Valid | - |
| Polynomial 8°a | Valid | - |
| Power | Valid | - |
| Hill | Warning | **Warnings**  • Zero degrees of freedom; saturated model  **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED! |
| Exponential M2 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0833 < 0.1) |
| Exponential M3 | Valid | - |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0228 < 0.1) |
| Exponential M5 | Warning | **Warnings**  • Zero degrees of freedom; saturated model |

a Recommended model

## Recommended model



====================================================================   
 Polynomial Model. (Version: 2.21; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-p6ullff7.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-p6ullff7.plt  
 Tue Apr 13 11:49:35 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = beta\_0 + beta\_1\*dose + beta\_2\*dose^2 + ...  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 rho is set to 0  
 The polynomial coefficients are restricted to be positive  
 A constant variance model is fit  
  
 Total number of dose groups = 4  
 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 = 1.04863  
 rho = 0 Specified  
 beta\_0 = -47.4623  
 beta\_1 = 0  
 beta\_2 = 0  
 beta\_3 = 0  
 beta\_4 = 0  
 beta\_5 = 0  
 beta\_6 = 0  
 beta\_7 = 0  
 beta\_8 = 0  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -rho -beta\_1 -beta\_2 -beta\_3 -beta\_4 -beta\_5 -beta\_6 -beta\_7   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 alpha beta\_0 beta\_8  
  
 alpha 1 -2.2e-007 1.1e-006  
  
 beta\_0 -2.2e-007 1 -0.45  
  
 beta\_8 1.1e-006 -0.45 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 alpha 0.919612 0.260106 0.409814 1.42941  
 beta\_0 12.4899 0.214445 12.0696 12.9102  
 beta\_1 0 NA  
 beta\_2 -0 NA  
 beta\_3 0 NA  
 beta\_4 0 NA  
 beta\_5 0 NA  
 beta\_6 3.13352e-022 NA  
 beta\_7 2.95604e-021 NA  
 beta\_8 0.130507 0.032492 0.0668242 0.194191  
  
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 12.7 12.5 1.21 0.959 0.624  
 0.15 5 12.5 12.5 0.962 0.959 -0.0697  
 0.5 5 12.1 12.5 0.733 0.959 -0.812  
 1.4 5 14.4 14.4 0.871 0.959 0.000211  
  
  
  
 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 -10.914174 5 31.828348  
 A2 -9.752573 8 35.505147  
 A3 -10.914174 5 31.828348  
 fitted -11.452455 3 28.904910  
 R -17.676651 2 39.353303  
  
  
 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 15.8482 6 0.01459  
 Test 2 2.3232 3 0.5081  
 Test 3 2.3232 3 0.5081  
 Test 4 1.07656 2 0.5838  
  
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 = 1.28313  
  
  
 BMDL = 0.82108  
  
  
 BMDU = 1.3887

# Male BMD Results for Table: Liver Weight Relative

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4a | 12a | 37a | 111a | 333a | 1000a |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 39.109 ± 2.37 | 38.879 ± 2.196 | 37.254 ± 1.955 | 43.959 ± 2.598 | 40.327 ± 1.915 | 40.142 ± 3.122 | 40.51 ± 1.873 | 42.47 ± 1.01 | 48.533 ± 1.747 | 47.017 ± 2.921 |

a Dose group removed in BMD modeling session

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear | 0.011 | 77.474 | 0.751 | 0.493 | Polynomial-8 recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° | 0.099 | 73.142 | 0.93 | 0.717 |
| Polynomial 3° | 0.198 | 71.763 | 1.051 | 0.802 |
| Polynomial 4° | 0.248 | 71.311 | 1.125 | 0.832 |
| Polynomial 5° | 0.268 | 71.157 | 1.175 | 0.839 |
| Polynomial 6° | 0.275 | 71.102 | 1.209 | 0.934 |
| Polynomial 7° | 0.278 | 71.083 | 1.235 | 0.89 |
| Polynomial 8°b | 0.279 | 71.076 | 1.254 | 0.844 |
| Power | 0.11 | 73.072 | 1.33 | 0.842 |
| Hill | 0.11 | 73.072 | 1.301 | 0.539 |
| Exponential M2 | 0.013 | 77.209 | 0.753 | 0.508 |
| Exponential M3 | 0.11 | 73.072 | 1.335 | -999 |
| Exponential M4 | 0.003 | 79.474 | 0.751 | 0.493 |
| Exponential M5 | -999 | 75.072 | 1.328 | 0.842 |

a Constant variance case presented (BMDS Test 2 p-value = 0.909, BMDS Test 3 p-value = 0.909).

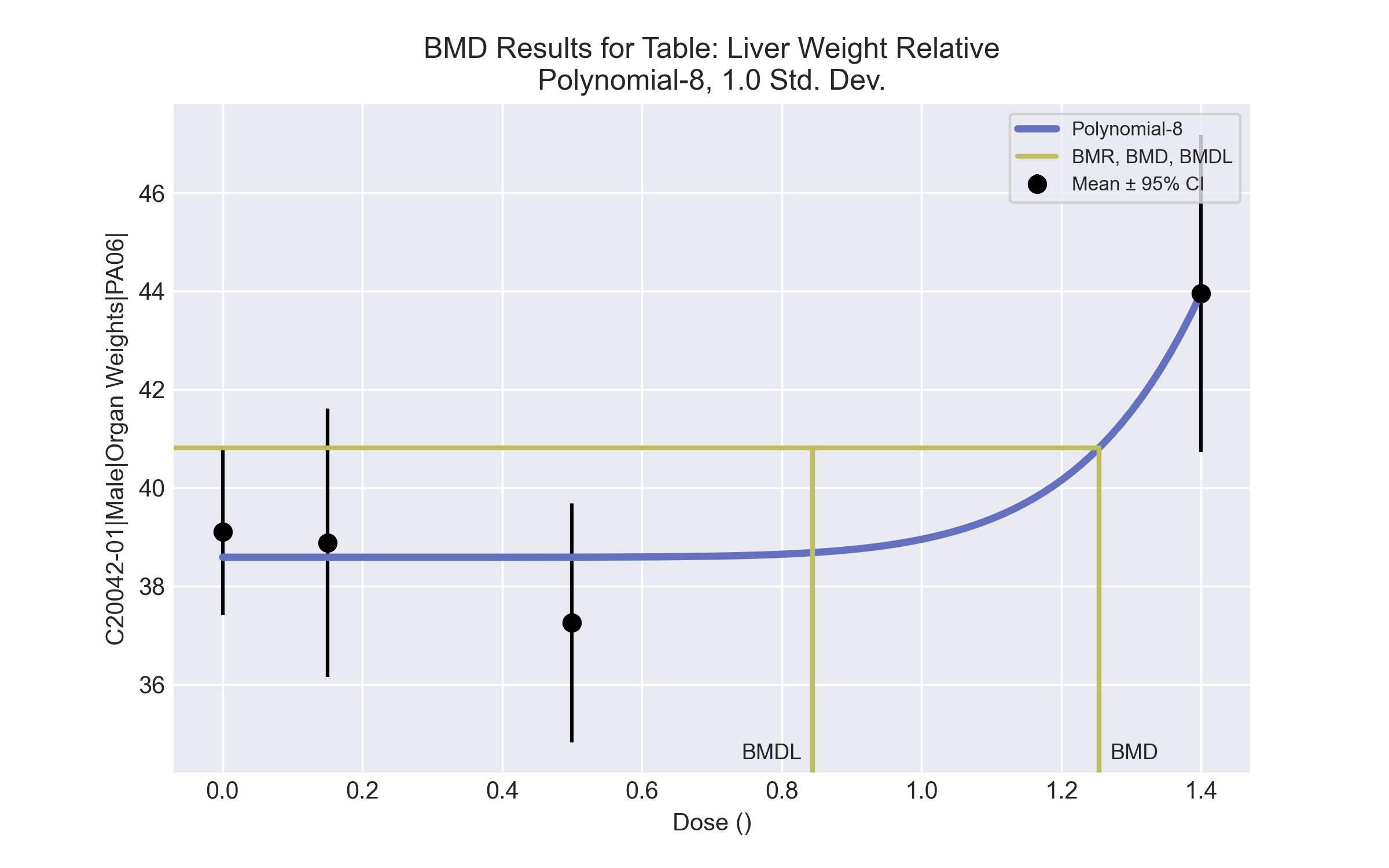
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0114 < 0.1) |
| Polynomial 2° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0993 < 0.1) |
| Polynomial 3° | Valid | - |
| Polynomial 4° | Valid | - |
| Polynomial 5° | Valid | - |
| Polynomial 6° | Valid | - |
| Polynomial 7° | Valid | - |
| Polynomial 8°a | Valid | - |
| Power | Valid | - |
| Hill | Valid | **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED! |
| Exponential M2 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.013 < 0.1) |
| Exponential M3 | Failure | **Failures**  • BMDL does not exist |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00277 < 0.1) |
| Exponential M5 | Warning | **Warnings**  • Zero degrees of freedom; saturated model |

a Recommended model

## Recommended model



====================================================================   
 Polynomial Model. (Version: 2.21; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-d9i15g4n.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-d9i15g4n.plt  
 Tue Apr 13 11:50:12 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = beta\_0 + beta\_1\*dose + beta\_2\*dose^2 + ...  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 rho is set to 0  
 The polynomial coefficients are restricted to be positive  
 A constant variance model is fit  
  
