**DATA SUMMARY**

***Initial dataset:***

**Number of effect sizes**: 2185

**Number of studies**: 92

**Number of species**: 36

**Number of observations with shared control group**: 2034

**Number of studies with shared control group**: 79

***Filtering initial dataset:***

After correcting sample size for shared control groups, 98 observations have sample size lower than 1 and are removed from dataset (sampling variance calculation only for n > 1). This leaves a dataset of 2087 observations, 90 studies and 36 species.

There are 5 observations with standard deviations for control and treatment groups of 0. These should be checked just in case these are typos/error in the dataset (and sample sizes for these observations are large, unlikely that SD is just 0). These observations are ‘Study.ID’: 1549, 1746, 2161, 2162, 2164. After double checking those values, I replace 0 by 0.01 (to make calculation of effect size possible) and retain these observations in the dataset.

Up until now, the dataset has 2087 observations, 90 studies and 36 species.

Then, I remove 5 studies that present correlative data (i.e., no experimental), these five studies account for 75 observations. After removing these five studies, the dataset has 2012 observations, 85 studies and 33 species

**Observations (and studies) by moderator levels:**

Biomarker and developmental stage:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Embryo** | **Tadpole** | **Adult** |
| **Enzymatic** | 97 (11) | 708 (45) | 547 (17) |
| **Indicator** | 5 (2) | 173 (25) | 168 (16) |
| **Non-enzymatic** | 22 (4) | 131 (15) | 161 (16) |

Biomarker, developmental stage and pollutant class:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Embryo** | **Tadpole** | **Adult** |
| **Herbicide** | **Enzymatic** | 5 (1) | 170 (12) | 10 (2) |
| **Indicator** | 0 (0) | 60 (10) | 2 (1) |
| **Non-enzymatic** | 0 (0) | 27 (2) | 0 (0) |
| **Metallic elements** | **Enzymatic** | 16 (2) | 196 (6) | 8 (2) |
| **Indicator** | 0 (0) | 3 (1) | 16 (4) |
| **Non-enzymatic** | 0 (0) | 44 (2) | 24 (7) |
| **Other inorganic compounds** | **Enzymatic** | 36 (4) | 51 (7) | 3 (1) |
| **Indicator** | 0 (0) | 14 (2) | 3 (1) |
| **Non-enzymatic** | 3 (1) | 6 (1) | 3 (1) |
| **Other organic compounds** | **Enzymatic** | 0 (0) | 16 (3) | 20 (2) |
| **Indicator** | 0 (0) | 4 (2) | 12 (2) |
| **Non-enzymatic** | 0 (0) | 2 (1) | 12 (2) |
| **Pesticide** | **Enzymatic** | 40 (5) | 275 (17) | 506 (12) |
| **Indicator** | 5 (2) | 92 (10) | 135 (9) |
| **Non-enzymatic** | 19 (3) | 52 (9) | 122 (6) |

**ANALYSIS SUMMARY**

***1 – Overall meta-analysis***

I first ran an overall meta-analysis with no moderators and the full dataset.

I get a warning message: “*Ratio of largest to smallest sampling variance extremely large. May not be able to obtain stable results”*

This message seems to mean that there are observations with very large and / or very small sampling variance and that causes problems. I inspect the data and indeed there are two observations (‘Study.ID’ 71 and 1756) that have very large sampling variance compared to the rest of the data set. It would be good to double check the data for these two effect sizes, just in case there is a type in the SD value of controls or treatments. For now, I have run a second model in which I have removed the top 10 and bottom 10 observations by their sampling variance. These second model does not generate the warning and the results are extremely similar to the first model (so, all good).

*These are the heterogeneity results:*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | ***I*2 total** | ***I*2 study ID** | ***I*2 species** | ***I*2 phylogeny** | ***I*2 residual** |
| **Full dataset**  **(k = 2007)** | 99.95 | 26.97 | 1.30 | 2.61 | 69.06 |
| **Trimmed data set**  **(k = 1987)** | 99.81 | 27.62 | 1.21 | 2.42 | 68.57 |

*These are the model coefficients:*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Full dataset**  **(k = 2007)** | 0.1489 | 0.2719 | 0.0258 | 0.018 |
| **Trimmed data set**  **(k = 1987)** | 0.1500 | 0.2710 | 0.0290 | 0.015 |

These estimates mean that overall treatments caused approximately a 16% increase in biomarker levels compared to controls.

