

Large Scale Metabolic Profiling identifies Novel Steroids linked to Rheumatoid Arthritis

Noha A. Yousri^{1,2}, Karim Bayoumy^{3,4}, Wessam Gad Elhaq^{3,14}, Robert P. Mohny⁵, Samar Al Emadi^{6,15}, Mohammed Hammoudeh^{6,15}, Hussein Halabi^{7,15}, Basel Masri^{8,15}, Humeira Badsha^{9,15}, Imad Uthman^{10,15}, Robert Plenge^{11,15}, Richa Saxena^{12,13,15}, Karsten Suhre¹, Thurayya Arayssi^{14,15}

¹Bioinformatics Core, Physiology and Biophysics, Weill Cornell Medicine- Qatar, Doha. ²Computers and Systems Engineering, Faculty of Engineering, Alexandria University, Egypt. ³Research Division, Weill Cornell Medical College-Qatar, Education City, Doha, Qatar. ⁴Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar. ⁵Metabolon Inc., Durham, NC, USA. ⁶Division of Rheumatology, Department of Medicine, Hamad Medical Corporation, Doha, Qatar. ⁷King Faisal Specialist Hospital & Research center, Jeddah, Kingdom of Saudi Arabia. ⁸Jordan Hospital, Amman, Jordan. ⁹Dr. Humeira Badsha Medical Center, Dubai, UAE. ¹⁰American University of Beirut, Faculty of Medicine, Beirut, Lebanon. ¹¹Merck, Boston, MA, USA, Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA. ¹²Center for Human Genetic Research, Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA. ¹³Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA. ¹⁴Department of Medicine, Weill Cornell Medical College-Qatar, Education City, Doha, Qatar. ¹⁵Member of the Middle East Rheumatoid Arthritis Consortium (MERAC)

Supplemental Information:

Supplemental Figure 1: GGM subnetworks where nodes correspond to metabolites and edges are significant partial correlations. Size of the node is proportional to its significance of association with RA. The color of the node indicates the superpathway of the metabolite according to the legend.

Supplemental Figure 2: Boxplots of 32 metabolites associated with RA for each of the RA groups with different corticosteroid treatment.

Supplemental Methods: Interaction Model.

Supplemental Table 1: Results of regression of all metabolites against case/control while including covariates and using interaction model.

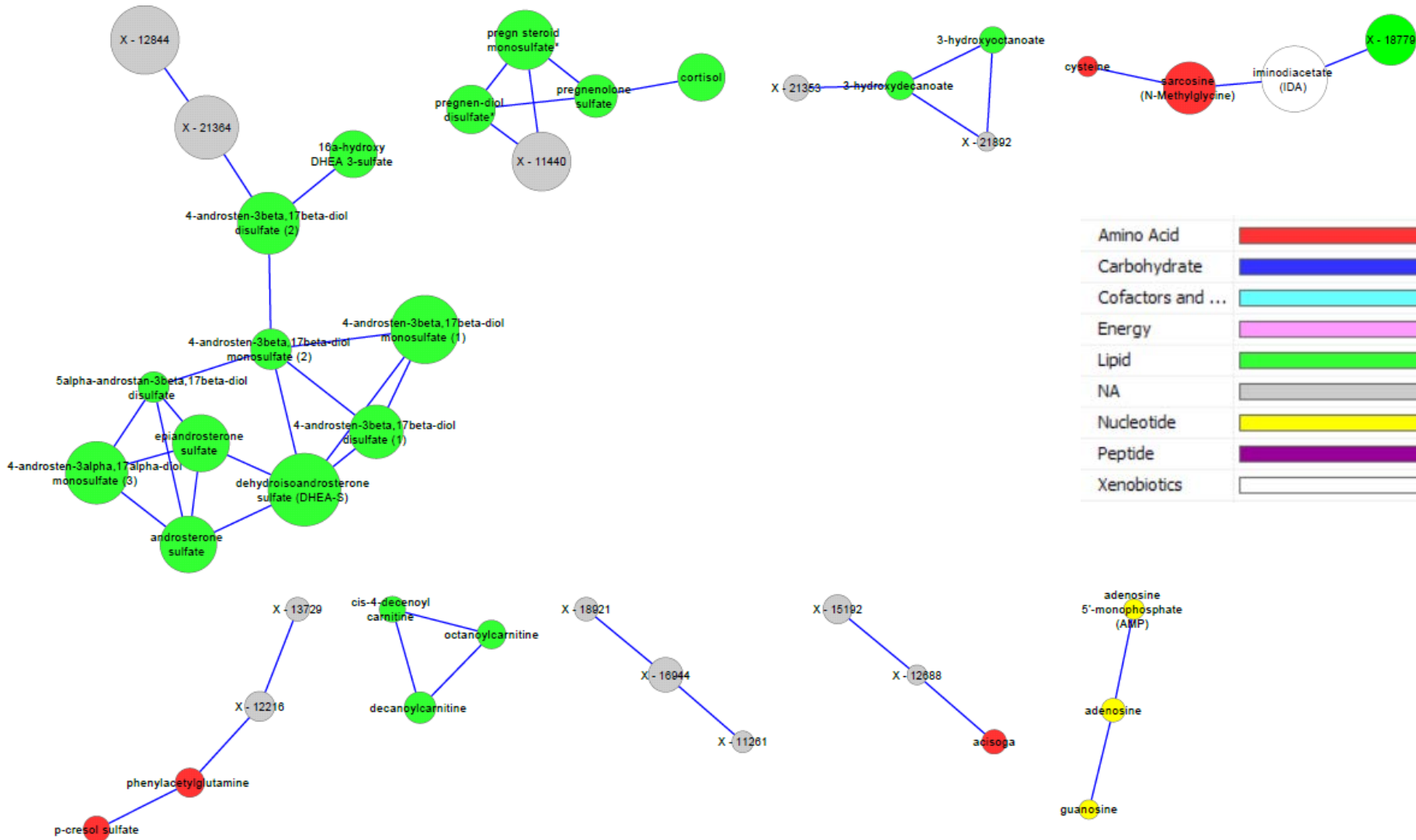
Supplemental Table 2: Output from OPLS-DA analysis using 96 metabolites and covariates.

Supplemental Table 3: SIMCA OPLS-DA output using all features (metabolites and covariates).

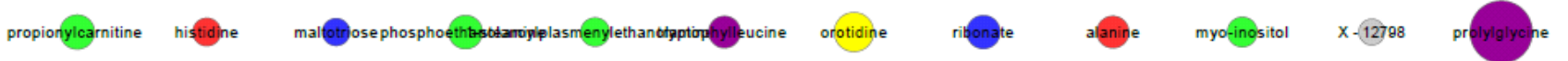
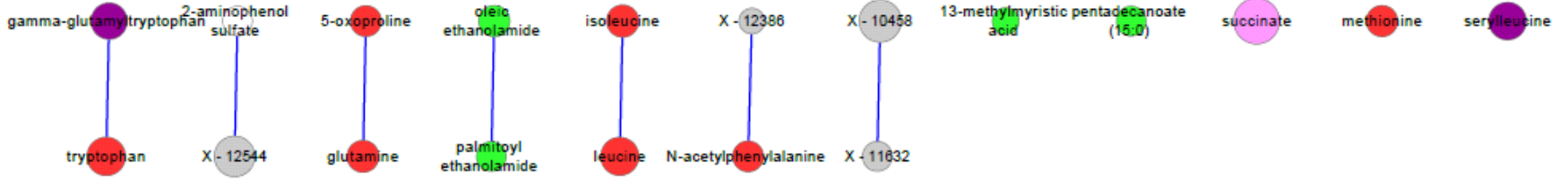
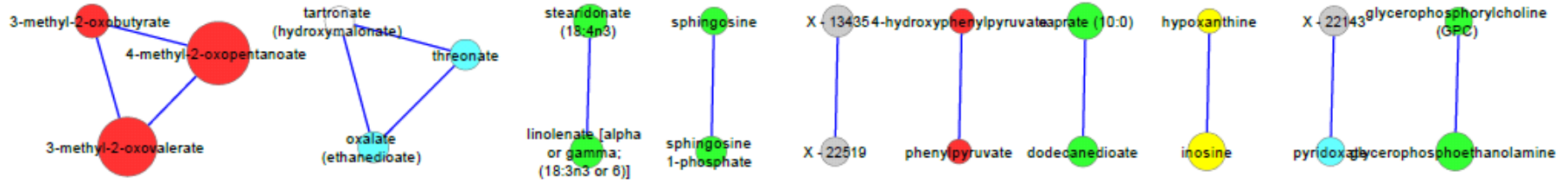
Supplemental Table 4: Results of regression of 32 RA metabolites in RA samples only using covariates according to feature selection.

Supplemental Table 5: Correlation of batch (KSA batch and Qatar batch) with different phenotypes.

Supplemental Figure 1: GGM subnetworks where nodes correspond to metabolites and edges are significant partial correlations. Size of the node is proportional to its significance of association with RA. The color of the node indicates the superpathway of the metabolite according to the legend.

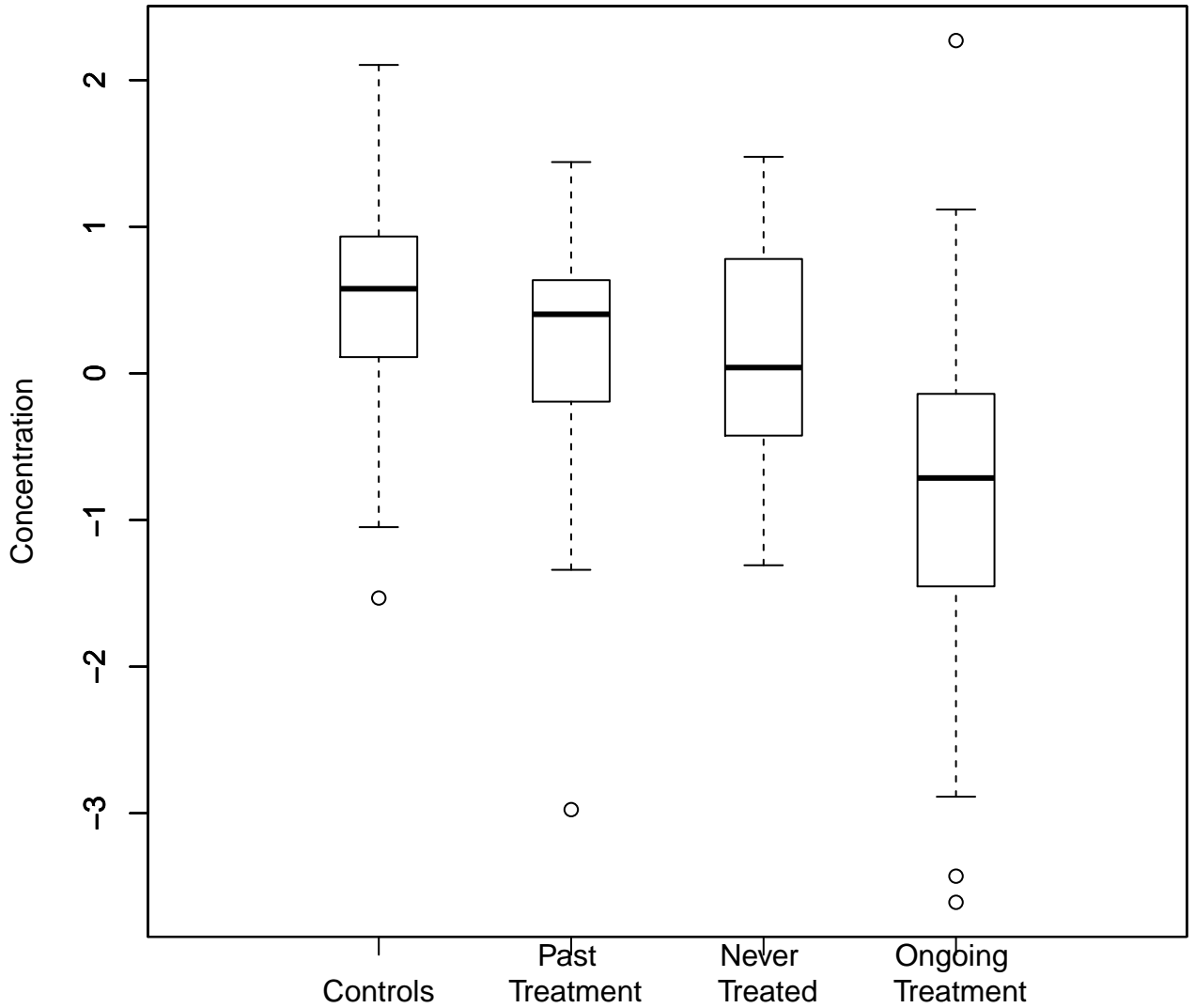


Amino Acid	
Carbohydrate	
Cofactors and ...	
Energy	
Lipid	
NA	
Nucleotide	
Peptide	
Xenobiotics	

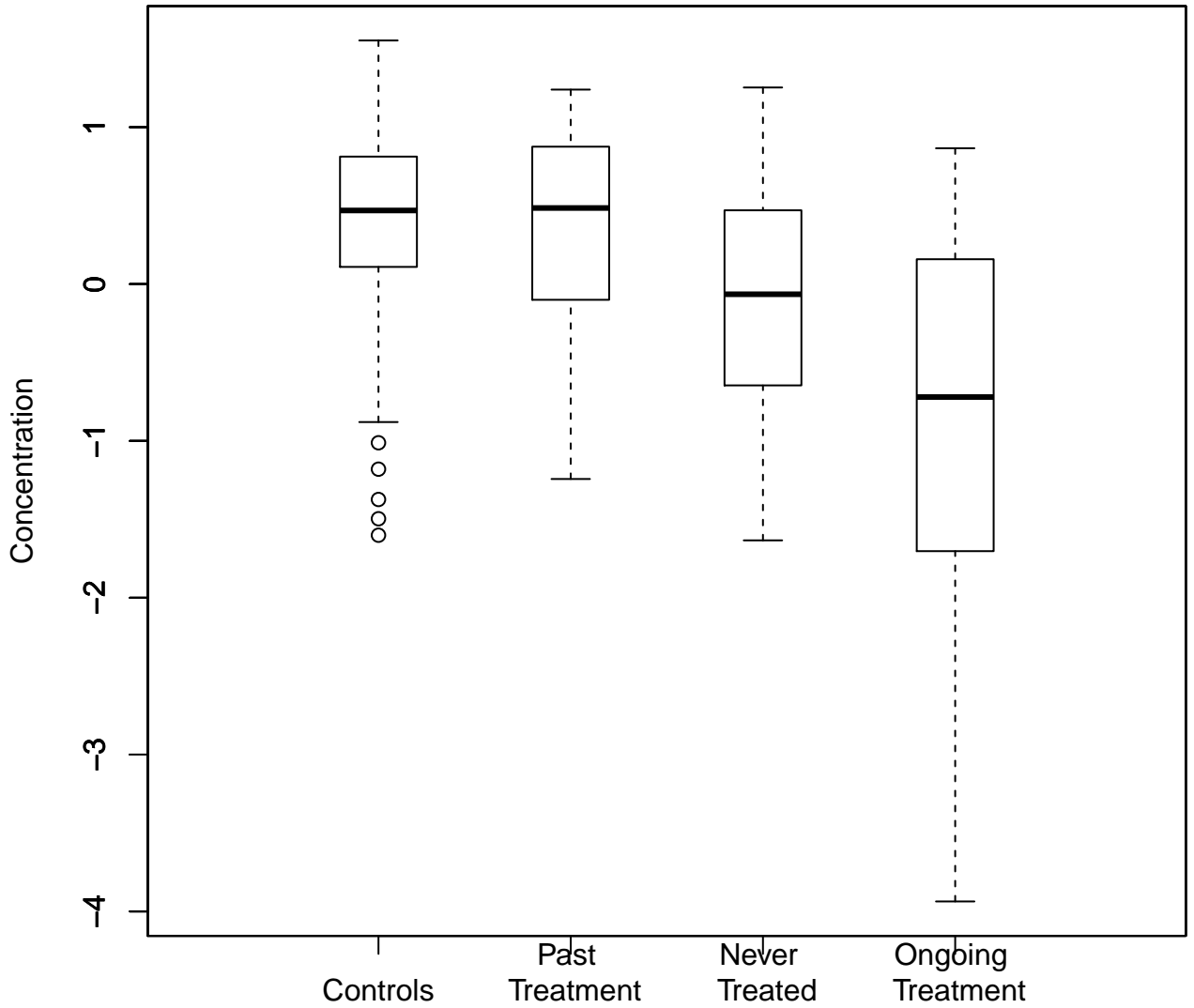


Supplemental Figure 2: Boxplots of 32 metabolites associated with RA for each of the RA groups with different corticosteroid treatment.