 Total number of dose groups = 4  
 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 = 5.34026  
 rho = 0 Specified  
 beta\_0 = -144.308  
 beta\_1 = 0  
 beta\_2 = 0  
 beta\_3 = 0  
 beta\_4 = 0  
 beta\_5 = 0  
 beta\_6 = 0  
 beta\_7 = 0  
 beta\_8 = 0  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -rho -beta\_1 -beta\_2 -beta\_3 -beta\_4 -beta\_5 -beta\_6 -beta\_7   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 alpha beta\_0 beta\_8  
  
 alpha 1 7.4e-007 -7.5e-008  
  
 beta\_0 7.4e-007 1 -0.45  
  
 beta\_8 -7.5e-008 -0.45 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 alpha 4.96814 1.4052 2.21399 7.72229  
 beta\_0 38.5875 0.498438 37.6106 39.5644  
 beta\_1 2.30843e-020 NA  
 beta\_2 0 NA  
 beta\_3 6.26087e-021 NA  
 beta\_4 -0 NA  
 beta\_5 0 NA  
 beta\_6 1.82648e-021 NA  
 beta\_7 0 NA  
 beta\_8 0.363929 0.0755216 0.215909 0.511949  
  
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 39.1 38.6 2.37 2.23 0.74  
 0.15 5 38.9 38.6 2.2 2.23 0.293  
 0.5 5 37.3 38.6 1.96 2.23 -1.34  
 1.4 5 44 44 2.6 2.23 0.000354  
  
  
  
 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 -31.261519 5 72.523038  
 A2 -30.989350 8 77.978701  
 A3 -31.261519 5 72.523038  
 fitted -32.538062 3 71.076124  
 R -40.749681 2 85.499363  
  
  
 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 19.5207 6 0.003369  
 Test 2 0.544338 3 0.909  
 Test 3 0.544338 3 0.909  
 Test 4 2.55309 2 0.279  
  
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 = 1.25425  
  
  
 BMDL = 0.844308  
  
  
 BMDU = 1.33981

# Male BMD Results for Table: A/G Ratio

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333a | 1000a |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 2.039 ± 0.212 | 1.989 ± 0.179 | 1.924 ± 0.28 | 2.032 ± 0.168 | 2.038 ± 0.089 | 1.959 ± 0.139 | 1.948 ± 0.056 | 1.89 ± 0.12 | 1.805 ± 0.127 | 1.88 ± 0.066 |

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°, 7°) | 0.657 | -115.416 | 155.225 | 90.396 | Polynomial-5 recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 5°b | <0.0001 | -64.708 | 47.003 | 11.049 |
| Polynomial 6° | <0.0001 | 396.127 | 3.805 | -999 |
| Polynomial 8° | <0.0001 | 659.363 | 11.722 | -999 |
| Hill | 0.976 | -117.215 | -999 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.548 | -113.472 | 156.383 | 89.278 |
| Exponential M4 | 0.93 | -115.096 | -999 | 0 |
| Exponential M5 | 0.93 | -115.096 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.024, BMDS Test 3 p-value = 0.115).

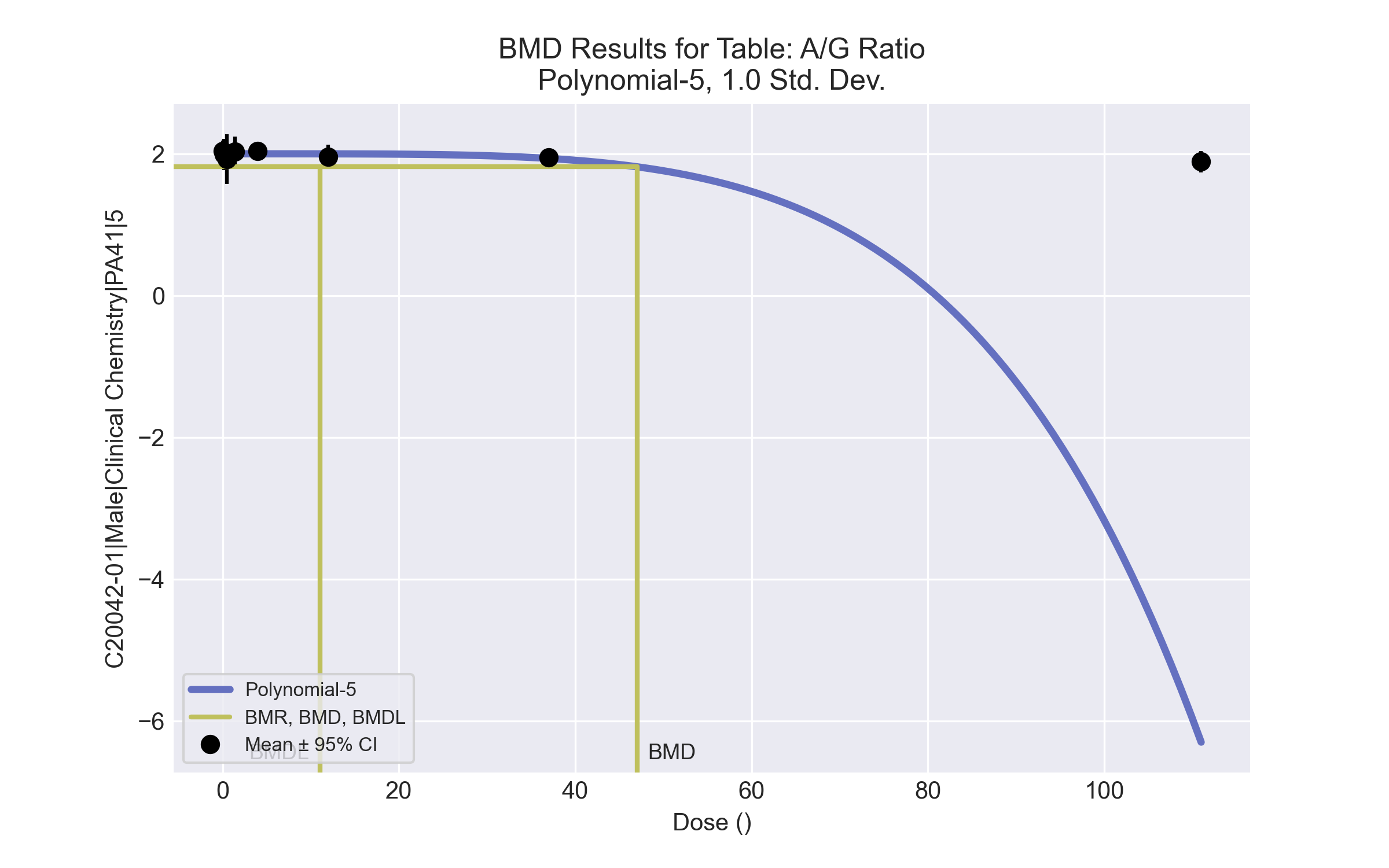
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 7°) | Warning | **Warnings**  • BMD/high dose ratio is greater than threshold (1.4 > 1.0) |
| Polynomial 5°a | Valid | - |
| Polynomial 6° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual of interest is greater than threshold (2.56 > 2.0)  • Residual at lowest dose is greater than threshold (2.74 > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (12.7 > 1.5)  **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMDL computation failed. |
| Polynomial 8° | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Residual at lowest dose is greater than threshold (3.43 > 2.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.28e+03 > 1.5)  **Cautions**  • Warning(s): 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 M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • BMD/high dose ratio is greater than threshold (1.41 > 1.0) |
| 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



====================================================================   
 Polynomial Model. (Version: 2.21; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-vkr05wpd.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-vkr05wpd.plt  
 Tue Apr 13 12:05:40 2021  
 ====================================================================   
  
 BMDS\_Model\_Run   
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~  
   
 The form of the response function is:   
  
 Y[dose] = beta\_0 + beta\_1\*dose + beta\_2\*dose^2 + ...  
  