*Plot of results:*

*Chart

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***2 – Overall effect per biomarker***

In the second meta-analysis, I include ‘Biomarker category’ as a moderator. I get a similar warning as before and check results with the trimmed dataset, also as above (both models provide very similar results).

Biomarker category only explains 1.57% of the variation in lnRR in the whole dataset (k = 2007 observations). The estimate for ‘Enzymatic’ and “Indicator’ are positive and significantly different from zero (table and plot below).

*These are the model coefficients:*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Full dataset**  **(k = 2007)** | **Enzymatic** | 0.120 | 0.008 | 0.232 | 0.035 |
| **Indicator** | 0.297 | 0.175 | 0.418 | < 0.001 |
| **Non-enzymatic** | 0.121 | -0.002 | 0.244 | 0.054 |
| **Trimmed data set**  **(k = 1987)** | **Enzymatic** | 0.121 | 0.011 | 0.231 | 0.031 |
| **Indicator** | 0.298 | 0.178 | 0.418 | <0.001 |
| **Non-enzymatic** | 0.121 | -0.001 | 0.242 | 0.051 |

*Chart

Description automatically generated*

***3 – Effect per biomarker and developmental stage***

Then, I do the analysis above, including biomarker category as a moderator, but for each developmental stage separately.

*Results for embryos:*

Biomarker category explains 8.2% of the variation in lnRR in the subset for embryos (k = 124 observations), and the estimate for ‘Non-enzymatic’ is positive and significantly different from zero (table and plot below).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Enzymatic** | 0.054 | -0.213 | 0.320 | 0.694 |
| **Indicator** | 0.221 | -0.205 | 0.646 | 0.309 |
| **Non-enzymatic** | 0.387 | 0.040 | 0.733 | 0.029 |

Chart, scatter chart

Description automatically generated

*Results for embryos combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant category:*

The model doesn’t converge. Not sure why, as the model just above did using the same data set.

*Results for tadpoles:*

Biomarker category only explains 0.59% of the variation in lnRR in the subset for tadpoles (k = 1011 observations), and none of the estimates are significantly different from zero (table and plot below). I get a similar warning as before and check results with a trimmed dataset, also as above (both models provide very similar results).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Full dataset**  **(k = 1011)** | **Enzymatic** | 0.179 | -0.012 | 0.370 | 0.066 |
| **Indicator** | 0.063 | -0.145 | 0.270 | 0.554 |
| **Non-enzymatic** | 0.203 | -0.010 | 0.416 | 0.061 |
| **Trimmed data set**  **(k = 991)** | **Enzymatic** | 0.181 | -0.001 | 0.370 | 0.060 |
| **Indicator** | 0.068 | -0.139 | 0.274 | 0.520 |
| **Non-enzymatic** | 0.203 | -0.008 | 0.414 | 0.060 |

***Chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category, ‘biomarker’ explains 0.5% of the variation in the response. There is some evidence that ‘Antioxidant’ has a non-zero estimate.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Antioxidant** | 0.183 | -0.006 | 0.372 | 0.058 |
| **Indicator** | 0.067 | -0.140 | 0.274 | 0.525 |

*Chart

Description automatically generated with low confidence*

*Results for adults:*

Biomarker category explains 10.02% of the variation in lnRR in the subset for adults (k = 872 observations), and the estimate for ‘Indicator’ is positive and significantly different from zero (table and plot below).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Enzymatic** | 0.071 | -0.080 | 0.223 | 0.358 |
| **Indicator** | 0.465 | 0.306 | 0.624 | < 0.001 |
| **Non-enzymatic** | 0.076 | -0.083 | 0.234 | 0.348 |

Chart

Description automatically generated

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category, ‘biomarker’ explains 10.48% of the variation in the response.