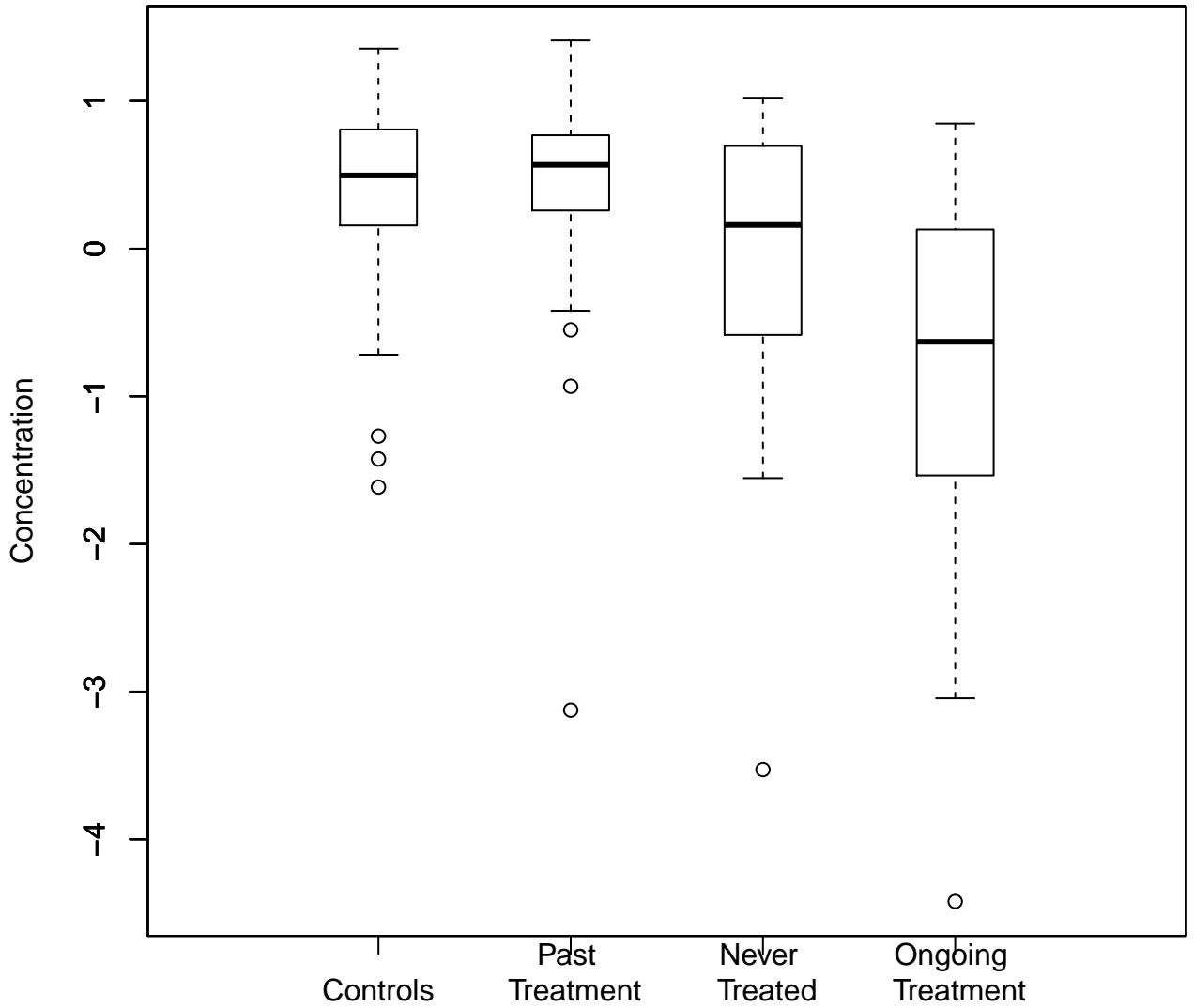
dehydroisoandrosterone sulfate (DHEA-S)



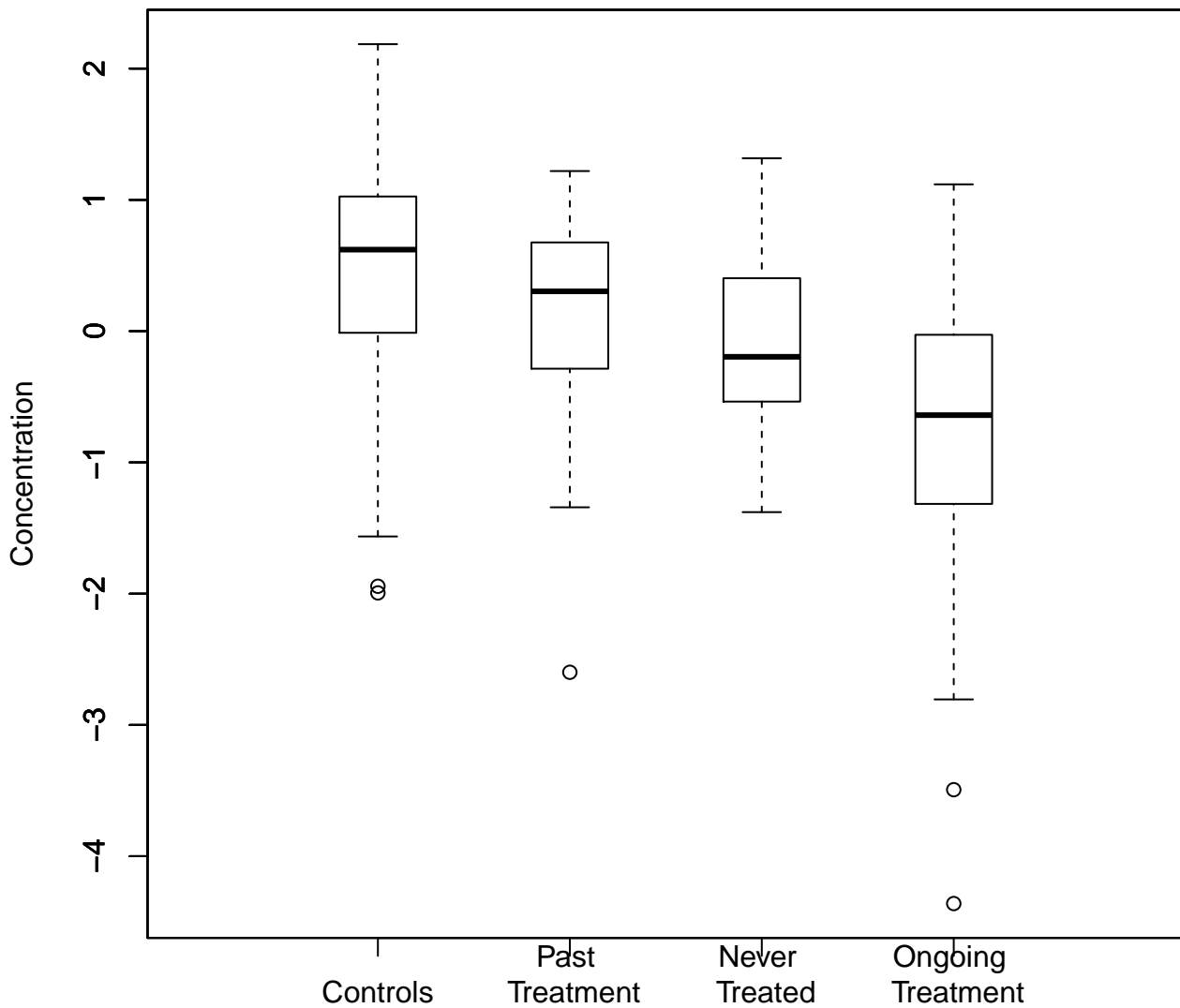
X - 11444



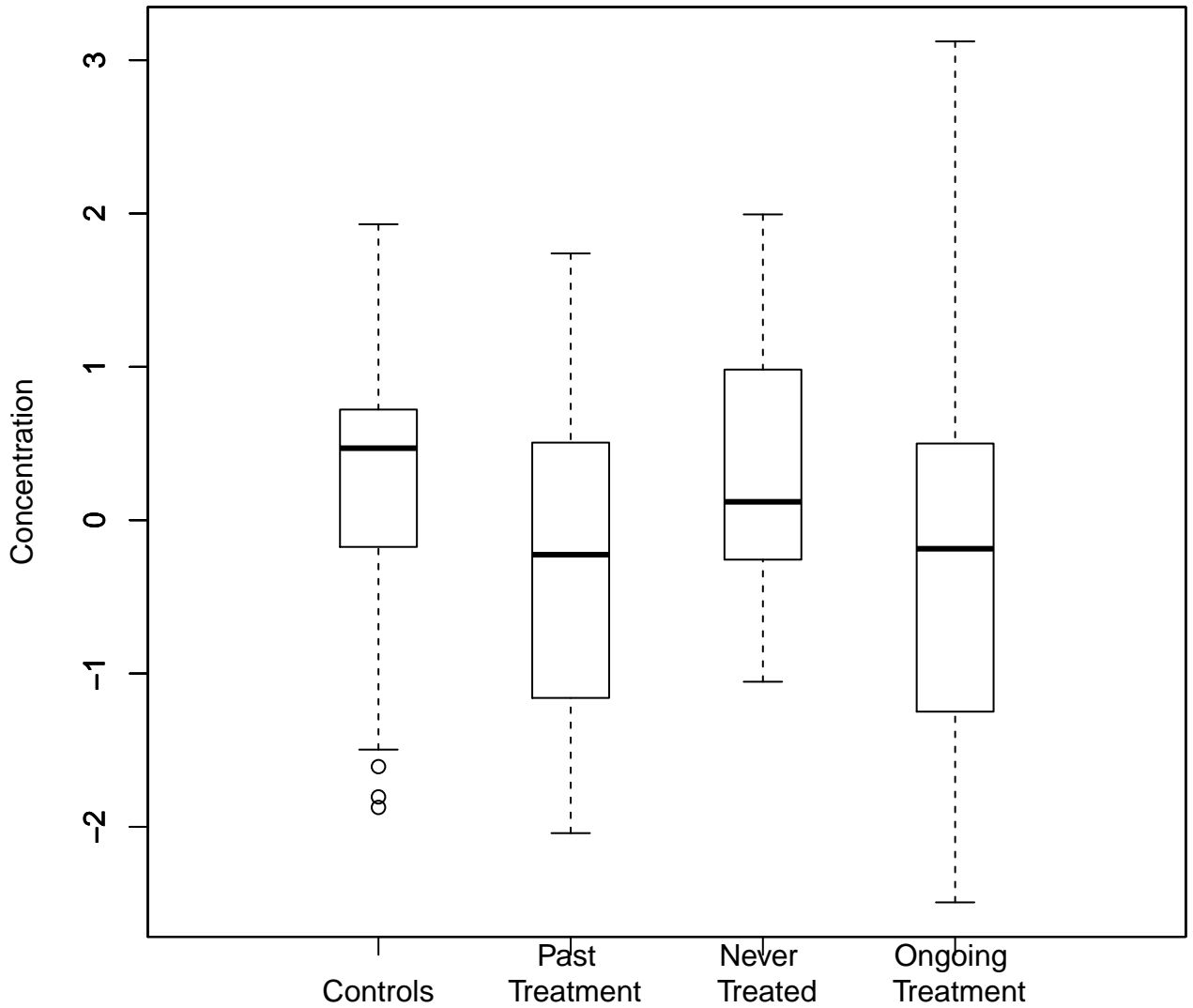
X - 12844



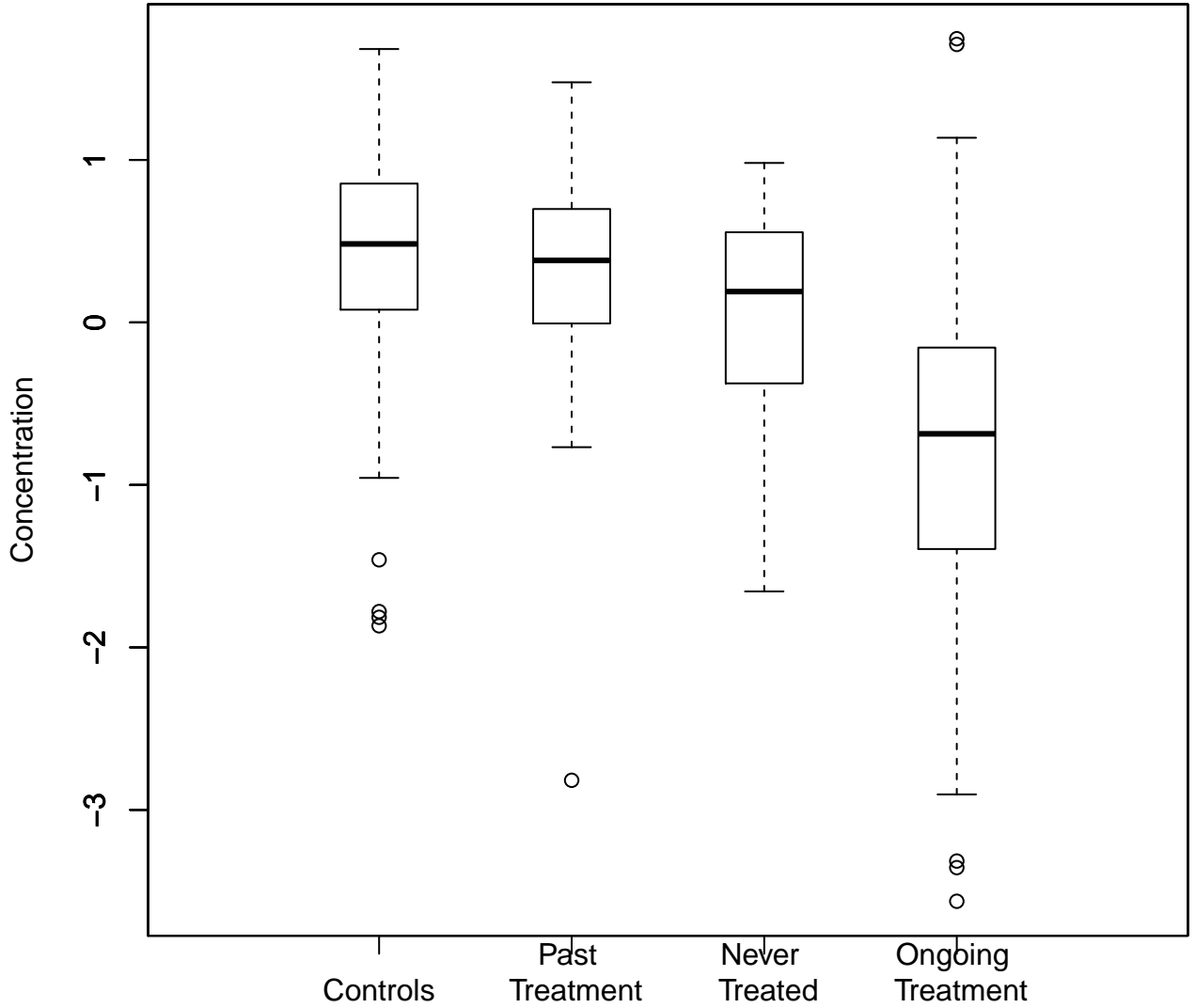
4-androsten-3beta,17beta-diol monosulfate (1)