  
 Dependent variable = Response  
 Independent variable = Dose  
 The polynomial coefficients are restricted to be negative  
 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 = -3.48303  
 rho = 0  
 beta\_0 = 1.9975  
 beta\_1 = -0.0153676  
 beta\_2 = 0  
 beta\_3 = -0.00115933  
 beta\_4 = 0  
 beta\_5 = -1.90913e-007  
  
  
!!! Warning: optimum may not have been found. !!!  
!!! You may want to try choosing different initial values. !!!  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -beta\_1 -beta\_2 -beta\_4   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 lalpha rho beta\_0 beta\_3 beta\_5  
  
 lalpha 1 -0.9 -0.029 -0.095 -0.0023  
  
 rho -0.9 1 0.021 0.048 0.14  
  
 beta\_0 -0.029 0.021 1 -0.4 0.4  
  
 beta\_3 -0.095 0.048 -0.4 1 -1  
  
 beta\_5 -0.0023 0.14 0.4 -1 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 lalpha -7.53623 0.412431 -8.34458 -6.72788  
 rho 5.96775 0.299987 5.37979 6.55572  
 beta\_0 2.0001 0.0310232 1.9393 2.06091  
 beta\_1 -7.71662e-022 NA  
 beta\_2 -3.74757e-023 NA  
 beta\_3 0 1.73288e-006 -3.39638e-006 3.39638e-006  
 beta\_4 -2.47885e-008 NA  
 beta\_5 -2.6917e-010 1.37365e-010 -5.38401e-010 6.05092e-014  
  
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 2.04 2 0.212 0.183 0.674  
 0.15 5 1.99 2 0.179 0.183 -0.138  
 0.5 5 1.92 2 0.28 0.183 -0.926  
 1.4 5 2.03 2 0.168 0.183 0.39  
 4 5 2.04 2 0.0893 0.183 0.46  
 12 5 1.96 2 0.139 0.183 -0.496  
 37 5 1.95 1.93 0.0555 0.166 0.178  
 111 5 1.89 -6.3 0.12 5.6 3.27  
  
  
  
 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 60.272458 9 -102.544915  
 A2 68.341814 16 -104.683627  
 A3 63.219064 10 -106.438129  
 fitted 37.353801 5 -64.707603  
 R 57.877773 2 -111.755546  
  
  
 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 20.9281 14 0.1035  
 Test 2 16.1387 7 0.02388  
 Test 3 10.2455 6 0.1147  
 Test 4 51.7305 5 <.0001  
  
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 less than .1. You may want to try a different   
model  
   
  
 Benchmark Dose Computation  
  
Specified effect = 1  
  
Risk Type = Estimated standard deviations from the control mean  
  
Confidence level = 0.95  
  
 BMD = 47.0028  
  
  
 BMDL = 11.0485  
  
   
BMDU computation failed.

# Male BMD Results for Table: Alanine aminotransferase

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333 | 1000 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 60.8 ± 14.861 | 57.2 ± 6.907 | 55 ± 11.247 | 64.2 ± 7.759 | 63.2 ± 11.904 | 57.6 ± 5.771 | 50.4 ± 5.32 | 52.6 ± 7.197 | 53.6 ± 6.269 | 52.4 ± 11.675 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 3°, 4°, 6°, 7°, 8°) | 0.027 | 316.347 | 1463.17 | 634.353 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 2° | 0.027 | 316.347 | 1463.16 | 634.353 |
| Polynomial 5° | 0.027 | 316.347 | 1463.18 | 634.353 |
| Hill | 0.433 | 308.041 | -999 | -999 |
| Exponential M2 | 0.028 | 316.285 | 1477.85 | 594.429 |
| Exponential M3 | 0.028 | 316.285 | 1477.84 | 594.429 |
| Exponential M4 | 0.328 | 309.132 | -999 | 0 |
| Exponential M5 | 0.324 | 310.041 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.079, BMDS Test 3 p-value = 0.483).

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 3°, 4°, 6°, 7°, 8°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0274 < 0.1)  • BMD/high dose ratio is greater than threshold (1.46 > 1.0) |
| Polynomial 2° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0274 < 0.1)  • BMD/high dose ratio is greater than threshold (1.46 > 1.0) |
| Polynomial 5° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0274 < 0.1)  • BMD/high dose ratio is greater than threshold (1.46 > 1.0) |
| Hill | Failure | **Failures**  • BMD does not exist  • BMDL does not exist  **Warnings**  • Residual of Interest does not exist  **Cautions**  • Warning(s): BMR value is not in the range of the mean function |
| Exponential M2 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.028 < 0.1)  • BMD/high dose ratio is greater than threshold (1.48 > 1.0) |
| Exponential M3 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.028 < 0.1)  • BMD/high dose ratio is greater than threshold (1.48 > 1.0) |
| 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.*

# Male BMD Results for Table: Cholesterol

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333 | 1000 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 114.9 ± 18.538 | 115.2 ± 4.97 | 119.6 ± 30.312 | 112.2 ± 17.796 | 123 ± 10.724 | 114.2 ± 7.662 | 117.8 ± 20.729 | 123.4 ± 13.164 | 131 ± 7.681 | 163.6 ± 15.915 |

## 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°) | 0.986 | 362.66 | 334.218 | 257.922 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Hill | 0.97 | 364.645 | 318.281 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.983 | 362.788 | 372.303 | 295.365 |
| Exponential M4 (equivalent models include Exponential M5) | 0.97 | 364.645 | 318.469 | 167.165 |

a Modeled variance case presented (BMDS Test 2 p-value = 0.004, BMDS Test 3 p-value = 0.003).

## 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 = 0.002918) |
| Hill | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.002918)  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.002918) |
| Exponential M4 (equivalent models include Exponential M5) | Warning | **Warnings**  • Variance model poorly fits dataset (p-value 3 = 0.002918) |

## Recommended model

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

# Male BMD Results for Table: Globulin (measured)

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333 | 1000 |
| N | 10 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean ± SD | 2.15 ± 0.227 | 2.16 ± 0.114 | 2.24 ± 0.344 | 2.12 ± 0.217 | 2.18 ± 0.045 | 2.2 ± 0.1 | 2.26 ± 0.089 | 2.26 ± 0.152 | 2.3 ± 0.141 | 2.3 ± 0.1 |

## 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°) | 0.043 | -135.711 | 1606.7 | 863.883 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Hill | 0.443 | -141.815 | -999 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.043 | -135.673 | 1592.17 | 873.591 |
| Exponential M4 | 0.44 | -142.74 | -999 | 0 |
| Exponential M5 | 0.442 | -141.806 | -999 | 0 |

a Modeled variance case presented (BMDS Test 2 p-value = 6.9E-04, BMDS Test 3 p-value = 0.097).