Chart

Description automatically generated

*Results across the three life stages for comparison (same plots as above but limits of the x axis are the same across the three plots):*

**Embryos**

***Chart, scatter chart

Description automatically generated***

**Tadpoles**

***Chart

Description automatically generated***

**Adults**

***Chart, diagram

Description automatically generated***

***4 – Effect of pollutants per biomarker***

*Results for herbicide:*

(k = 274 observations / 5 embryos obs / 257 tadpoles obs / 12 adults obs

Biomarker category explains 5.7% of the variation in lnRR in the subset for herbicide (k = 274 observations). There is a significant and positive change in ‘Non-enzymatic’.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Herbicide dataset**  **(k = 274)** | **Enzymatic** | 0.060 | -0.111 | 0.231 | 0.489 |
| **Indicator** | 0.136 | -0.081 | 0.352 | 0.219 |
| **Non-enzymatic** | 0.492 | 0.174 | 0.810 | 0.002 |

Chart, scatter chart

Description automatically generated

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

*A picture containing text, light, day

Description automatically generated*

*Results for Metallic elements:*

(k = 307 observations / 16 embryos obs / 243 tadpoles obs / 48 adults obs

Biomarker category only explains 0.27% of the variation in lnRR in the subset for metallic elements (k = 307 observations) and none of the estimates are significantly different from zero.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Metallic element dataset**  **(k = 307)** | **Enzymatic** | 0.144 | -0.030 | 0.318 | 0.104 |
| **Indicator** | 0.265 | -0.048 | 0.579 | 0.097 |
| **Non-enzymatic** | 0.177 | -0.019 | 0.372 | 0.077 |

Chart, scatter chart

Description automatically generated

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

*Chart

Description automatically generated*

*Results for other* *inorganic elements:*

(k = 119 observations / 39 embryos obs / 71 tadpoles obs / 9 adults obs

Biomarker category explains 5.3% of the variation in lnRR in the subset for other inorganic elements (k = 119 observations). There is a significant and positive change in ‘Non-enzymatic’.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Inorganic element dataset**  **(k = 119)** | **Enzymatic** | -0.038 | -0.278 | 0.202 | 0.758 |
| **Indicator** | 0.112 | -0.261 | 0.486 | 0.555 |
| **Non-enzymatic** | 0.426 | 0.050 | 0.802 | 0.0264 |

***Chart, scatter chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

***Chart, scatter chart

Description automatically generated***

*Results for other organic elements:*

(k = 66 observations / 0 embryos obs / 22 tadpoles obs / 44 adults obs

Biomarker category explains 1.06% of the variation in lnRR in the subset for other organic elements (k = 66 observations) and none of the estimates are significantly different from zero.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Organic element dataset**  **(k = 66)** | **Enzymatic** | 0.231 | -0.129 | 0.589 | 0.208 |
| **Indicator** | 0.229 | -0.196 | 0.654 | 0.291 |
| **Non-enzymatic** | 0.404 | -0.045 | 0.853 | 0.078 |

***Chart, scatter chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

Chart, scatter chart

Description automatically generated

*Results for pesticide:*

(k = 1246 observations / 64 embryos obs / 419 tadpoles obs / 763 adults obs

Biomarker category explains 4.0% of the variation in lnRR in the subset for pesticide (k = 1246 observations). There is a significant and positive change in ‘Enzymatic’ and ‘indicator’.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Pesticide dataset**  **(k = 1246)** | **Enzymatic** | 0.171 | 0.051 | 0.291 | 0.005 |
| **Indicator** | 0.382 | 0.252 | 0.512 | <0.001 |
| **Non-enzymatic** | 0.076 | -0.058 | 0.209 | 0.265 |

***Chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

***Diagram, schematic

Description automatically generated***

***5 – Effects per specific biomarker inside ‘Enzymatic’ for tadpoles and adults***

I have looked at how specific biomarkers vary for tadpoles and adults. I chose these two developmental stages because they are data rich. In general, ‘Specific biomarker’ explains little variation (5.01% for tadpoles and 3.05% for adults) and no biomarker stands out as being highly modified by the treatment.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Biomarker** | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Tadpoles**  **(k = 708)** | **CAT** | 0.160 | -0.313 | 0.633 | 0.506 |
| **GPx** | 0.478 | -0.003 | 0.958 | 0.052 |
| **GR** | 0.428 | -0.070 | 0.926 | 0.092 |
| **GST** | 0.181 | -0.297 | 0.659 | 0.458 |
| **SOD** | -0.038 | -0.511 | 0.435 | 0.875 |
| **Adults**  **(k = 547)** | **CAT** | 0.098 | -0.202 | 0.399 | 0.522 |
| **GPx** | -0.049 | -0.345 | 0.248 | 0.747 |
| **GR** | 0.028 | -0.278 | 0.334 | 0.177 |
| **GST** | 0.038 | -0.256 | 0.332 | 0.800 |
| **SOD** | 0.184 | -0.112 | 0.480 | 0.222 |

***TADPOLES:***

***Diagram

Description automatically generated***

***ADULTS:***

***Chart, diagram

Description automatically generated***

***6 – Effects per specific biomarker inside ‘Enzymatic’ across pollutants***

Samples sizes:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Biomarker** | **Herbicide** | **Metallic elements** | **Others Inorganic compound** | **Others organic compound** | **Pesticide** |
| **CAT** | 68 | 56 | 22 | 4 | 178 |
| **GPx** | 9 | 50 | 5 | 14 | 135 |
| **GR** | 17 | 9 | 6 | 2 | 65 |
| **GST** | 28 | 34 | 37 | 10 | 242 |
| **SOD** | 63 | 71 | 20 | 6 | 201 |

For other inorganic and organic compounds, I don’t think there is enough sample size to do these analyses (see plots below).

Chart, scatter chart

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***Chart, scatter chart

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Description automatically generatedA picture containing text, sky, screenshot

Description automatically generatedChart, scatter chart

Description automatically generated***

***7 – Effects per specific biomarker inside ‘Enzymatic’ across pollutants***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Full dataset**  **(k = 2012)** | **Antioxidant mechanims** | 0.120 | 0.013 | 0.226 | 0.028 |
| **Indicator** | 0.300 | 0.182 | 0.417 | < 0.001 |

***Chart

Description automatically generated***

***8 – General effects for tissues with more than 50 effect sizes***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Brain (k = 88)** | 0.152 | -0.031 | 0.335 | 0.105 |
| **Heart (k = 80)** | 0.284 | 0.094 | 0.473 | 0.003 |
| **Kidney (k = 133)** | 0.165 | -0.002 | 0.330 | 0.052 |
| **Liver (k = 413)** | 0.157 | 0.021 | 0.294 | 0.024 |
| **Muscle (k = 182)** | 0.143 | -0.015 | 0.300 | 0.075 |
| **Whole body (k = 860)** | 0.123 | 0.014 | 0.232 | 0.027 |

***Chart

Description automatically generated***

***9 - General effects for tissues per biomarker***

*Brain:*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Brain**  **(k = 88)** | **Enzymatic** | 0.218 | -0.781 | 1.218 | 0.669 |
| **Indicator** | 1.355 | 0.334 | 2.377 | 0.009 |
| **Non-enzymatic** | -0.022 | -1.042 | 0.998 | 0.966 |

***Chart, scatter chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

Chart, scatter chart

Description automatically generated

*Heart (only 2 studies and 1 species):*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Heart**  **(k = 80)** | **Enzymatic** | -0.095 | -0.192 | 0.002 | 0.055 |
| **Indicator** | 0.733 | 0.561 | 0.904 | <0.001 |
| **Non-enzymatic** | -0.173 | -0.352 | 0.007 | 0.060 |

***Chart, scatter chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

Chart, scatter chart

Description automatically generated

*Kidney*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Kidney**  **(k = 133)** | **Enzymatic** | -0.152 | -0.373 | 0.070 | 0.178 |
| **Indicator** | 0.693 | 0.382 | 1.003 | <0.001 |
| **Non-enzymatic** | -0.104 | -0.376 | 0.167 | 0.452 |