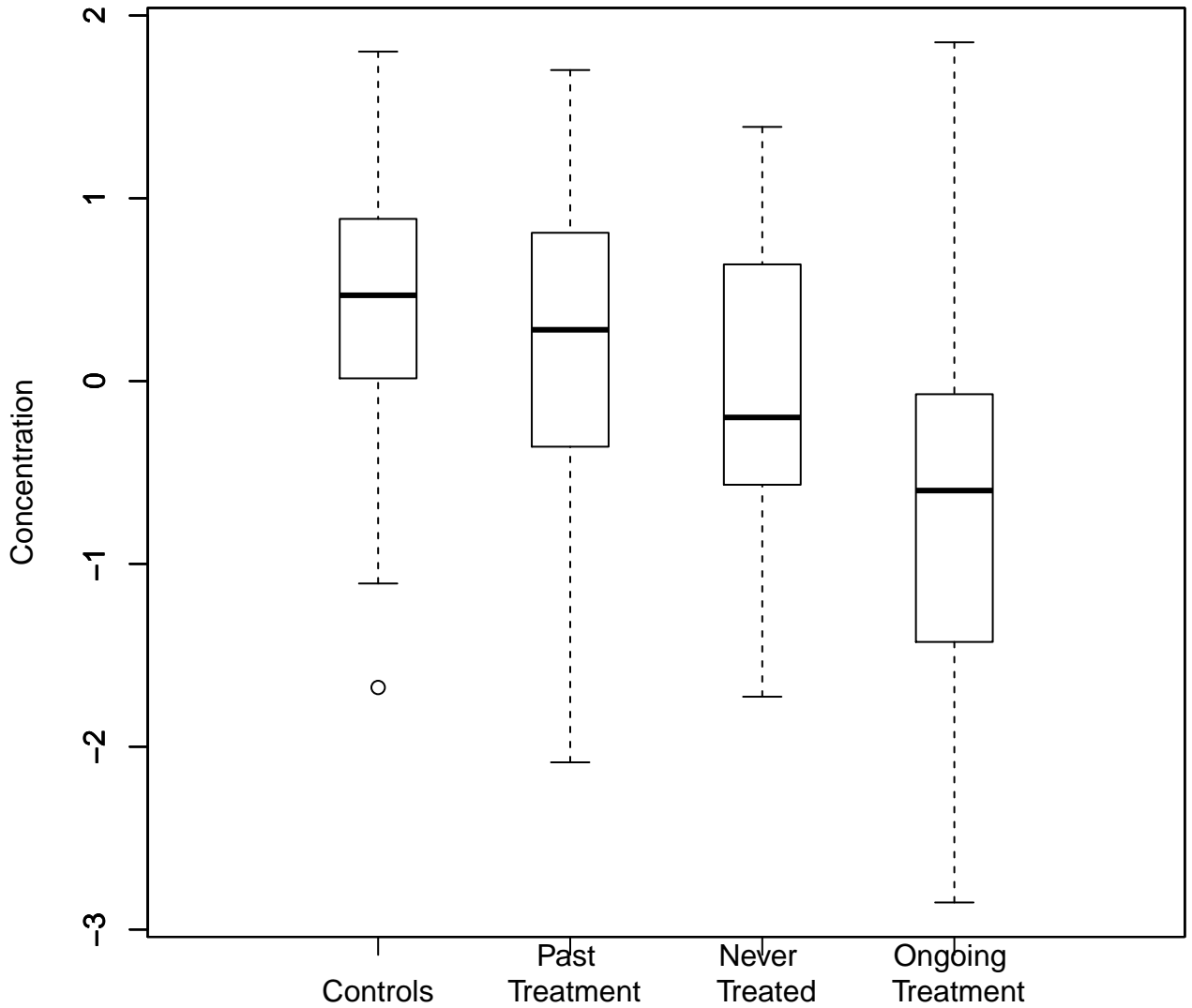
iminodiacetate (IDA)



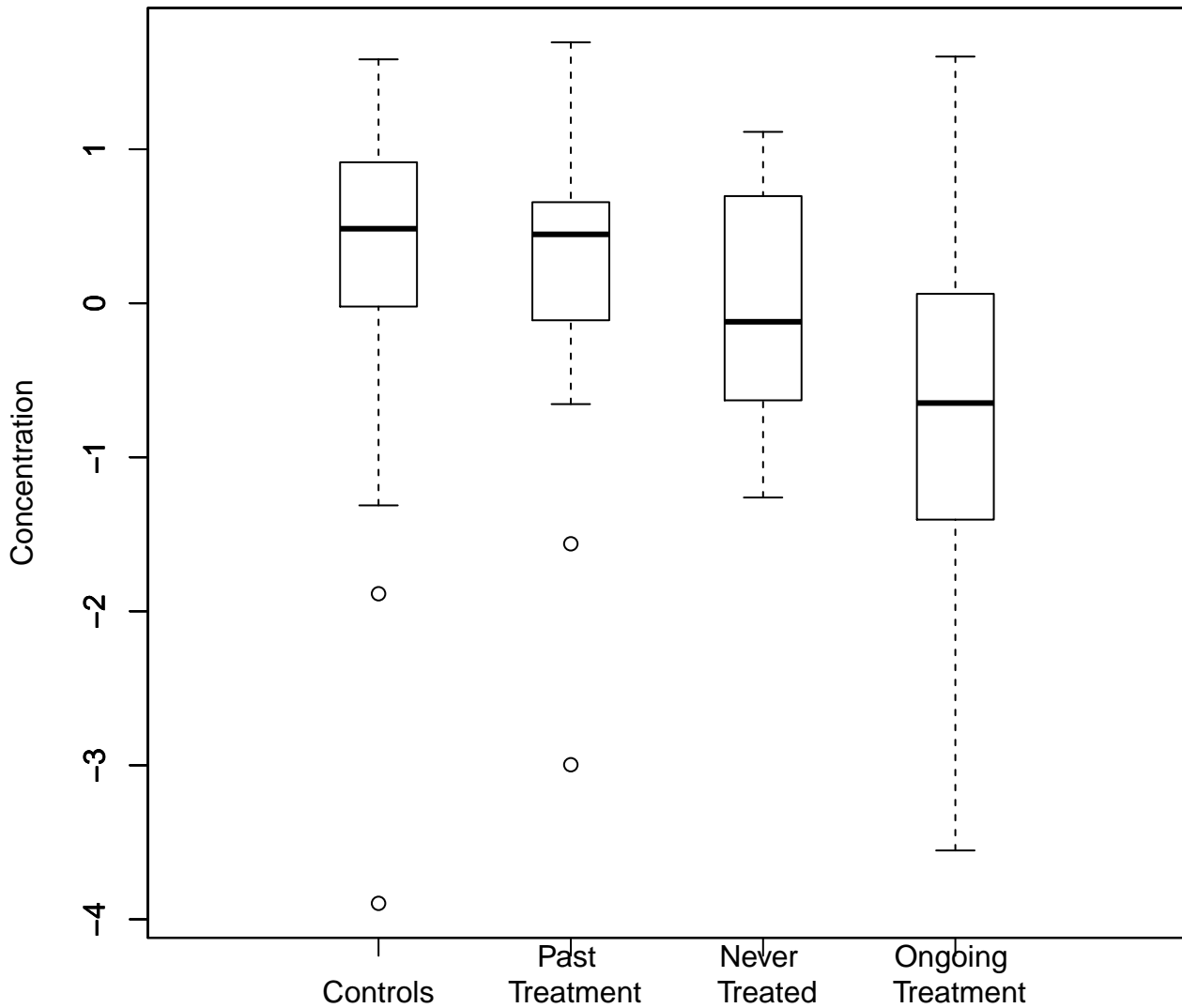
X - 21364



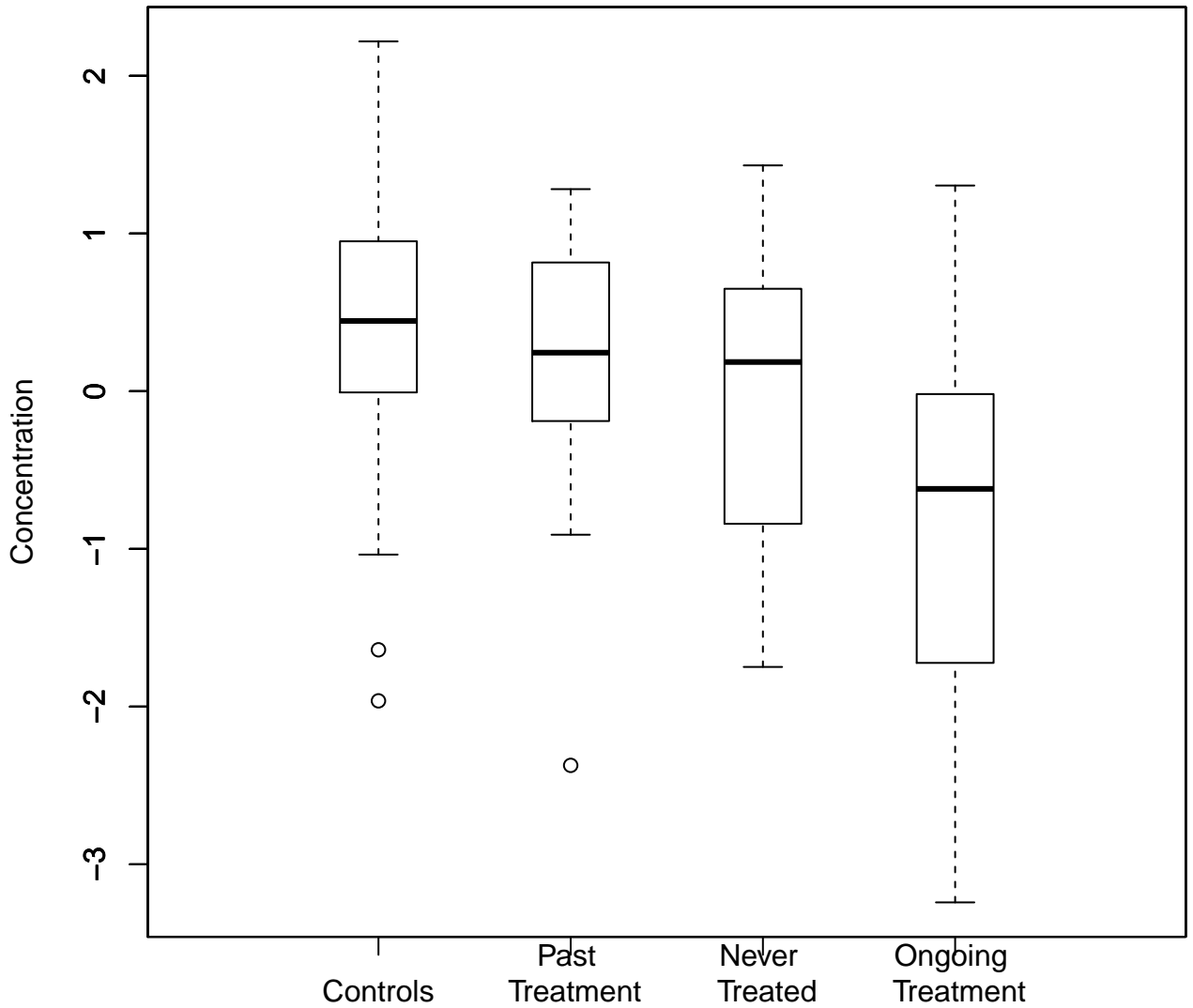
4-androsten-3alpha,17alpha-diol monosulfate (3)



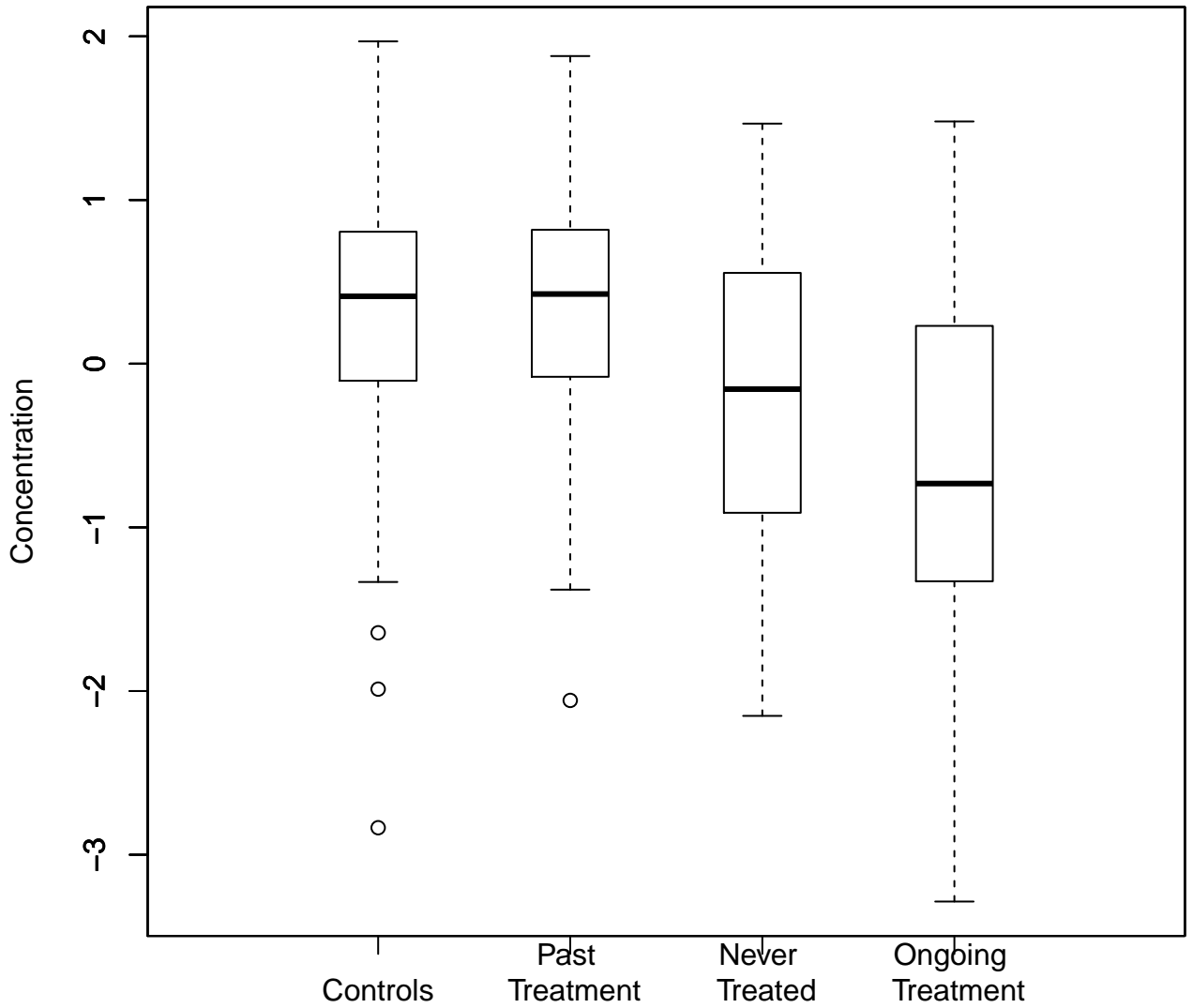
4-androsten-3beta,17beta-diol disulfate (2)