## 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 = 0.09691)  • Goodness of fit p-value is less than threshold (0.0434 < 0.1)  • BMD/high dose ratio is greater than threshold (1.61 > 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 = 0.09691)  **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 = 0.09691)  • Goodness of fit p-value is less than threshold (0.0429 < 0.1)  • BMD/high dose ratio is greater than threshold (1.59 > 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 = 0.09691) |
| Exponential M5 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist  • Variance model poorly fits dataset (p-value 3 = 0.09691) |

## Recommended model

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

# Male BMD Results for Table: Eosinophil count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12a | 37a | 111a | 333a | 1000a |
| N | 9 | 5 | 5 | 4 | 5 | 5 | 5 | 5 | 5 | 4 |
| Mean ± SD | 0.1 ± 0.057 | 0.068 ± 0.029 | 0.09 ± 0.045 | 0.22 ± 0.28 | 0.098 ± 0.027 | 0.056 ± 0.027 | 0.084 ± 0.059 | 0.058 ± 0.036 | 0.05 ± 0.029 | 0.037 ± 0.01 |

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°, 7°, 8°) | <0.0001 | -96.377 | 1.077 | 0.498 | Exponential-M5 recommended as best-fitting model on the basis of the lowest AIC. |
| Power | <0.0001 | -98.437 | 5.405 | 5.259 |
| Hill | <0.0001 | -110.423 | 0.859 | -999 |
| Exponential M2 | <0.0001 | -87.791 | 1 | -999 |
| Exponential M3 | <0.0001 | -91.356 | 2.47 | 0.939 |
| Exponential M4 | <0.0001 | -101.419 | -999 | 0 |
| Exponential M5b | <0.0001 | -108.424 | 1.194 | 0.522 |

a Modeled variance case presented (BMDS Test 2 p-value = <0.0001, BMDS Test 3 p-value = 0.585).

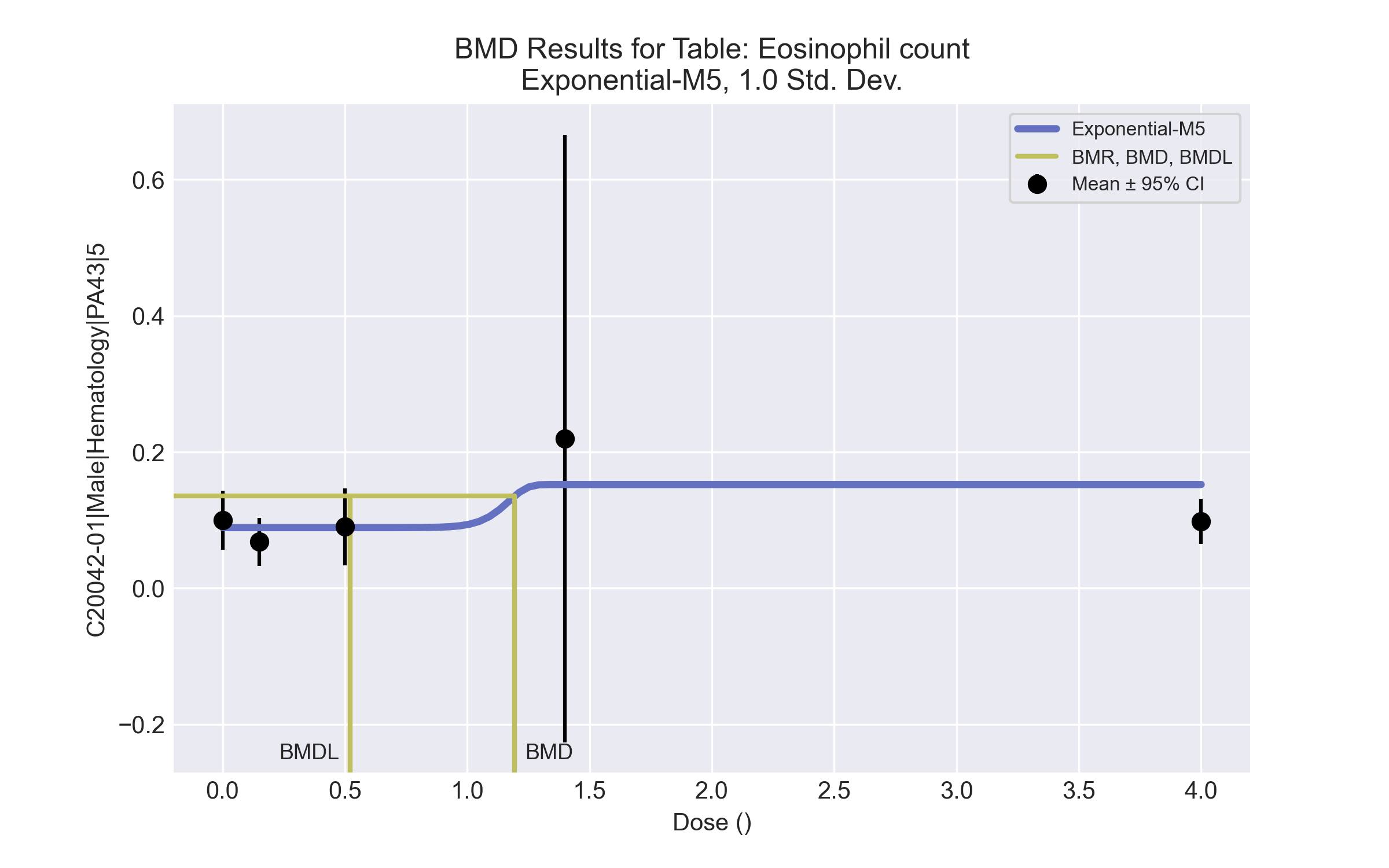
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Polynomial 2°, 3°, 4°, 5°, 6°, 7°, 8°) | Valid | - |
| Power | Warning | **Warnings**  • BMD/high dose ratio is greater than threshold (1.35 > 1.0)  • Ratio of modeled to actual stdev. at control is greater than threshold (2.14 > 1.5)  **Cautions**  • BMDL/high dose ratio is greater than threshold (1.31 > 1.0) |
| 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 is greater than threshold (2.02 > 2.0) |
| Exponential M3 | Valid | - |
| Exponential M4 | Failure | **Failures**  • BMD does not exist  **Warnings**  • Residual of Interest does not exist |
| Exponential M5a | Valid | - |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-qlzieysu.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 12:08:59 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 = 5  
 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 3.41631   
 rho 4.08536   
 a 0.0646   
 b 0.262454   
 c 3.57585   
 d 1   
  
  
  
 Parameter Estimates  
  
 Variable Model 5 Std. Err.  
 -------- ------- ---------  
 lnalpha 5.79772 9.03777  
 rho 4.93927 3.81659  
 a 0.0889474 0.0105761  
 b 0.851382 12.2345  
 c 1.71136 0.682262  
 d 16.5291 860.665  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 9 0.1 0.05657  
 0.15 5 0.068 0.02864  
 0.5 5 0.09 0.04528  
 1.4 4 0.22 0.2804  
 4 5 0.098 0.02683  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 0.08895 0.0461 0.7193  
 0.15 0.08895 0.0461 -1.016  
 0.5 0.08895 0.0461 0.05105  
 1.4 0.1522 0.1738 0.7801  
 4 0.1522 0.1738 -0.6977  
  
  
  
 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 50.68597 6 -89.37194  
 A2 71.04723 10 -122.0945  
 A3 70.07675 7 -126.1535  
 R 47.89547 2 -91.79094  
 5 60.21213 6 -108.4243  
  
  
 Additive constant for all log-likelihoods = -25.73. 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 46.3 8 < 0.0001  
 Test 2 40.72 4 < 0.0001  
 Test 3 1.941 3 0.5848  
 Test 7a 19.73 1 < 0.0001  
  
  
 The p-value for Test 1 is less than .05. There appears to be a  
 difference between response and/or variances among the dose  
 levels, it seems appropriate to model the data.  
  
 The p-value for Test 2 is less than .1. A non-homogeneous  
 variance model appears to be appropriate.  
  
 The p-value for Test 3 is greater than .1. The modeled  
 variance appears to be appropriate here.  
  
 The p-value for Test 7a is less than .1. Model 5 may not adequately  
 describe the data; you may want to consider another model.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 1.19358  
  
 BMDL = 0.521706  
  
 BMDU = 40000

# Male BMD Results for Table: Platelet count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333 | 1000 |
| N | 9 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 4 | 4 |
| Mean ± SD | 868.889 ± 150.507 | 1029.2 ± 131.201 | 926.2 ± 53.765 | 954 ± 179.094 | 904 ± 356.4 | 974.6 ± 59.919 | 877 ± 190.162 | 883.4 ± 146.189 | 1061 ± 84.546 | 1177.75 ± 59.236 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 3°, 4°, 5°, 6°, 7°, 8°) | 0.013 | 579.966 | 673.733 | 511.633 | No model was recommended as a best-fitting model. Doses were dropped until there were only 3 remaining dose-groups. |
| Polynomial 2° | 0.013 | 579.966 | 673.734 | 511.633 |
| Hill | 0.005 | 583.126 | 547.392 | -999 |
| Exponential M2 (equivalent models include Exponential M3) | 0.012 | 580.189 | 702.207 | 549.076 |
| Exponential M4 | 0.009 | 581.331 | 526.639 | 279.699 |
| Exponential M5 | 0.009 | 581.612 | 359.119 | 270.336 |

a Modeled variance case presented (BMDS Test 2 p-value = 2.4E-04, BMDS Test 3 p-value = 0.213).