**Chart, scatter chart

Description automatically generated**

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

***Chart, scatter chart

Description automatically generated***

*Liver*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Liver**  **(k = 413)** | **Enzymatic** | 0.072 | -0.068 | 0.212 | 0.312 |
| **Indicator** | 0.412 | 0.237 | 0.586 | <0.001 |
| **Non-enzymatic** | 0.123 | -0.054 | 0.300 | 0.173 |

***Chart, scatter chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

***Chart, scatter chart

Description automatically generated***

*Muscle*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Muscle**  **(k = 182)** | **Enzymatic** | 0.051 | -0.230 | 0.332 | 0.723 |
| **Indicator** | 0.006 | -0.309 | 0.321 | 0.970 |
| **Non-enzymatic** | 0.136 | -0.175 | 0.446 | 0.392 |

***Chart, scatter chart, box and whisker chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

***Chart, scatter chart

Description automatically generated***

*Whole body*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Whole body**  **(k = 860)** | **Enzymatic** | 0.178 | -0.006 | 0.362 | 0.057 |
| **Indicator** | 0.034 | -0.164 | 0.232 | 0.734 |
| **Non-enzymatic** | 0.210 | 0.003 | 0.418 | 0.047 |

***Chart

Description automatically generated***

Combining ‘enzymatic’ and ‘non-enzymatic’ in an ‘antioxidant’ category:

***Chart

Description automatically generated***

***10 – Effects per biomarker, tissue and life stage (for liver and whole body)***

***Whole body: (tadpoles and embryo)***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Whole Body** | **Embryo**  **(k = 118)** | **Enzymatic** | 0.032 | -0.239 | 0.303 | 0.815 |
| **Indicator** | 0.205 | -0.225 | 0.636 | 0.350 |
| **Non-enzymatic** | 0.379 | 0.029 | 0.728 | 0.034 |
| **Tadpoles**  **(k = 721)** | **Enzymatic** | 0.192 | -0.002 | 0.3865 | 0.053 |
| **Indicator** | 0.040 | -0.169 | 0.249 | 0.708 |
| **Non-enzymatic** | 0.177 | -0.044 | 0.398 | 0.117 |

***Chart, scatter chart

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***Chart, scatter chart

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***Liver: (tadpoles and adults)***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Liver** | **Tadpoles**  **(k = 118)** | **Enzymatic** | 0.044 | -0.454 | 0.543 | 0.861 |
| **Indicator** | 0.373 | -0.230 | 0.977 | 0.225 |
| **Non-enzymatic** | 0.053 | -0.556 | 0.663 | 0.864 |
| **Adults**  **(k = 289)** | **Enzymatic** | 0.056 | -0.228 | 0.339 | 0.700 |
| **Indicator** | 0.398 | 0.098 | 0.698 | 0.009 |
| **Non-enzymatic** | 0.128 | -0.172 | 0.428 | 0.403 |

***Chart, scatter chart, box and whisker chart

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***11 – Effect of pollutants (organic* versus *inorganic) per biomarker***

*Results for inorganic compounds:*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Inorganic compounds**  **(k = 484)** | **Enzymatic** | 0.131 | -0.019 | 0.280 | 0.086 |
| **Indicator** | 0.177 | -0.017 | 0.371 | 0.074 |
| **Non-enzymatic** | 0.191 | 0.010 | 0.372 | 0.038 |

***Chart, scatter chart

Description automatically generated***

*Results for organic compounds:*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Estimate** | **Low 95%CI** | **High 95%CI** | **p** |
| **Organic compounds**  **(k = 1528)** | **Enzymatic** | 0.123 | -0.004 | 0.250 | 0.058 |
| **Indicator** | 0.330 | 0.194 | 0.467 | <0.001 |
| **Non-enzymatic** | 0.093 | -0.047 | 0.233 | 0.191 |

**Chart

Description automatically generated**