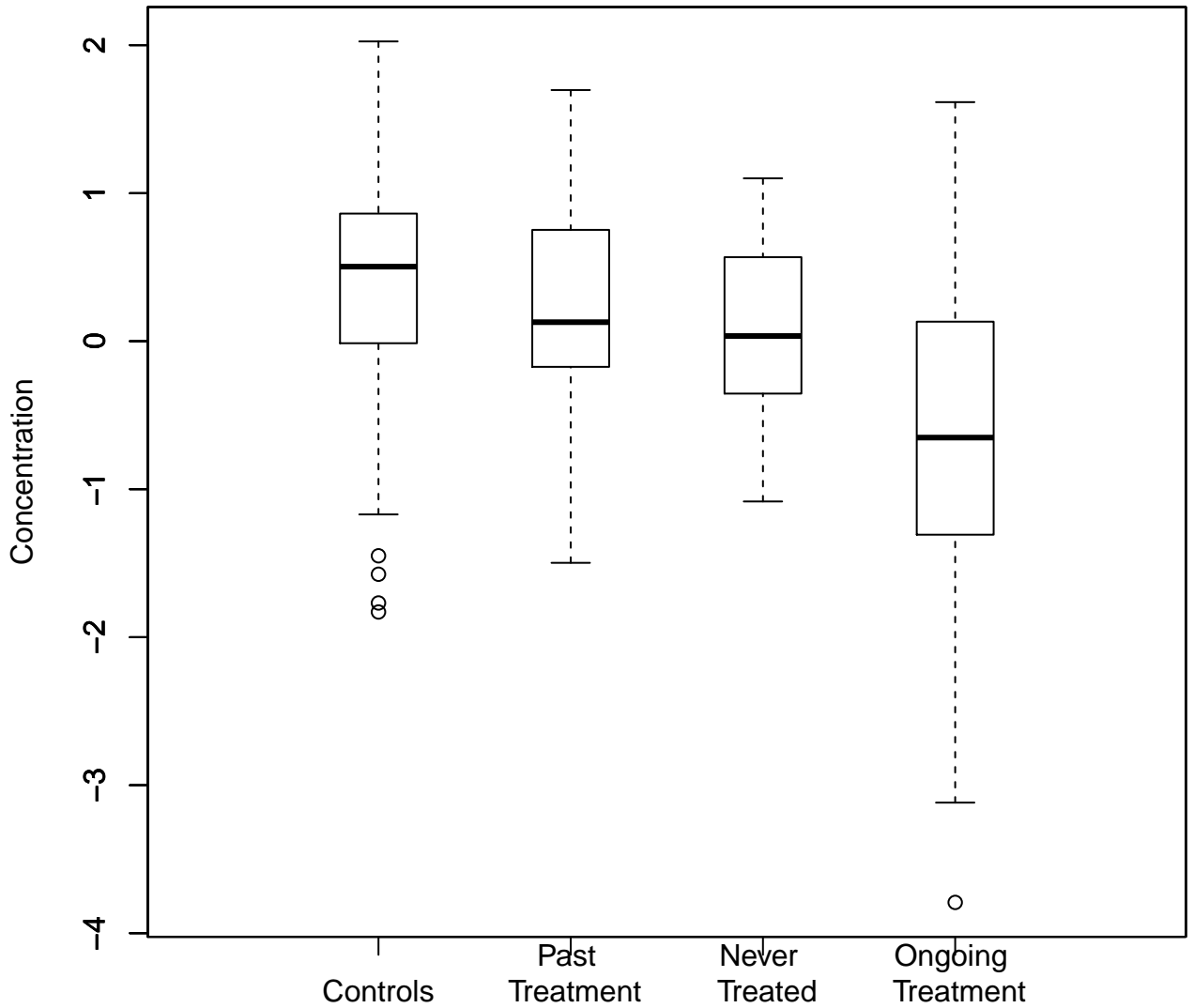
pregn steroid monosulfate*



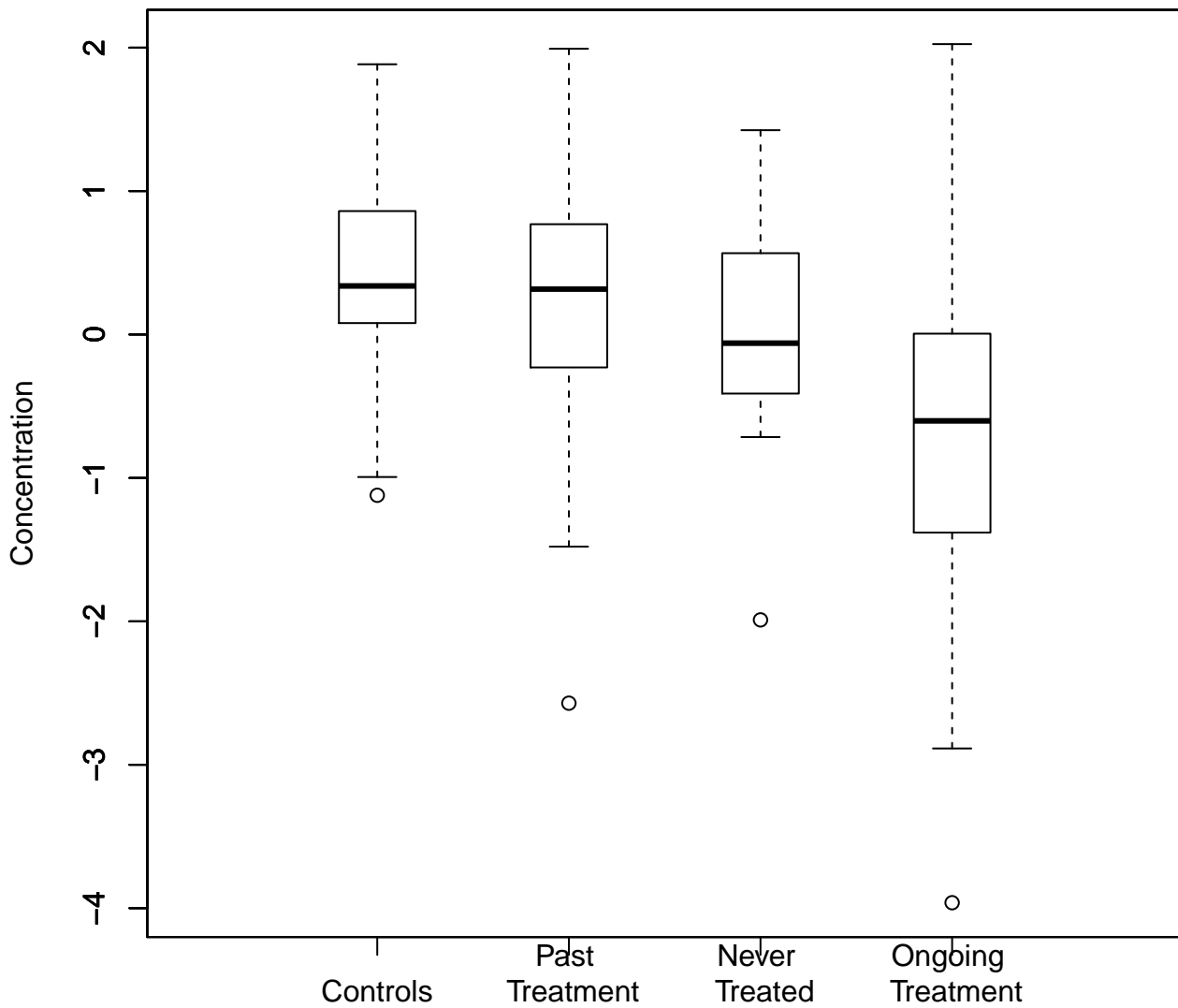
X - 12846



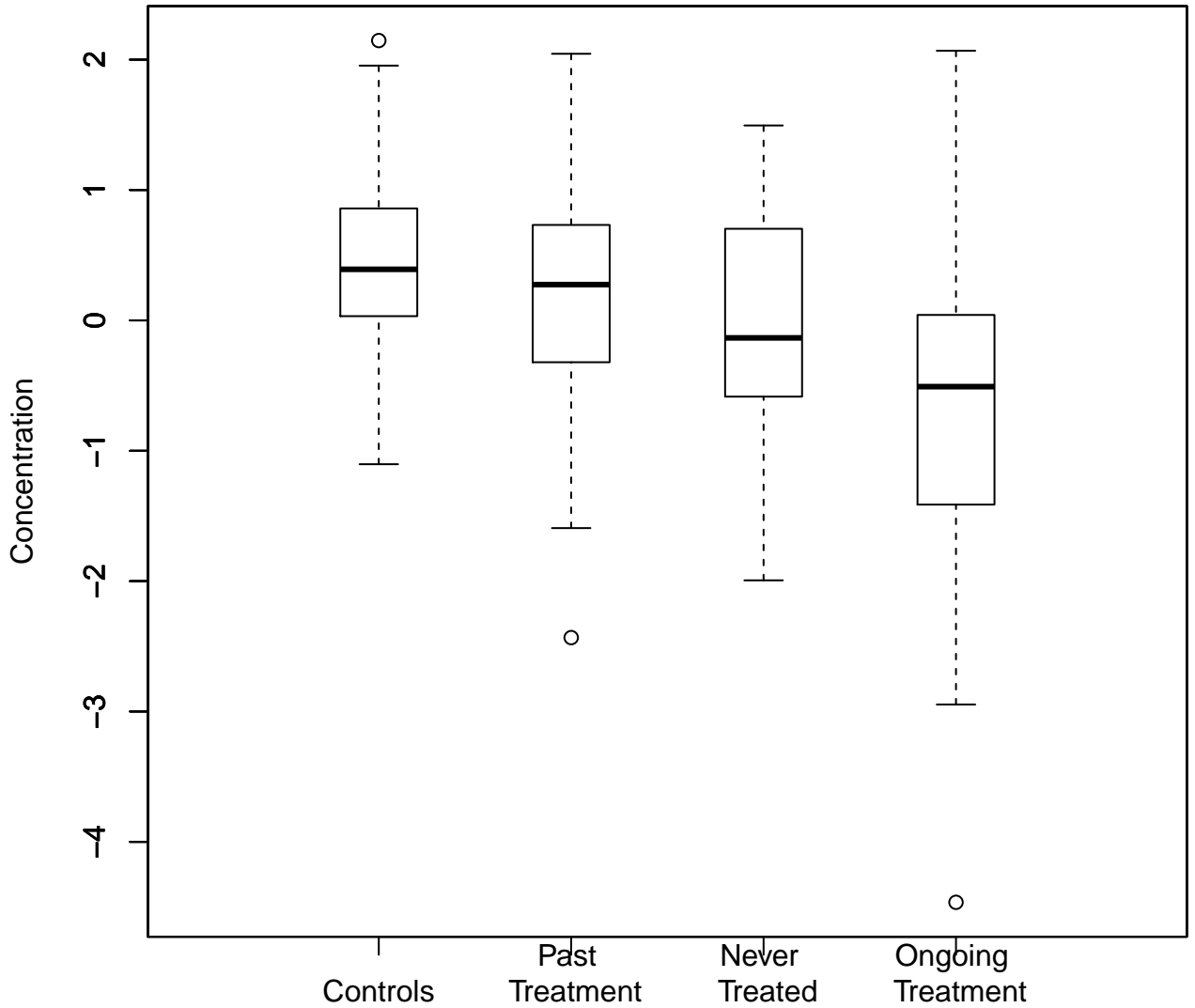
X - 11440



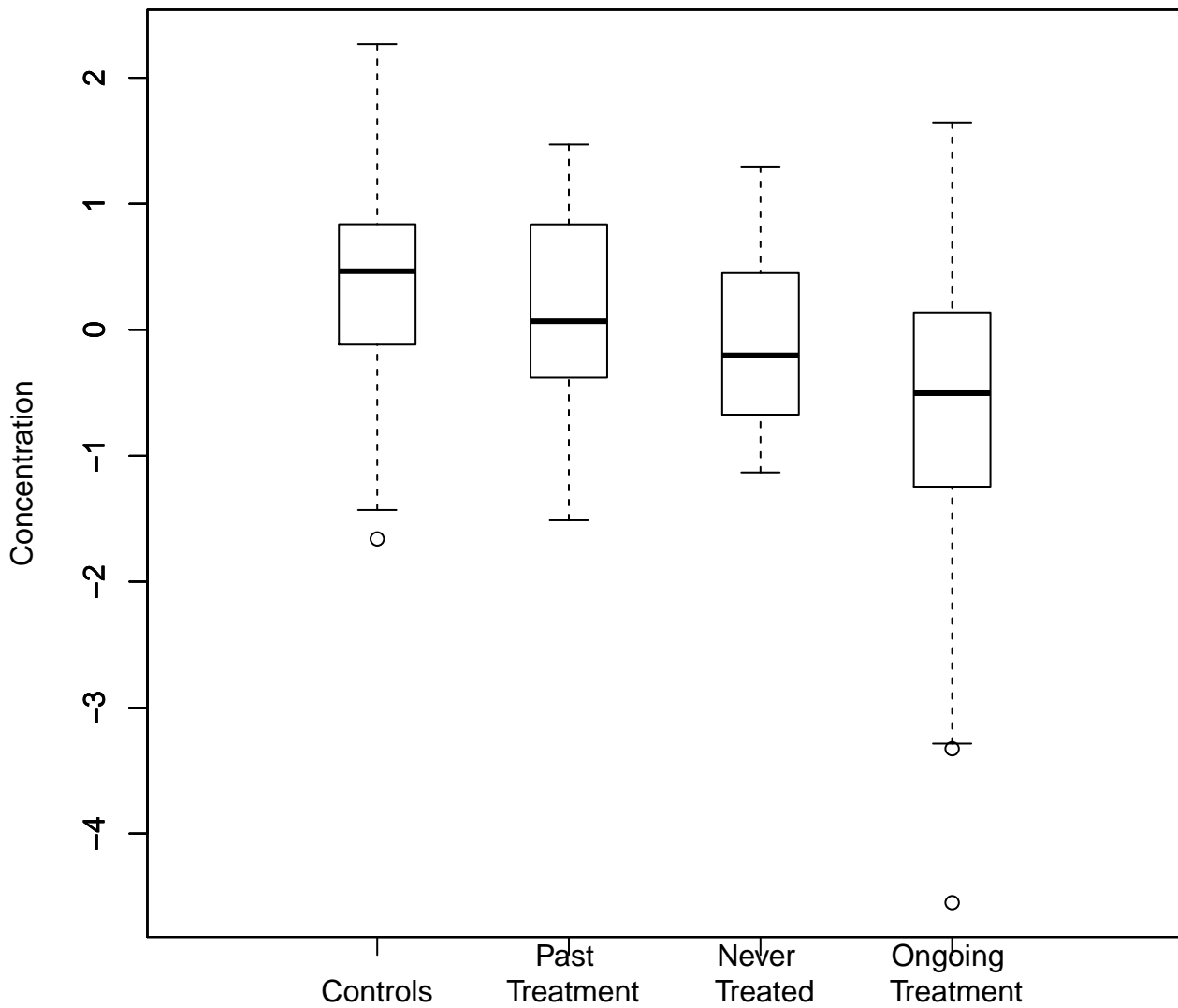
epiandrosterone sulfate



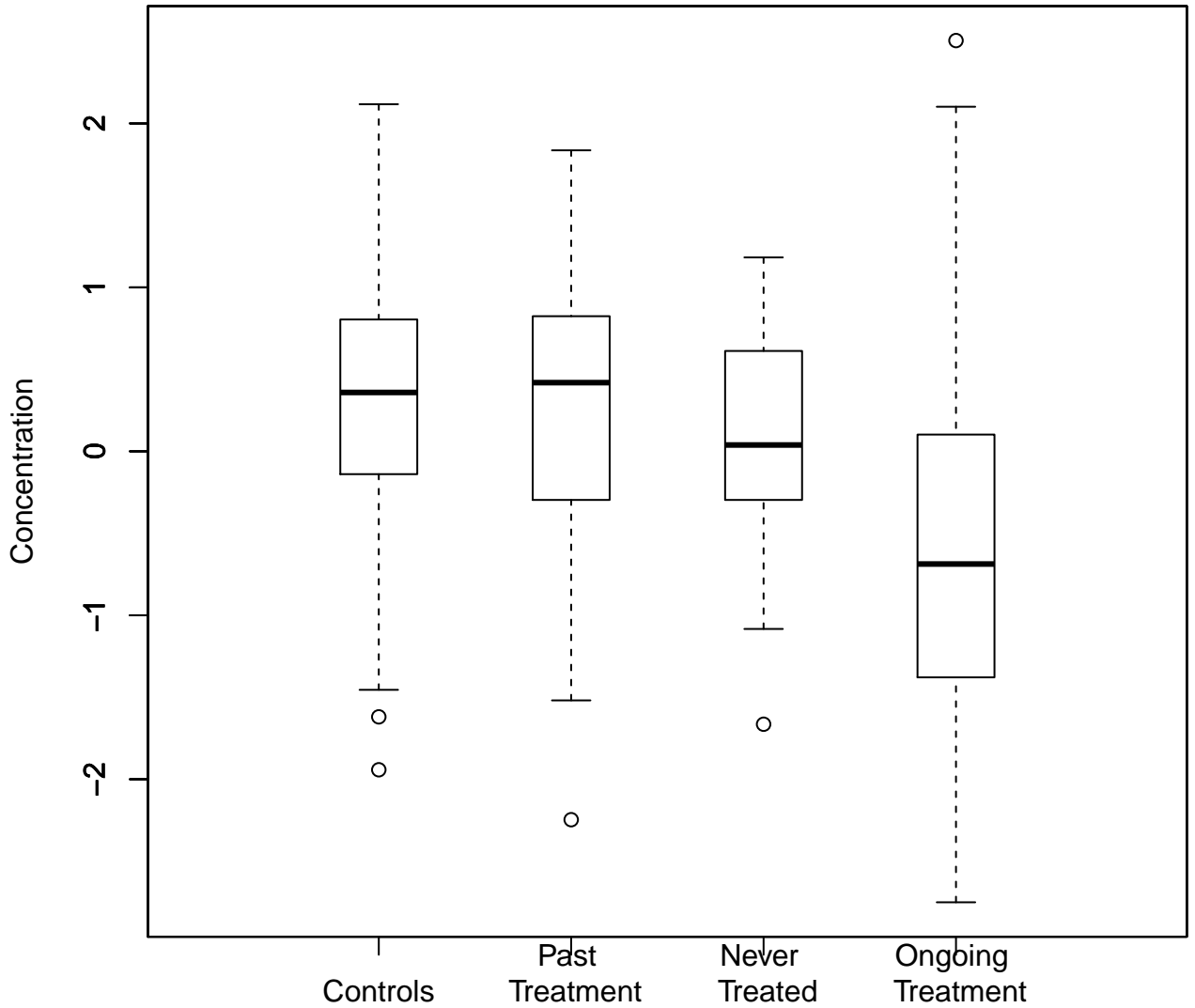