## 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 (0.0128 < 0.1) |
| Polynomial 2° | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0128 < 0.1) |
| Hill | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Goodness of fit p-value is less than threshold (0.00495 < 0.1)  **Cautions**  • Warning(s): THE MODEL HAS PROBABLY NOT CONVERGED!!!; THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!; BMDL computation failed. |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0118 < 0.1) |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00891 < 0.1) |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.00907 < 0.1) |

## Recommended model

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

# Male BMD Results for Table: Reticulocyte count

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333 | 1000 |
| N | 9 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 4 |
| Mean ± SD | 244.7 ± 21.461 | 247.22 ± 47.71 | 232.6 ± 28.537 | 212.3 ± 27.996 | 258.34 ± 31.852 | 210.78 ± 31.508 | 168.74 ± 19.588 | 147 ± 24.588 | 138.5 ± 14.982 | 122.425 ± 29.794 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 5°) | <0.0001 | 454.346 | 341.771 | 257.016 | Exponential-M4 recommended as best-fitting model on the basis of the lowest BMDL. |
| Polynomial 2° (equivalent models include Polynomial 3°, 4°, 6°) | <0.0001 | 454.346 | 341.77 | 257.016 |
| Polynomial 7° | <0.0001 | 454.346 | 341.773 | 257.016 |
| Polynomial 8° | <0.0001 | 454.359 | 345.622 | 256.86 |
| Hill | 0.095 | 417.488 | 13.542 | 6.061 |
| Exponential M2 (equivalent models include Exponential M3) | <0.0001 | 449.005 | 197.918 | 130.422 |
| Exponential M4b | 0.108 | 416.483 | 11.837 | 6.978 |
| Exponential M5 | 0.07 | 418.372 | 14.169 | 7.05 |

a Constant variance case presented (BMDS Test 2 p-value = 0.432, BMDS Test 3 p-value = 0.432).

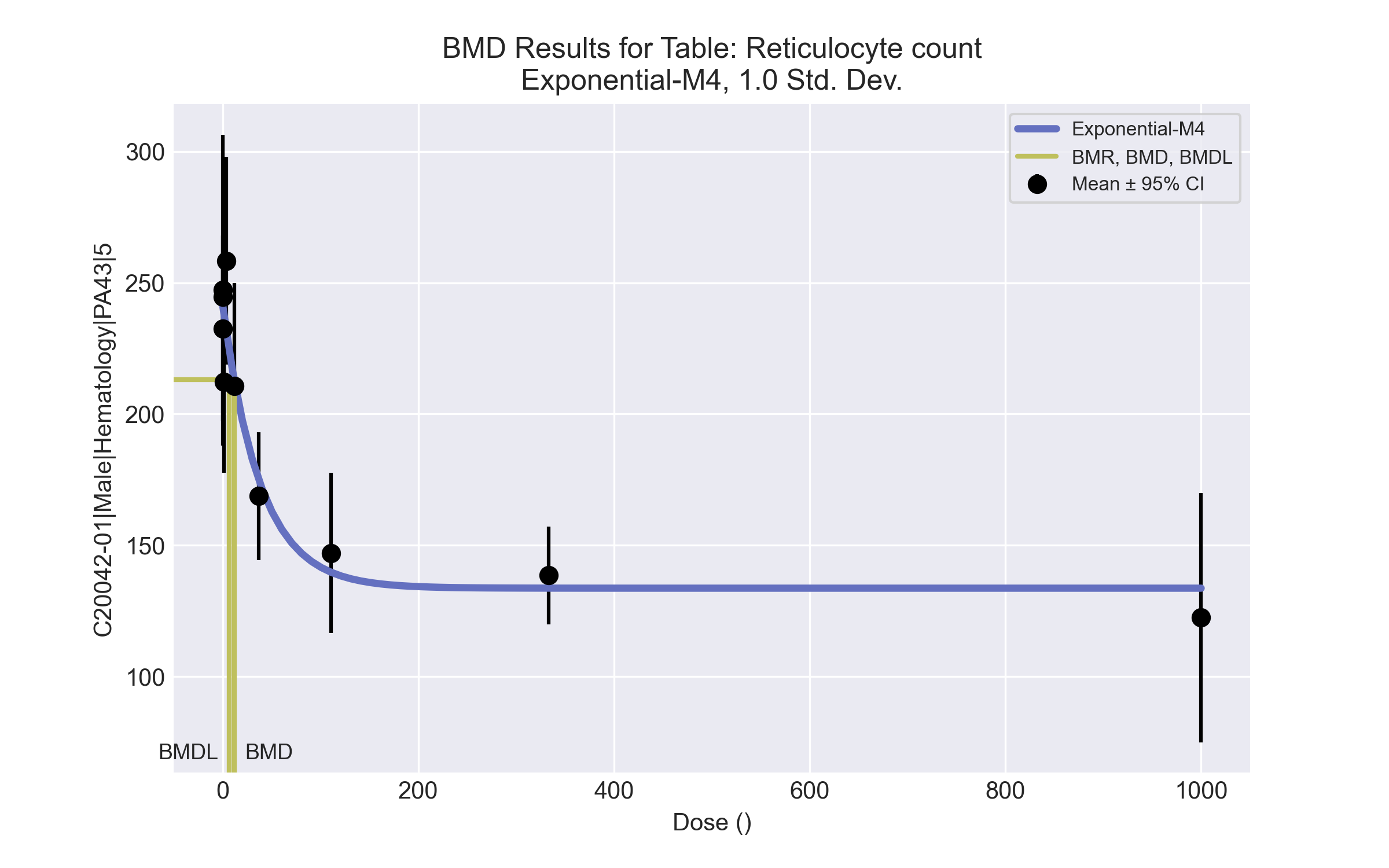
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Power, Polynomial 5°) | Warning | **Warnings**  • Ratio of modeled to actual stdev. at control is greater than threshold (1.94 > 1.5) |
| Polynomial 2° (equivalent models include Polynomial 3°, 4°, 6°) | Warning | **Warnings**  • Ratio of modeled to actual stdev. at control is greater than threshold (1.94 > 1.5) |
| Polynomial 7° | Warning | **Warnings**  • Ratio of modeled to actual stdev. at control is greater than threshold (1.94 > 1.5) |
| Polynomial 8° | Warning | **Warnings**  • Ratio of modeled to actual stdev. at control is greater than threshold (1.96 > 1.5) |
| Hill | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0952 < 0.1) |
| Exponential M2 (equivalent models include Exponential M3) | Valid | - |
| Exponential M4a | Valid | - |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0697 < 0.1) |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-g5z4\_5sw.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 12:09:50 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 6.48492   
 rho 0 Specified  
 a 271.257   
 b 0.00369601   
 c 0.429833   
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 4 Std. Err.  
 -------- ------- ---------  
 lnalpha 6.70723 158.961  
 a 241.74 5.62349  
 b 0.0259732 0.00870846  
 c 0.552918 0.0369698  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 9 244.7 21.46  
 0.15 5 247.2 47.71  
 0.5 5 232.6 28.54  
 1.4 5 212.3 28  
 4 5 258.3 31.85  
 12 5 210.8 31.51  
 37 5 168.7 19.59  
 111 5 147 24.59  
 333 5 138.5 14.98  
 1000 4 122.4 29.79  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 241.7 28.61 0.3104  
 0.15 241.3 28.61 0.4612  
 0.5 240.3 28.61 -0.6055  
 1.4 237.9 28.61 -2  
 4 231.1 28.61 2.131  
 12 212.8 28.61 -0.1578  
 37 175 28.61 -0.4896  
 111 139.7 28.61 0.5697  
 333 133.7 28.61 0.3766  
 1000 133.7 28.61 -0.7857  
  
  
  
 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 -198.3505 11 418.701  
 A2 -193.8237 20 427.6475  
 A3 -198.3505 11 418.701  
 R -236.9292 2 477.8584  
 4 -204.2416 4 416.4833  
  
  
 Additive constant for all log-likelihoods = -48.7. 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 86.21 18 < 0.0001  
 Test 2 9.054 9 0.4323  
 Test 3 9.054 9 0.4323  
 Test 6a 11.78 7 0.108  
  
  
 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 = 11.8372  
  
 BMDL = 6.97754  
  
 BMDU = 21.822

# Male BMD Results for Table: Free Thyroxine

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12a | 37a | 111a | 333a | 1000a |
| N | 8 | 5 | 5 | 4 | 5 | 5 | 4 | 3 | 4 | 3 |
| Mean ± SD | 7.067 ± 0.884 | 6.102 ± 2.048 | 8.47 ± 3.144 | 14.438 ± 11.318 | 9.842 ± 4.748 | 14.388 ± 3.313 | 10.803 ± 2.829 | 8.383 ± 2.254 | 13.957 ± 1.314 | 10.353 ± 5.036 |

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 5°, 8°) | 3.9E-04 | 104.818 | 0.367 | 0.199 | Exponential-M2 recommended as best-fitting model on the basis of the lowest AIC. |
| Polynomial 2° (equivalent models include Power, Polynomial 3°, 4°, 6°, 7°) | 3.9E-04 | 104.818 | 0.367 | 0.199 |
| Hill | 0.05 | 94.429 | 0.489 | -999 |
| Exponential M2b (equivalent models include Exponential M3) | <0.0001 | 113.451 | 0.79 | 0.395 |
| Exponential M4 | 0.084 | 93.535 | 0.3 | 0.072 |
| Exponential M5 | 0.052 | 94.361 | 0.437 | 0.101 |

a Modeled variance case presented (BMDS Test 2 p-value = <0.0001, BMDS Test 3 p-value = 0.138).

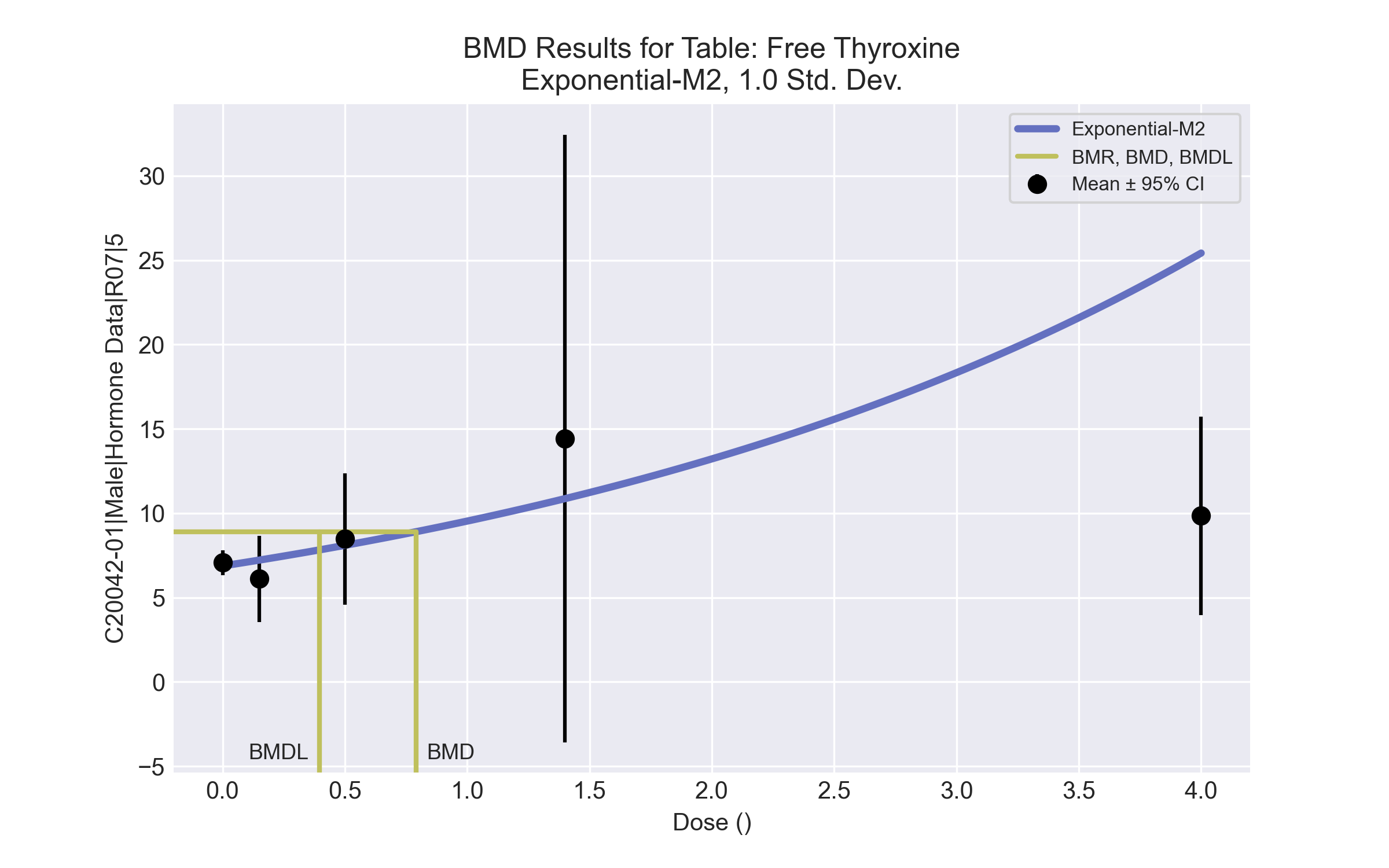
b Recommended model

## Model recommendation details

|  |  |  |
| --- | --- | --- |
| Model | Bin | Notes |
| Linear (equivalent models include Polynomial 5°, 8°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000392 < 0.1)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.72 > 1.5) |
| Polynomial 2° (equivalent models include Power, Polynomial 3°, 4°, 6°, 7°) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.000392 < 0.1)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.72 > 1.5) |
| Hill | Failure | **Failures**  • BMDL does not exist  **Warnings**  • Goodness of fit p-value is less than threshold (0.0497 < 0.1)  • Ratio of modeled to actual stdev. at control is greater than threshold (1.57 > 1.5)  **Cautions**  • Warning(s): BMDL computation failed. |
| Exponential M2a (equivalent models include Exponential M3) | Valid | - |
| Exponential M4 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0838 < 0.1) |
| Exponential M5 | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0518 < 0.1) |

a Recommended model

## Recommended model



====================================================================   
 Exponential Model. (Version: 1.11; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-m196arm0.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 12:15:12 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 = 5  
 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 -8.69261   
 rho 5.05734   
 a 7.53732   
 b 0.102114   
 c 0 Specified  
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 2 Std. Err.  
 -------- ------- ---------  
 lnalpha -6.82714 2.91461  
 rho 4.2741 1.39576  
 a 6.8743 0.561425  
 b 0.326944 0.135612  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 8 7.067 0.8837  
 0.15 5 6.102 2.048  
 0.5 5 8.47 3.144  
 1.4 4 14.44 11.32  
 4 5 9.842 4.748  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 6.874 2.026 0.2697  
 0.15 7.22 2.25 -1.111  
 0.5 8.095 2.874 0.2917  
 1.4 10.86 5.389 1.326  
 4 25.42 33.15 -1.051  
  
  
  
 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 -53.84791 6 119.6958  
 A2 -36.53264 10 93.06528  
 A3 -39.28873 7 92.57745  
 R -58.00647 2 120.0129  
 2 -52.72524 4 113.4505  
  
  
 Additive constant for all log-likelihoods = -24.81. 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 42.95 8 < 0.0001  
 Test 2 34.63 4 < 0.0001  
 Test 3 5.512 3 0.1379  
 Test 4 26.87 3 < 0.0001  
  
  
 The p-value for Test 1 is less than .05. There appears to be a  
 difference between response and/or variances among the dose  
 levels, it seems appropriate to model the data.  
  
 The p-value for Test 2 is less than .1. A non-homogeneous  
 variance model appears to be appropriate.  
  
 The p-value for Test 3 is greater than .1. The modeled  
 variance appears to be appropriate here.  
  