androsterone sulfate



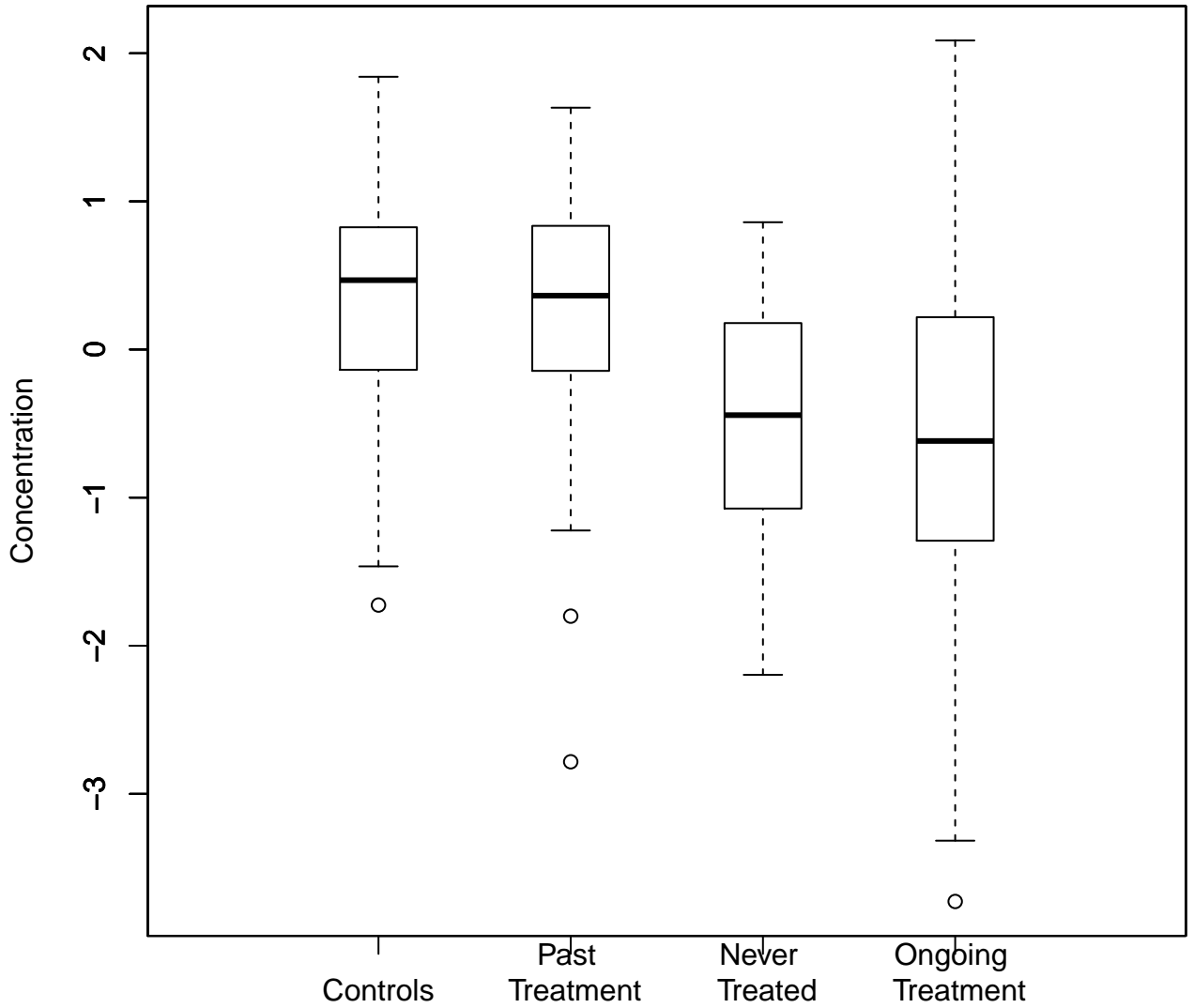
4-androsten-3beta,17beta-diol disulfate (1)



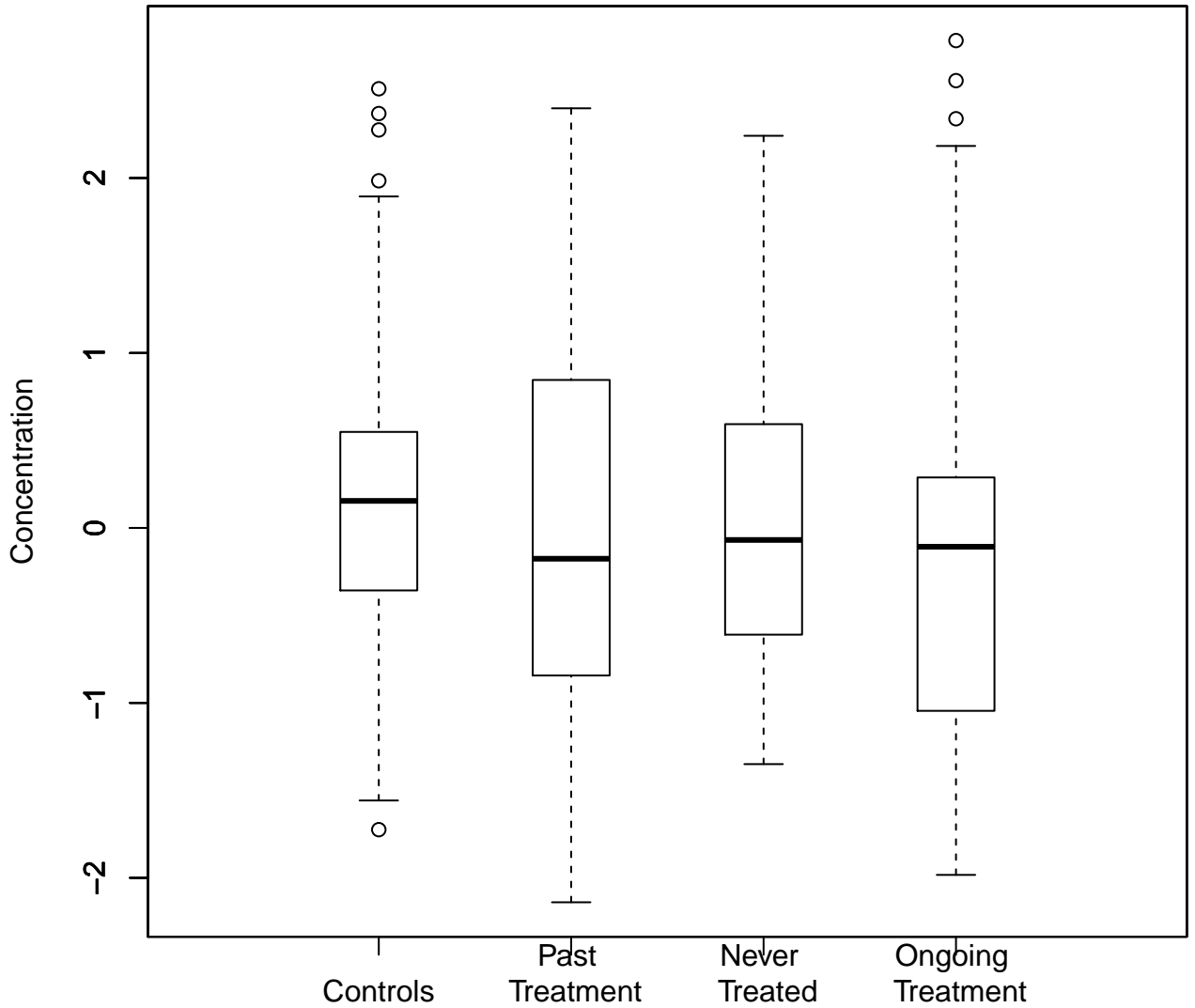
X - 21470



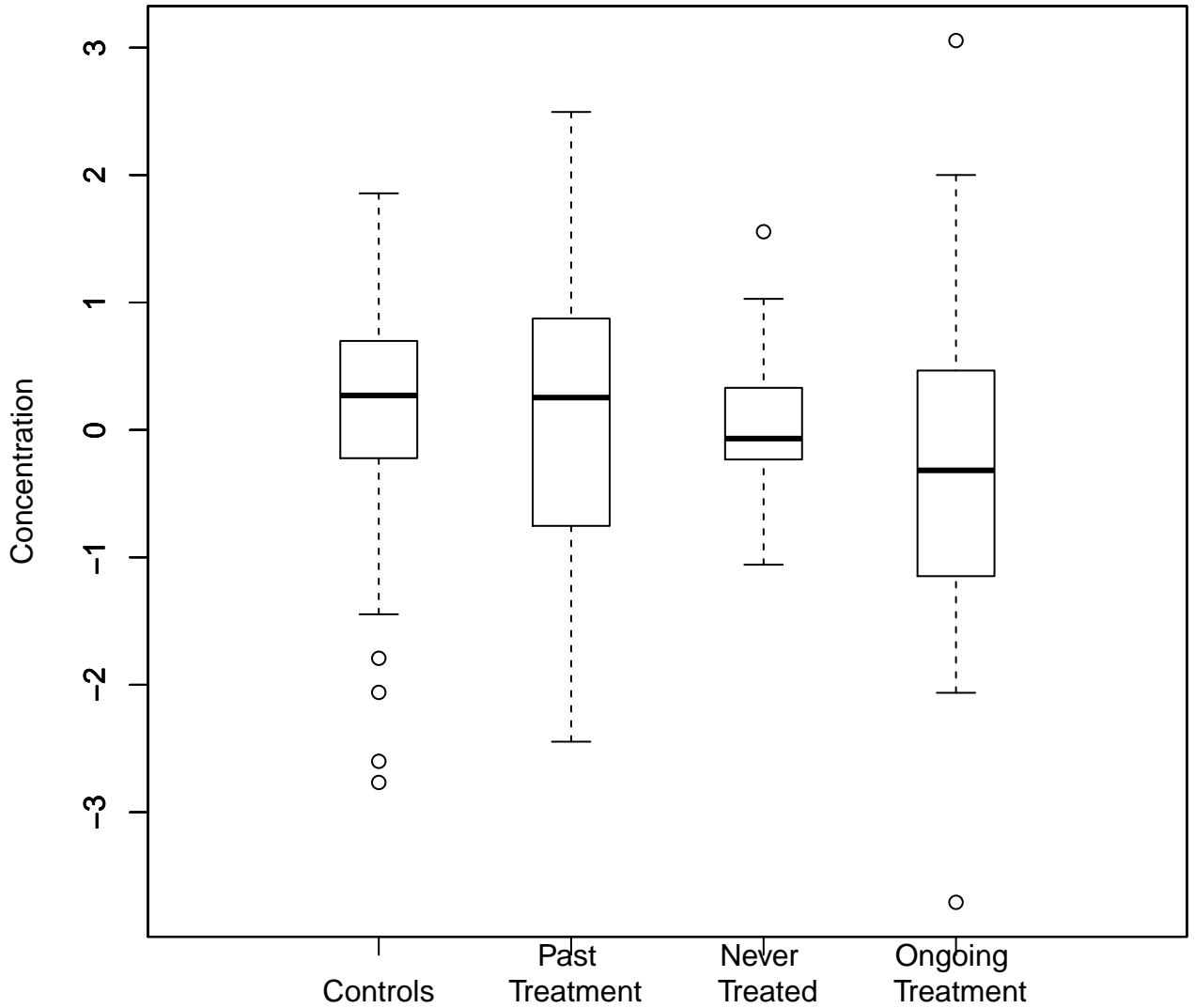
X - 21410



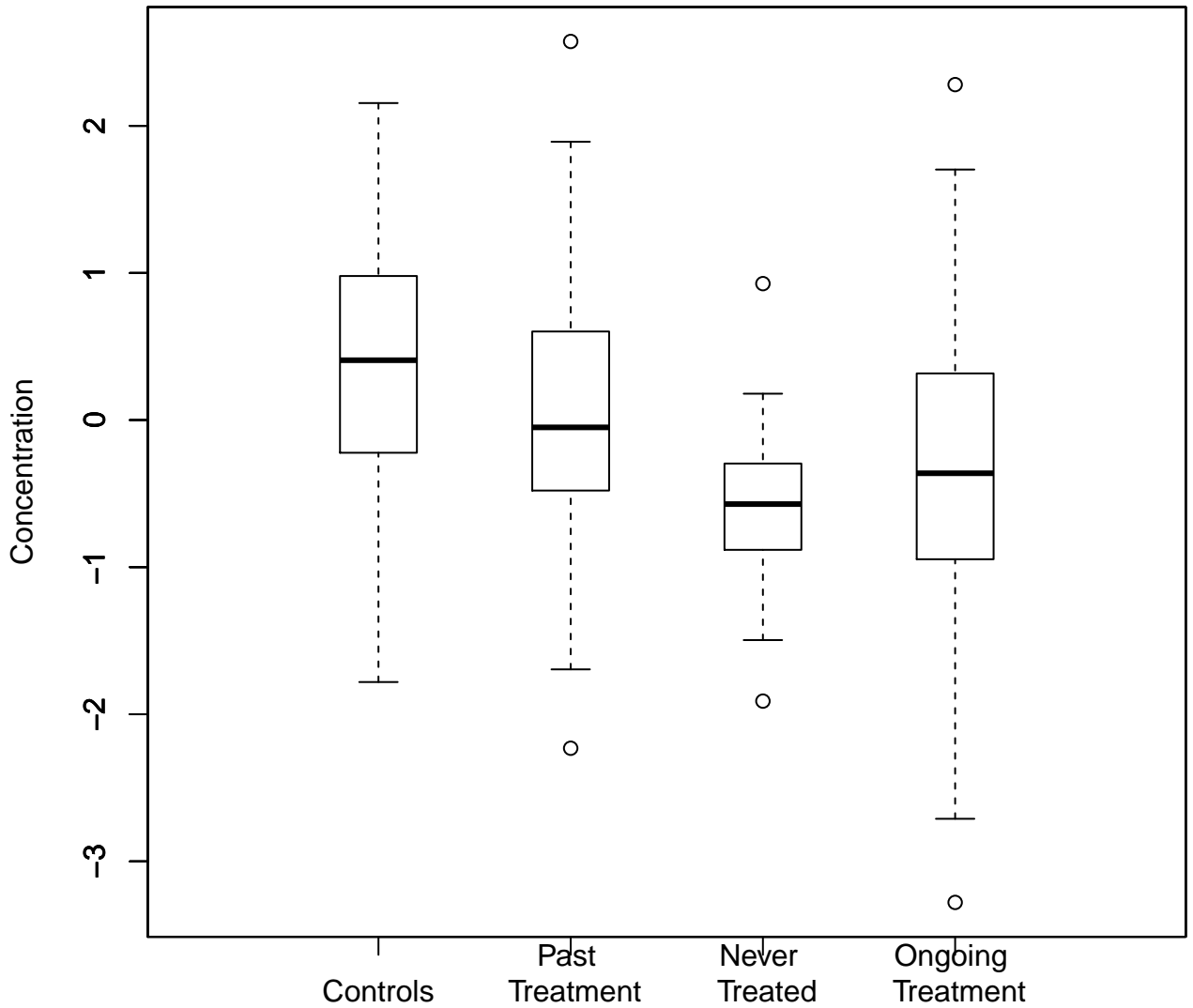
sarcosine (N-Methylglycine)