 The p-value for Test 4 is less than .1. Model 2 may not adequately  
 describe the data; you may want to consider another model.  
  
  
 Benchmark Dose Computations:  
  
 Specified Effect = 1.000000  
  
 Risk Type = Estimated standard deviations from control  
  
 Confidence Level = 0.950000  
  
 BMD = 0.790135  
  
 BMDL = 0.395036  
  
 BMDU = 3.42982

# Male BMD Results for Table: Thyroid Stimulating Hormone

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333 | 1000 |
| N | 8 | 5 | 5 | 4 | 5 | 5 | 4 | 3 | 4 | 3 |
| Mean ± SD | 2.95 ± 1.746 | 3.76 ± 3.238 | 4.26 ± 1.568 | 3.275 ± 2.241 | 2.76 ± 0.792 | 3.9 ± 2.281 | 4.525 ± 1.889 | 7.033 ± 1.106 | 7.5 ± 2.146 | 7.233 ± 1.75 |

## 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°) | 0.044 | 120.572 | 459.181 | 312.019 | Exponential-M4 recommended as best-fitting model on the basis of the lowest AIC. |
| Hill | 0.831 | 111.506 | 48.208 | 20.314 |
| Exponential M2 (equivalent models include Exponential M3) | 0.023 | 122.472 | 611.164 | 455.531 |
| Exponential M4b | 0.853 | 110.013 | 44.526 | 19.298 |
| Exponential M5 | 0.841 | 111.425 | 50.667 | 21.201 |

a Constant variance case presented (BMDS Test 2 p-value = 0.249, BMDS Test 3 p-value = 0.249).

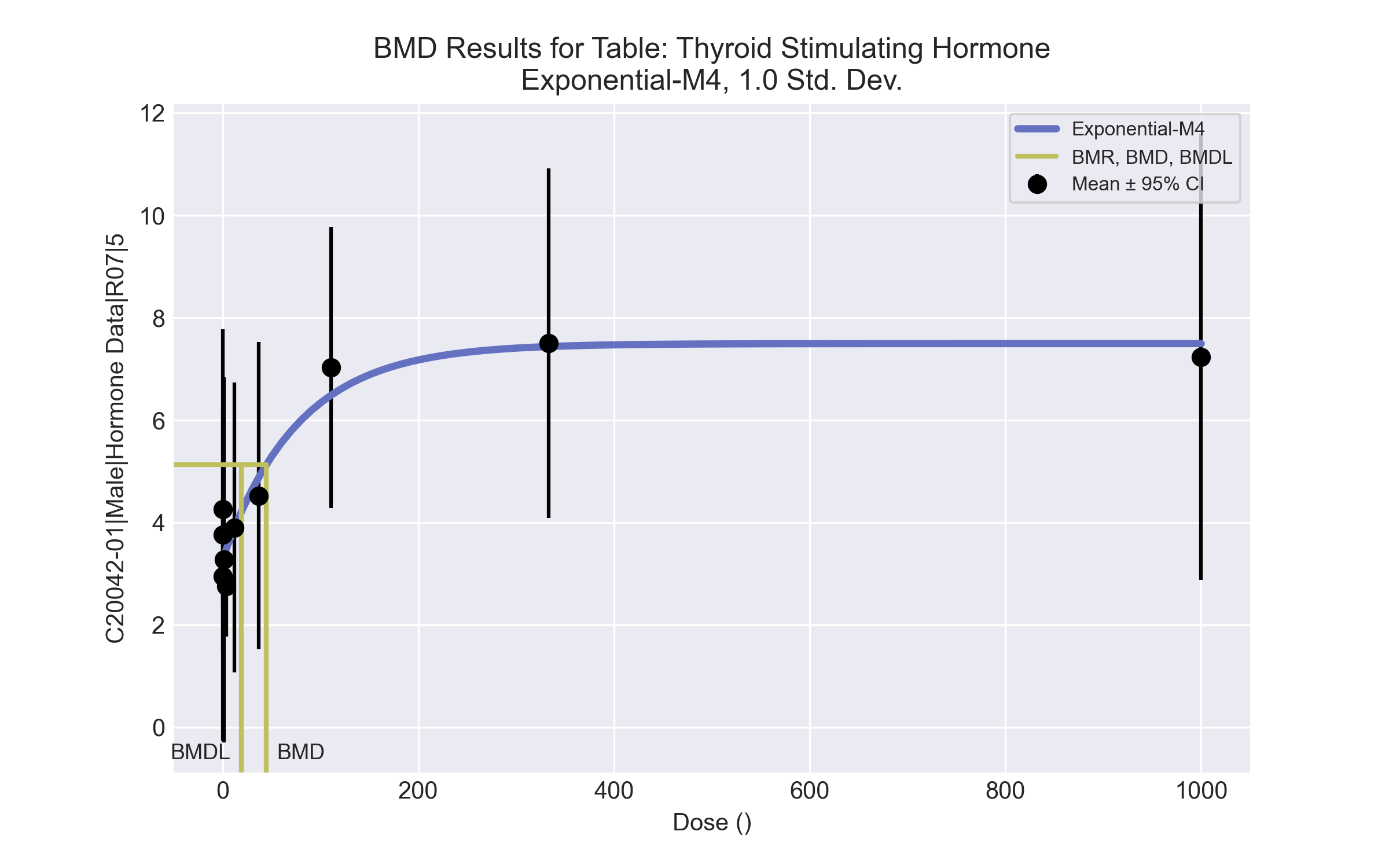
b Recommended model

## 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 (0.044 < 0.1) |
| Hill | Valid | - |
| Exponential M2 (equivalent models include Exponential M3) | Warning | **Warnings**  • Goodness of fit p-value is less than threshold (0.0229 < 0.1)  • Residual of interest is greater than threshold (2.28 > 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-p2\_hclwc.(d)   
 Gnuplot Plotting File:   
 Tue Apr 13 12:15:18 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 1.14536   
 rho 0 Specified  
 a 2.622   
 b 0.00284976   
 c 3.00343   
 d 1 Specified  
  
  
  
 Parameter Estimates  
  
 Variable Model 4 Std. Err.  
 -------- ------- ---------  
 lnalpha 1.21768 0.704638  
 a 3.28751 0.347892  
 b 0.0128951 0.00706172  
 c 2.2801 0.316531  
  
 NC = No Convergence  
  
  
 Table of Stats From Input Data  
  
 Dose N Obs Mean Obs Std Dev  
 ----- --- ---------- -------------  
 0 8 2.95 1.746  
 0.15 5 3.76 3.238  
 0.5 5 4.26 1.568  
 1.4 4 3.275 2.241  
 4 5 2.76 0.7925  
 12 5 3.9 2.281  
 37 4 4.525 1.889  
 111 3 7.033 1.106  
 333 4 7.5 2.146  
 1000 3 7.233 1.75  
  
  
 Estimated Values of Interest  
  
 Dose Est Mean Est Std Scaled Residual  
 ------ ---------- --------- ----------------  
 0 3.288 1.838 -0.5193  
 0.15 3.296 1.838 0.5648  
 0.5 3.315 1.838 1.15  
 1.4 3.363 1.838 -0.09552  
 4 3.499 1.838 -0.899  
 12 3.891 1.838 0.01116  
 37 4.884 1.838 -0.3909  
 111 6.49 1.838 0.5118  
 333 7.438 1.838 0.06704  
 1000 7.496 1.838 -0.2473  
  
  
  
 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 -49.34328 11 120.6866  
 A2 -43.64357 20 127.2871  
 A3 -49.34328 11 120.6866  
 R -63.42016 2 130.8403  
 4 -51.00655 4 110.0131  
  
  
 Additive constant for all log-likelihoods = -42.27. 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 39.55 18 0.0024  
 Test 2 11.4 9 0.2493  
 Test 3 11.4 9 0.2493  
 Test 6a 3.327 7 0.8532  
  
  
 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 = 44.5258  
  
 BMDL = 19.2976  
  
 BMDU = 122.566

# Male BMD Results for Table: Total Thyroxine

BMDS version: BMDS v2.7.0

## Input dataset

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Dose | 0 | 0.15 | 0.5 | 1.4 | 4 | 12 | 37 | 111 | 333 | 1000 |
| N | 8 | 5 | 5 | 4 | 5 | 5 | 4 | 3 | 4 | 3 |
| Mean ± SD | 2.795 ± 0.568 | 2.592 ± 0.539 | 2.714 ± 0.492 | 3.155 ± 0.494 | 2.82 ± 0.865 | 2.718 ± 0.616 | 2.53 ± 0.704 | 1.973 ± 0.405 | 1.647 ± 0.248 | 1.717 ± 0.284 |

## Summary table

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modela | Goodness of fit | | BMD | BMDL | Comments |
| *p*-value | AIC |
| Linear (equivalent models include Power, Polynomial 2°, 3°, 4°, 5°, 7°, 8°) | 0.102 | 2.659 | 451.101 | 308.027 | Hill recommended as best-fitting model on the basis of the lowest BMDL. |
| Polynomial 6° | 0.102 | 2.659 | 451.1 | 308.027 |
| Hillb | 0.81 | -3.636 | 61.426 | 24.276 |
| Exponential M2 (equivalent models include Exponential M3) | 0.184 | 0.698 | 309.877 | 179.923 |
| Exponential M4 | 0.858 | -5.343 | 60.953 | 24.743 |
| Exponential M5 | 0.815 | -3.678 | 66.028 | 26.194 |

a Constant variance case presented (BMDS Test 2 p-value = 0.35, BMDS Test 3 p-value = 0.35).

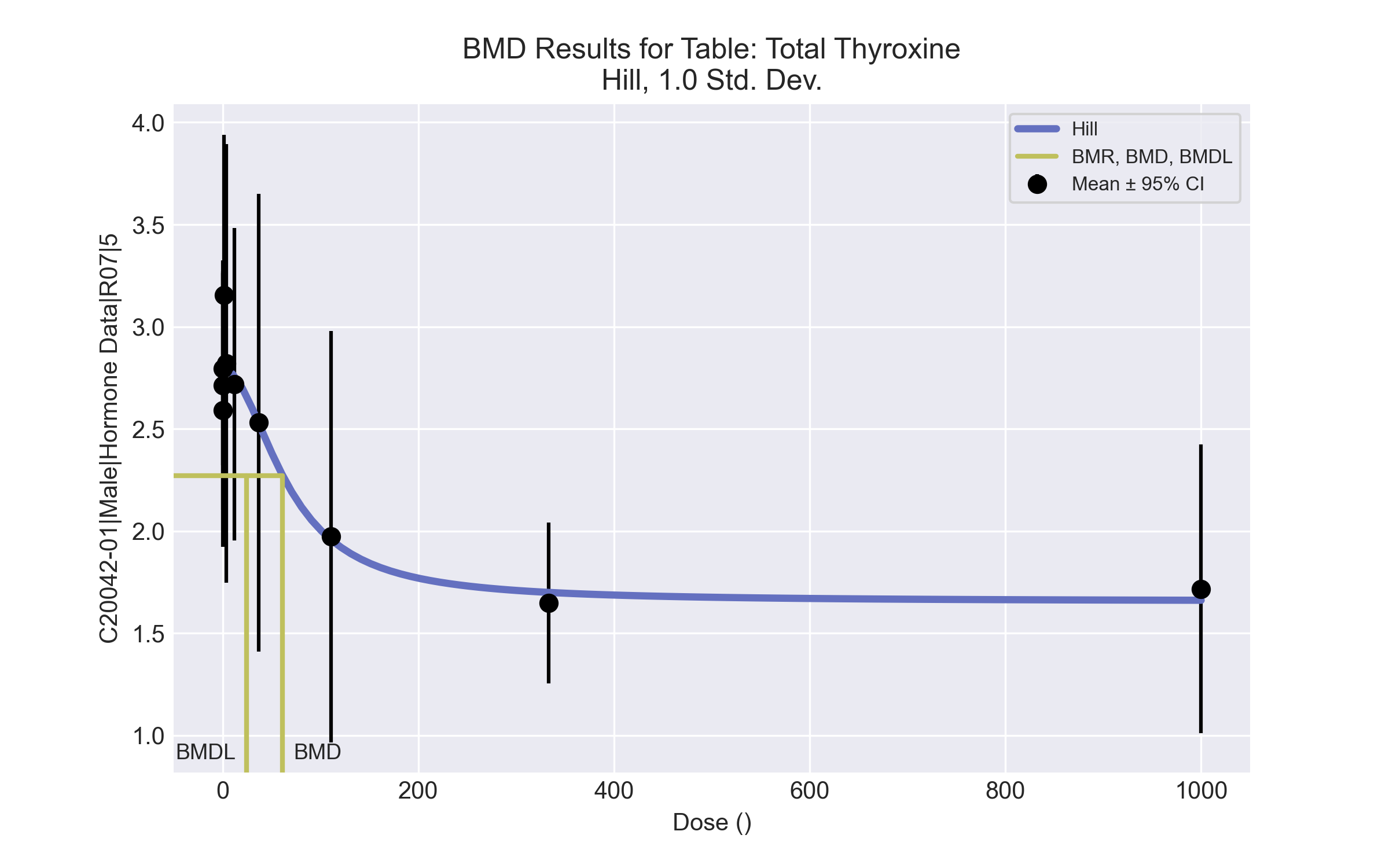
b Recommended model

## Model recommendation details

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

a Recommended model

## Recommended model



====================================================================   
 Hill Model. (Version: 2.18; Date: 03/14/2017)   
 Input Data File: C:\Windows\TEMP\bmds-r78c\_ihp.(d)   
 Gnuplot Plotting File: C:\Windows\TEMP\bmds-r78c\_ihp.plt  
 Tue Apr 13 12:15:22 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 = 0.327472  
 rho = 0 Specified  
 intercept = 2.795  
 v = -1.1475  
 n = 1.24608  
 k = 78.0434  
  
  
 Asymptotic Correlation Matrix of Parameter Estimates  
  
 ( \*\*\* The model parameter(s) -rho   
 have been estimated at a boundary point, or have been specified by the user,  
 and do not appear in the correlation matrix )  
  
 alpha intercept v n k  
  
 alpha 1 -1.1e-008 8.7e-008 4.2e-008 -2e-009  
  
 intercept -1.1e-008 1 -0.44 -0.28 -0.21  
  
 v 8.7e-008 -0.44 1 0.53 -0.42  
  
 n 4.2e-008 -0.28 0.53 1 -0.22  
  
 k -2e-009 -0.21 -0.42 -0.22 1  
  
  
  
 Parameter Estimates  
  
 95.0% Wald Confidence Interval  
 Variable Estimate Std. Err. Lower Conf. Limit Upper Conf. Limit  
 alpha 0.273508 0.0570304 0.161731 0.385285  
 intercept 2.79441 0.0979412 2.60244 2.98637  
 v -1.1383 0.264438 -1.65659 -0.620009  
 n 2.0054 1.64611 -1.2209 5.23171  
 k 66.6137 38.146 -8.15102 141.378  
  
  
  
 Table of Data and Estimated Values of Interest  
  
 Dose N Obs Mean Est Mean Obs Std Dev Est Std Dev Scaled Res.  
------ --- -------- -------- ----------- ----------- ----------  
  
 0 8 2.79 2.79 0.568 0.523 0.00321  
 0.15 5 2.59 2.79 0.539 0.523 -0.865  
 0.5 5 2.71 2.79 0.492 0.523 -0.344  
 1.4 4 3.15 2.79 0.494 0.523 1.38  
 4 5 2.82 2.79 0.865 0.523 0.127  
 12 5 2.72 2.76 0.616 0.523 -0.175  
 37 4 2.53 2.53 0.704 0.523 0.0127  
 111 3 1.97 1.96 0.405 0.523 0.0544  
 333 4 1.65 1.7 0.248 0.523 -0.199  
 1000 3 1.72 1.66 0.284 0.523 0.184  
  
  
  
 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 8.313929 11 5.372142  
 A2 13.314424 20 13.371152  
 A3 8.313929 11 5.372142  
 fitted 6.817765 5 -3.635530  
 R -4.657175 2 13.314350  
  
  
 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 35.9432 18 0.007175  
 Test 2 10.001 9 0.3504  
 Test 3 10.001 9 0.3504  
 Test 4 2.99233 6 0.8098  
  
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 = 61.4259  
  
 BMDL = 24.2755  
  
 BMDU = 158.988