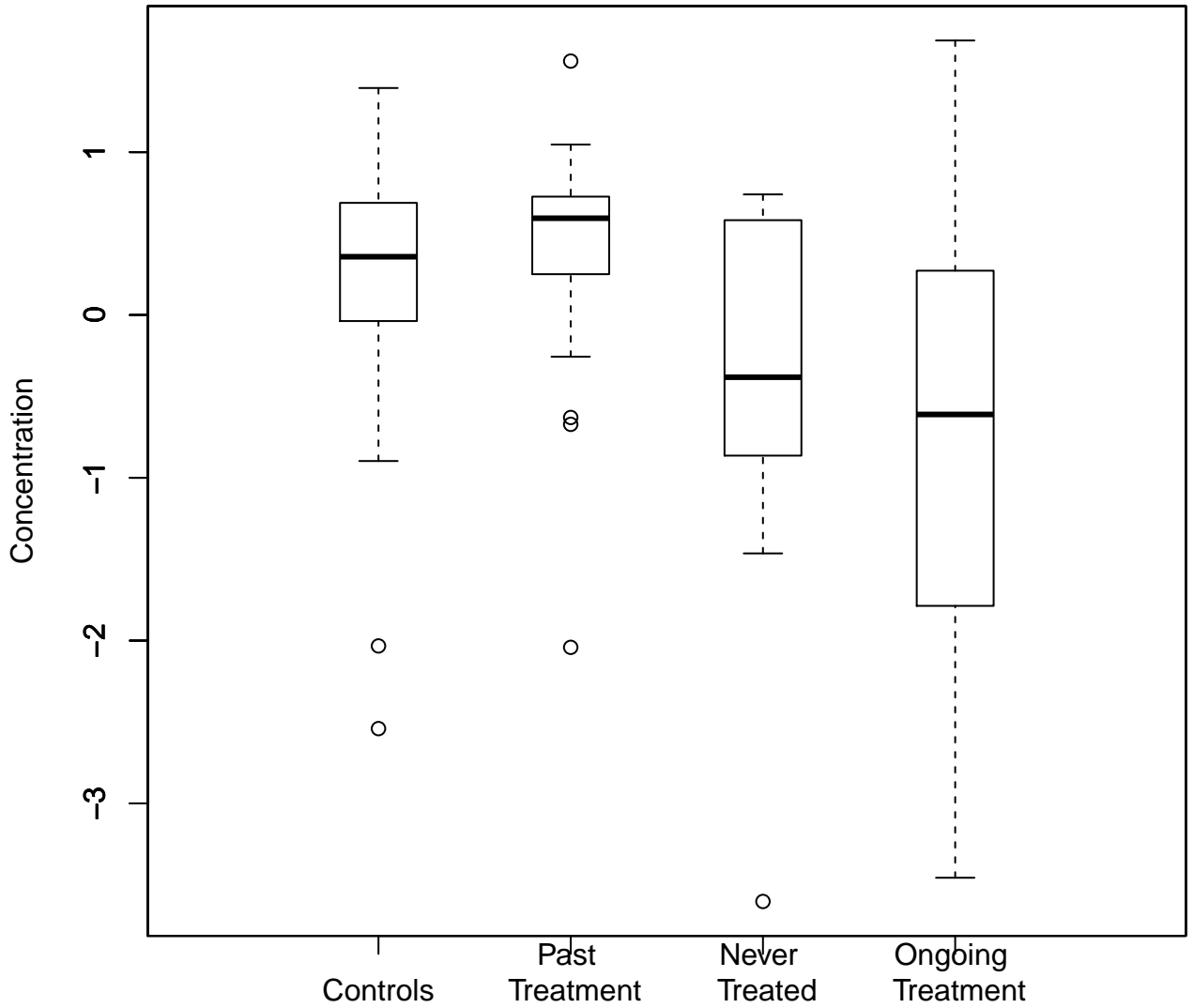
X - 18779



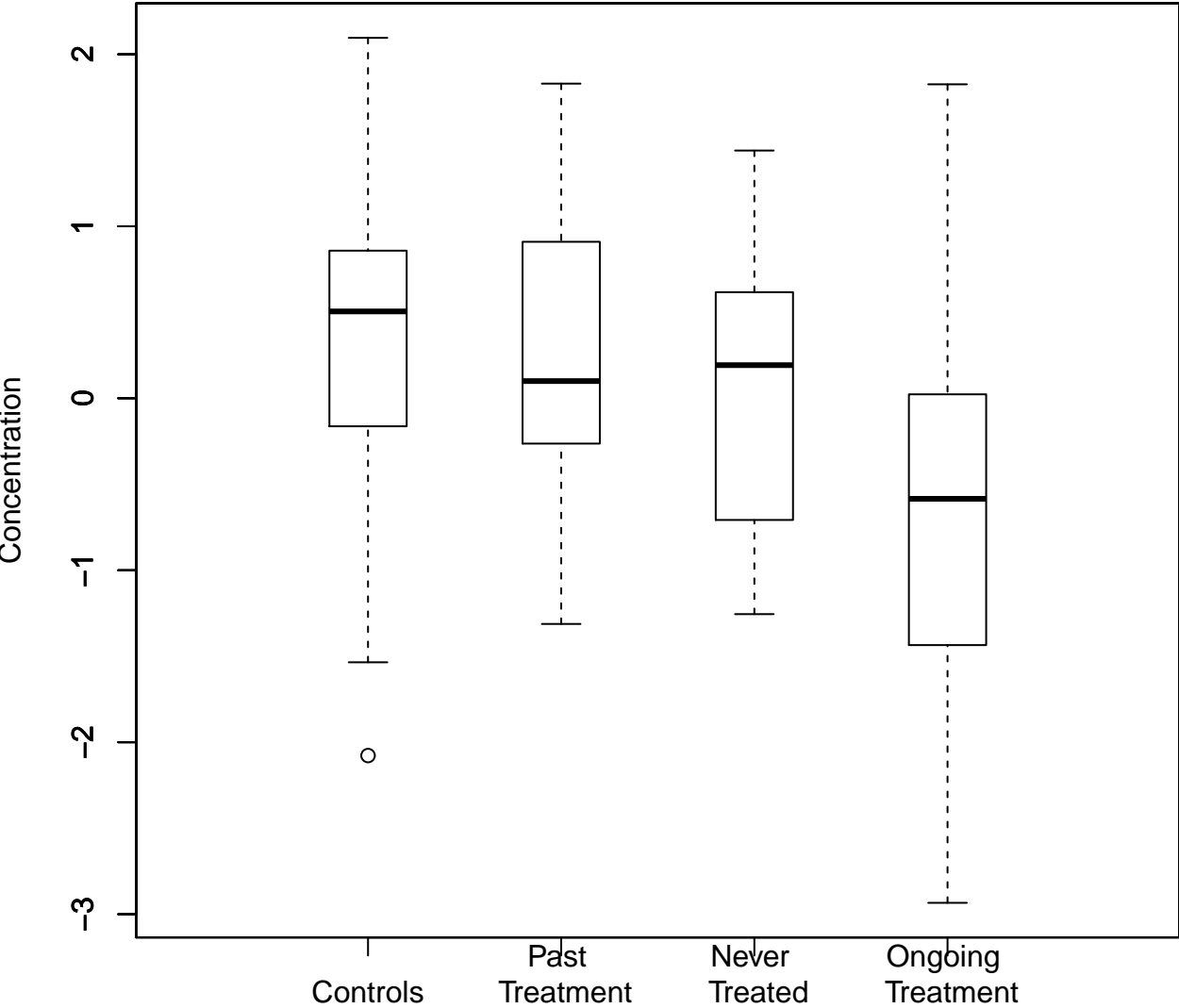
4-methyl-2-oxopentanoate



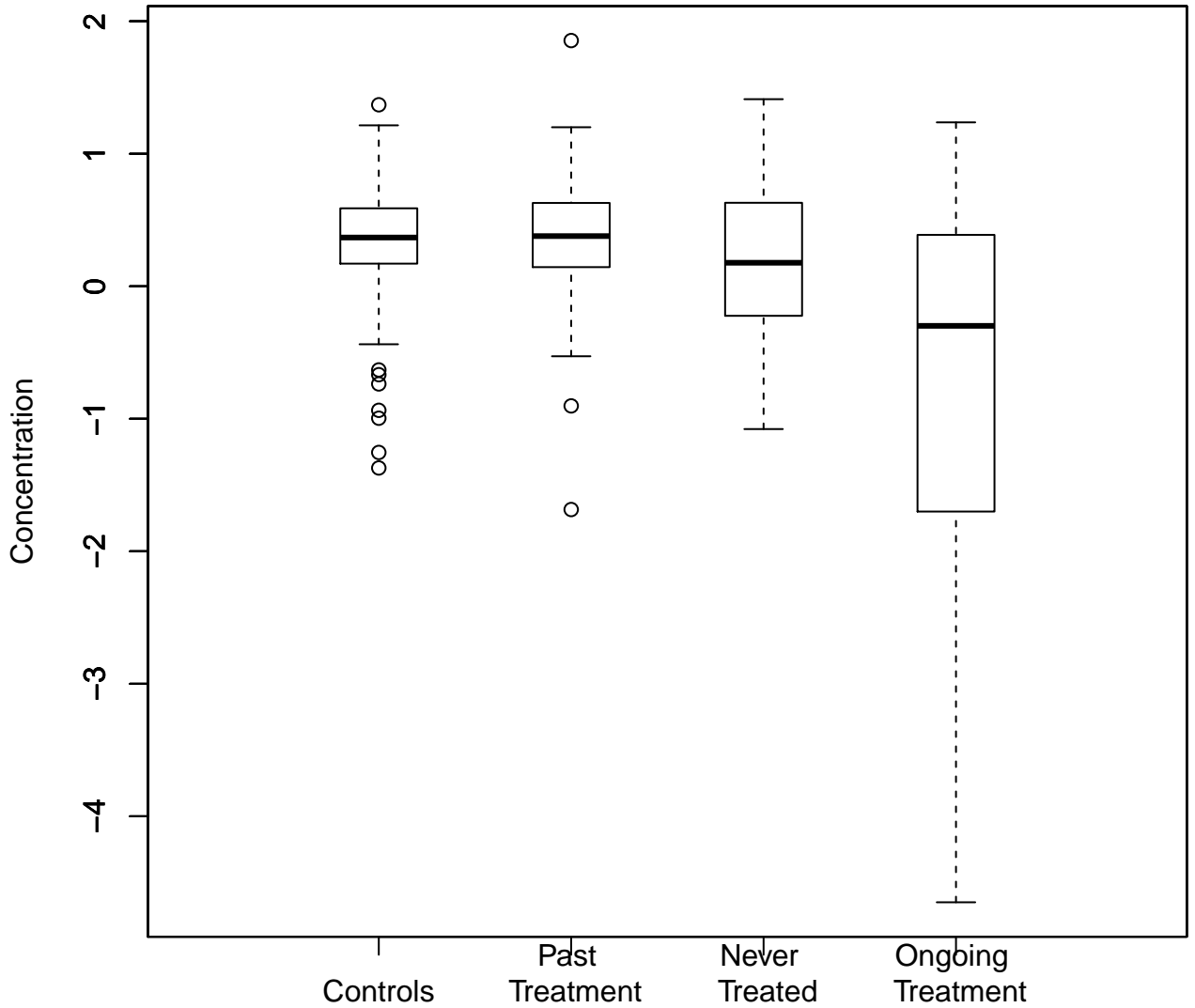
X - 17359



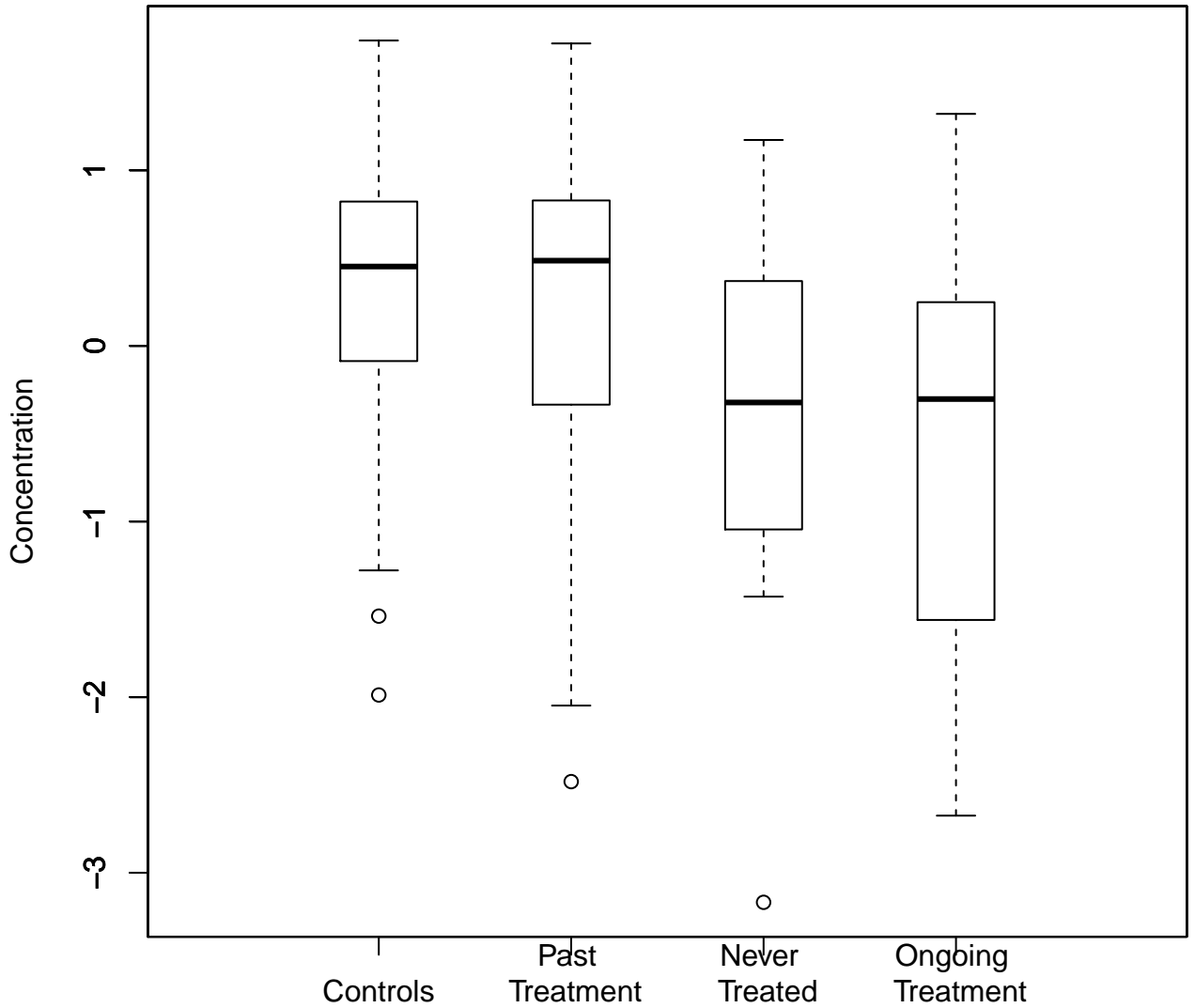
pregnen-diol disulfate*



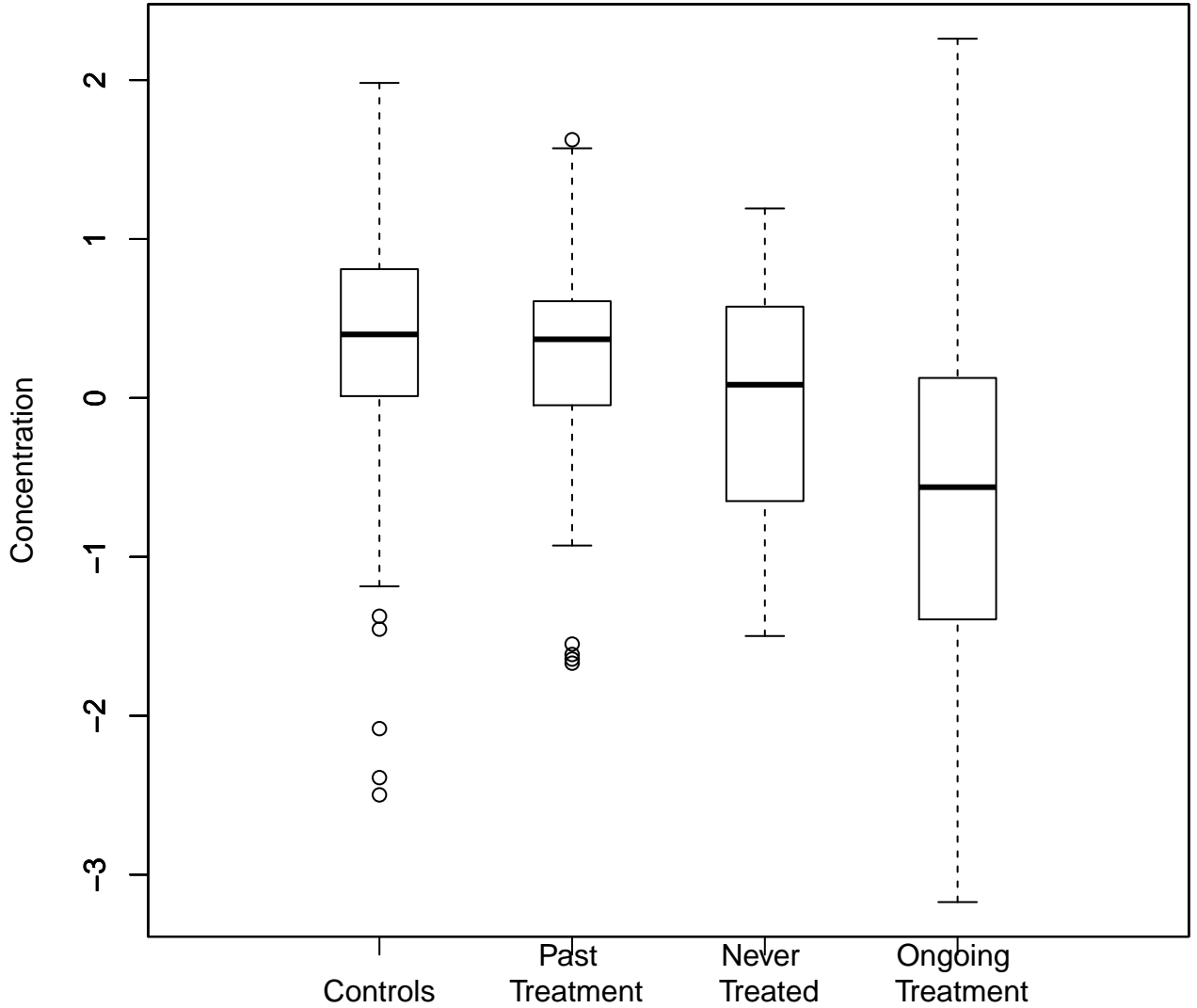
cortisol



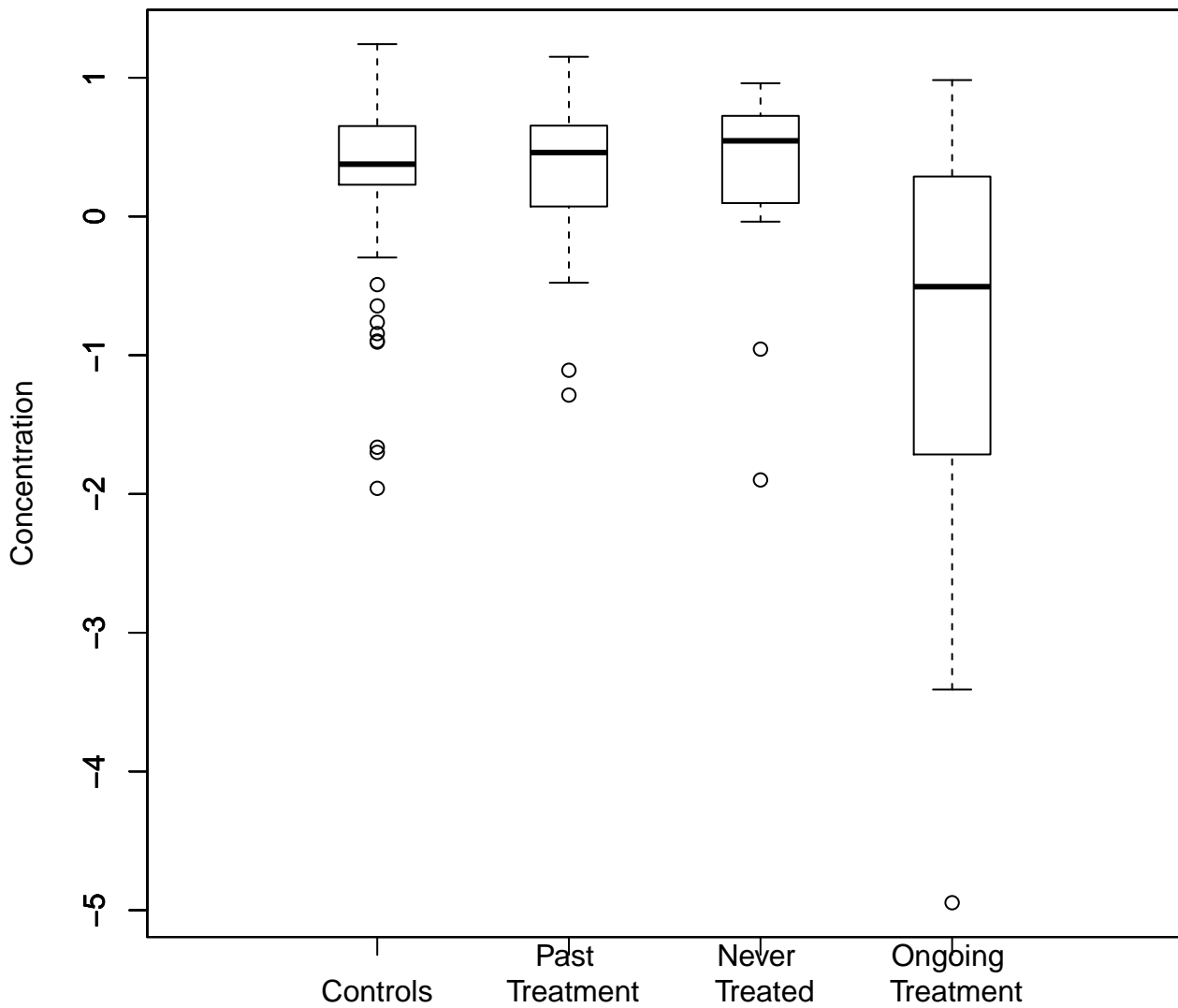
X - 17340



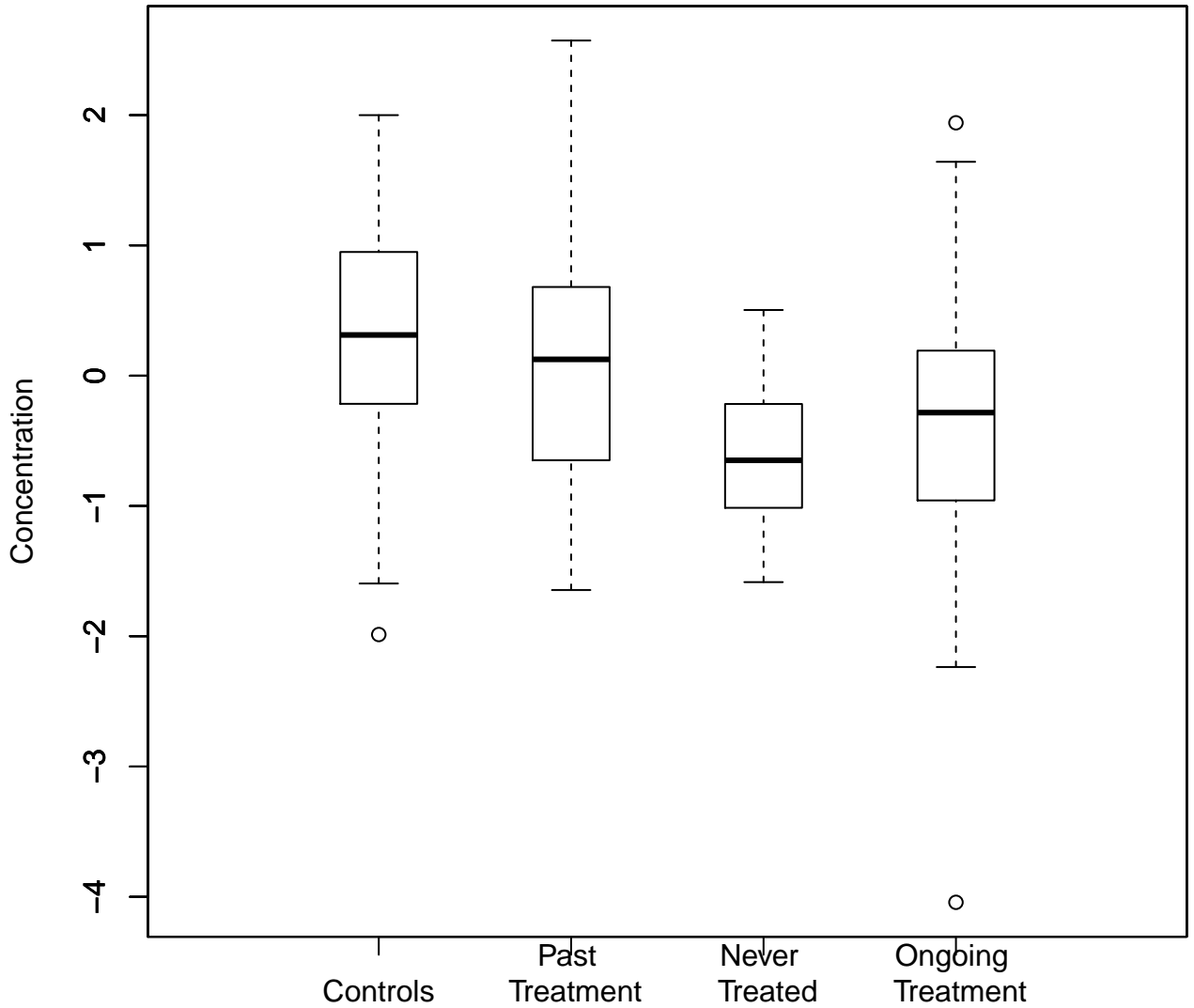
16 α -hydroxy DHEA 3-sulfate



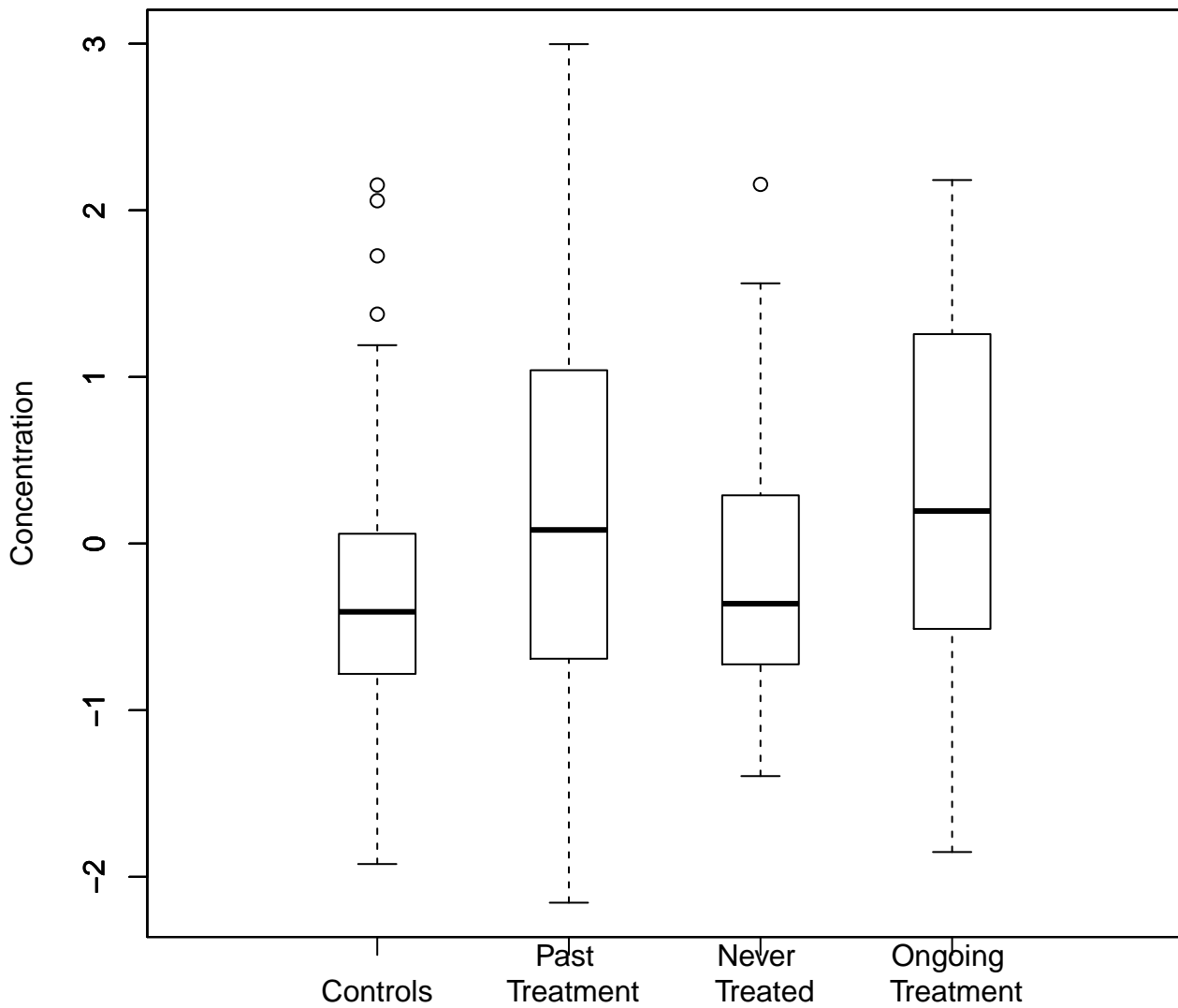
cortisone



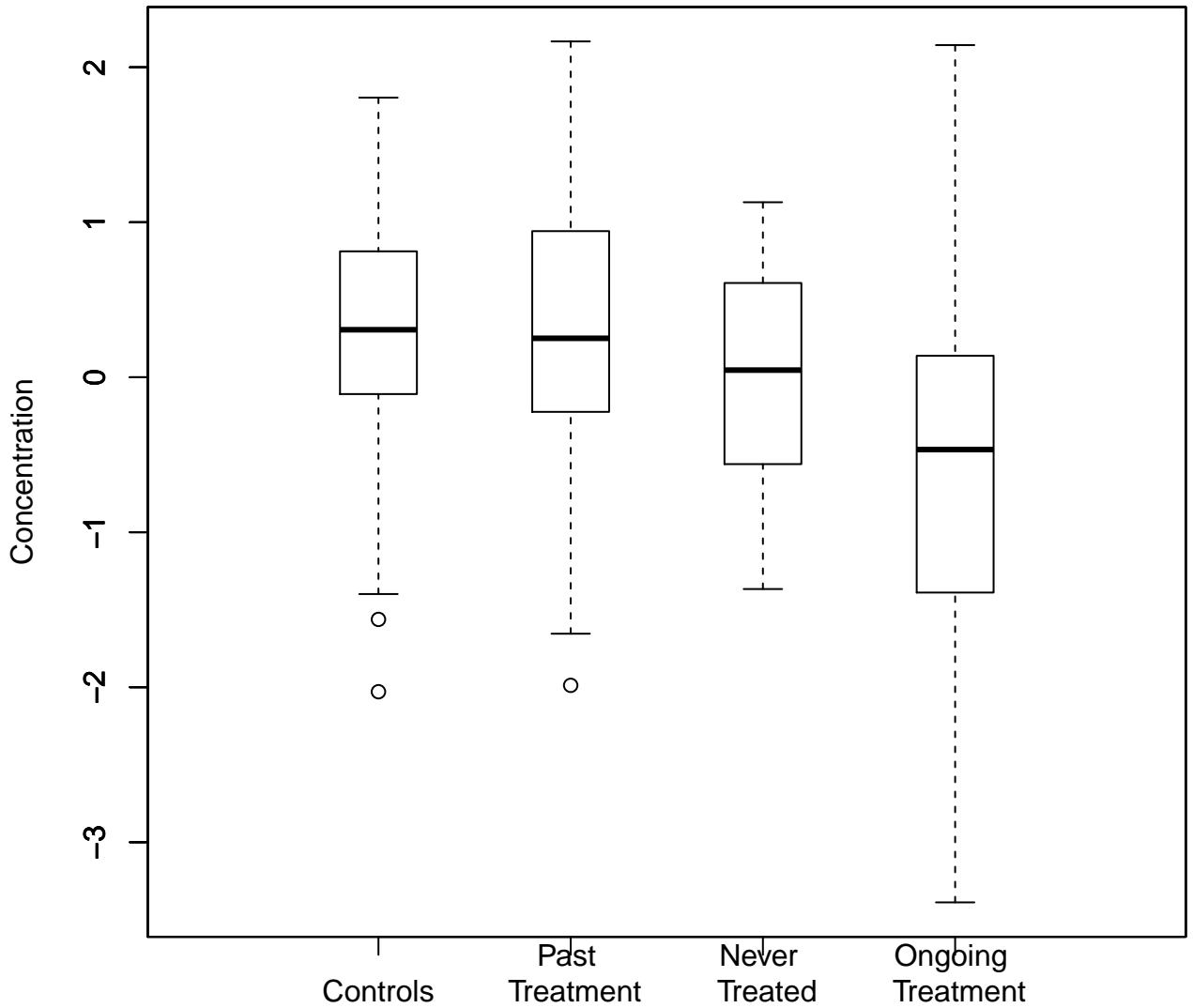
3-methyl-2-oxovalerate



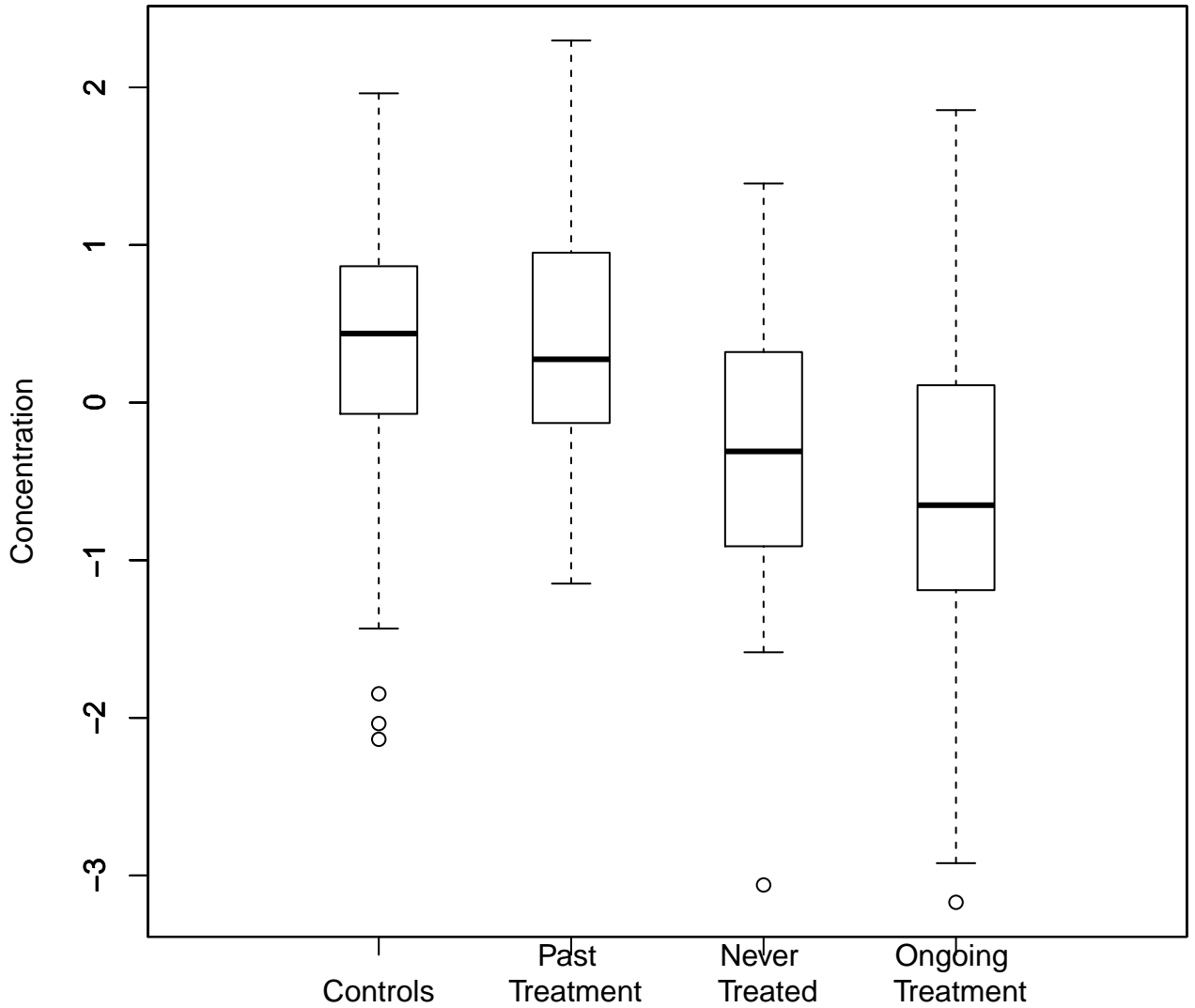
prolylglycine



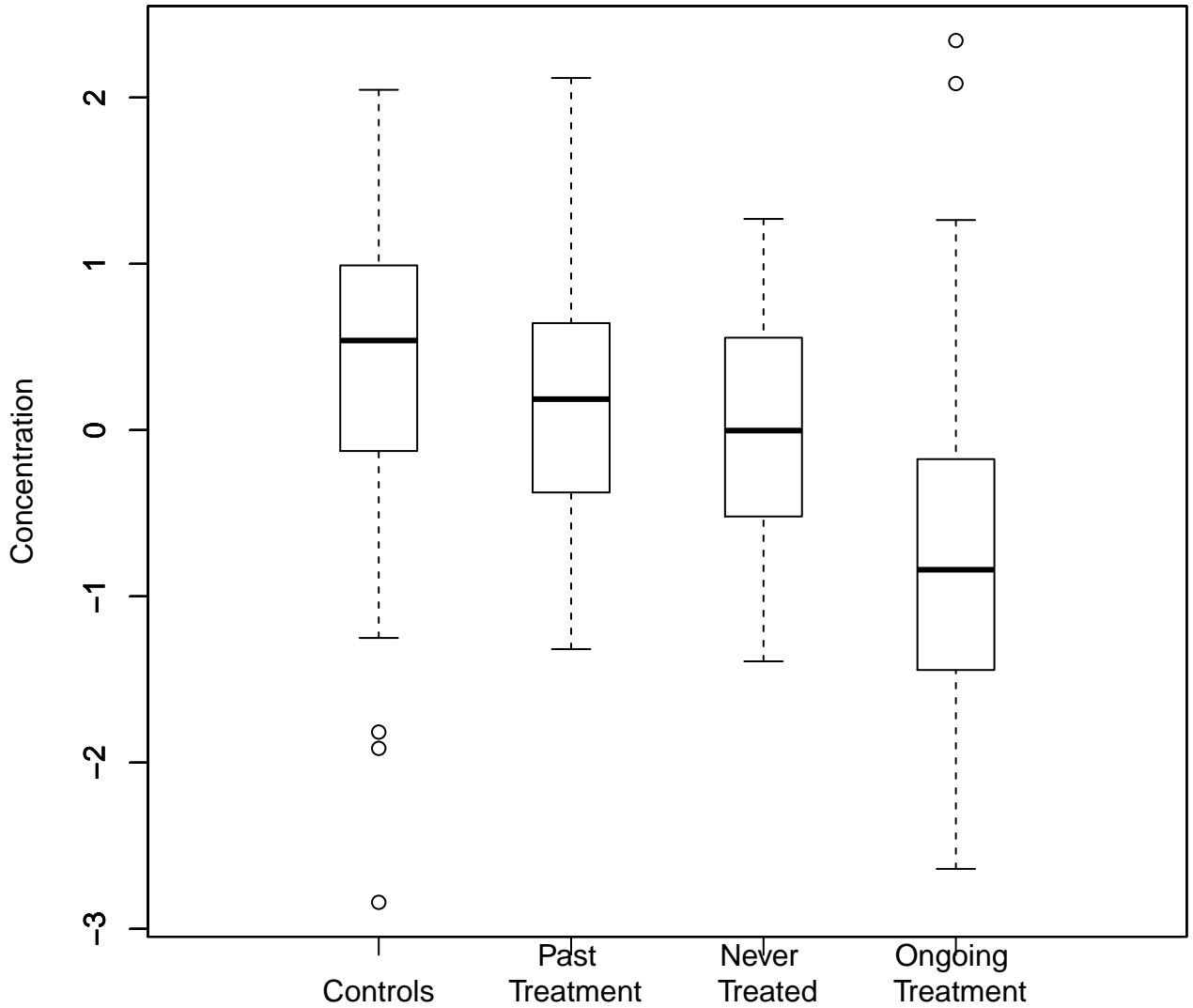
etiocholanolone glucuronide



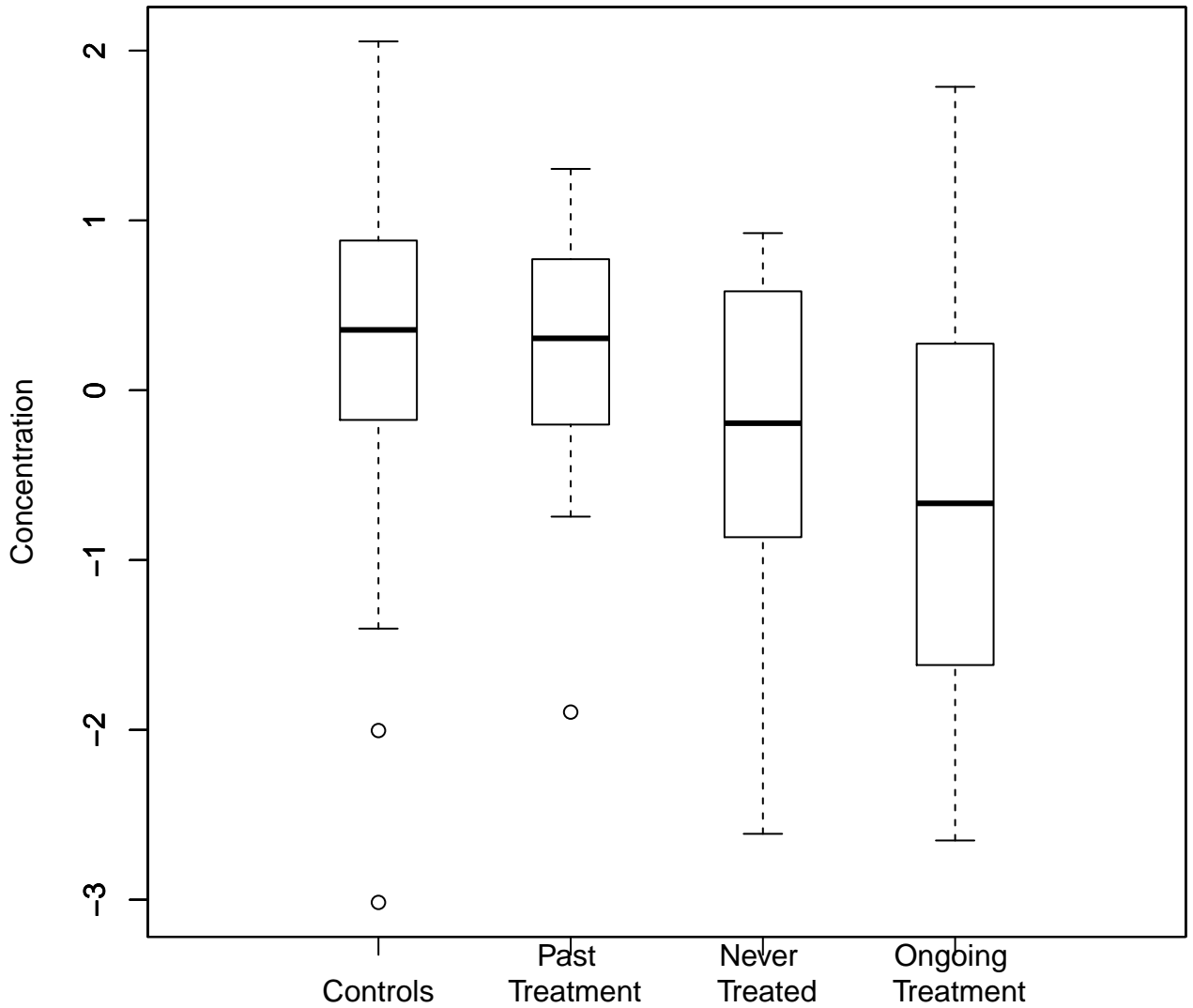
X - 21441



21-hydroxypregnenolone disulfate



4-androsten-3alpha,17alpha-diol monosulfate (2)



pregnenolone sulfate

