

Table S1. Pre-bronchodilator spirometry between baseline and week 12, as assessed by Wilcoxon signed rank test.

Variables	Baseline median (IQR)	Post intervention median (IQR)	p value
Lung function			
Pre BD FEV1 (litres)	2.91 (2.39, 3.37)	3.2 (2.5, 3.6)	0.173
Pre BD FVC (litres)	3.98 (3.12, 4.32)	4.29 (3.36, 4.42)	0.028*
FEV1/FVC ratio	77 (74, 82)	77 (72, 82)	0.916
% change FEV1 post BD	8 (3.8, 13.3)	3 (2.3, 6.3)	0.043*

*= statistically significant.

Abbreviations: BD; bronchodilator, FEV1; forced expiratory volume in 1 second, FVC; forced vital capacity, IQR; interquartile range

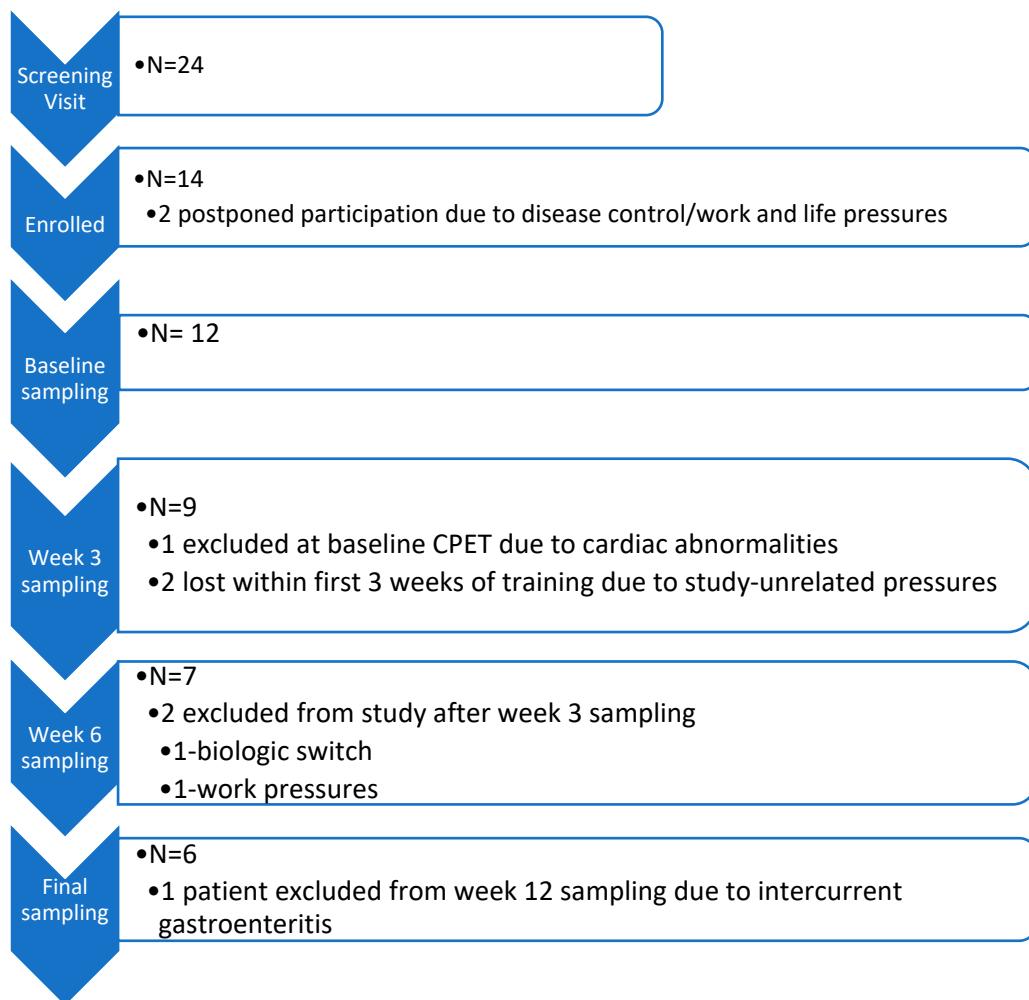


Figure S1. Flow chart of patient enrolment and sampling, including numbers and reasons for withdrawal/exclusion

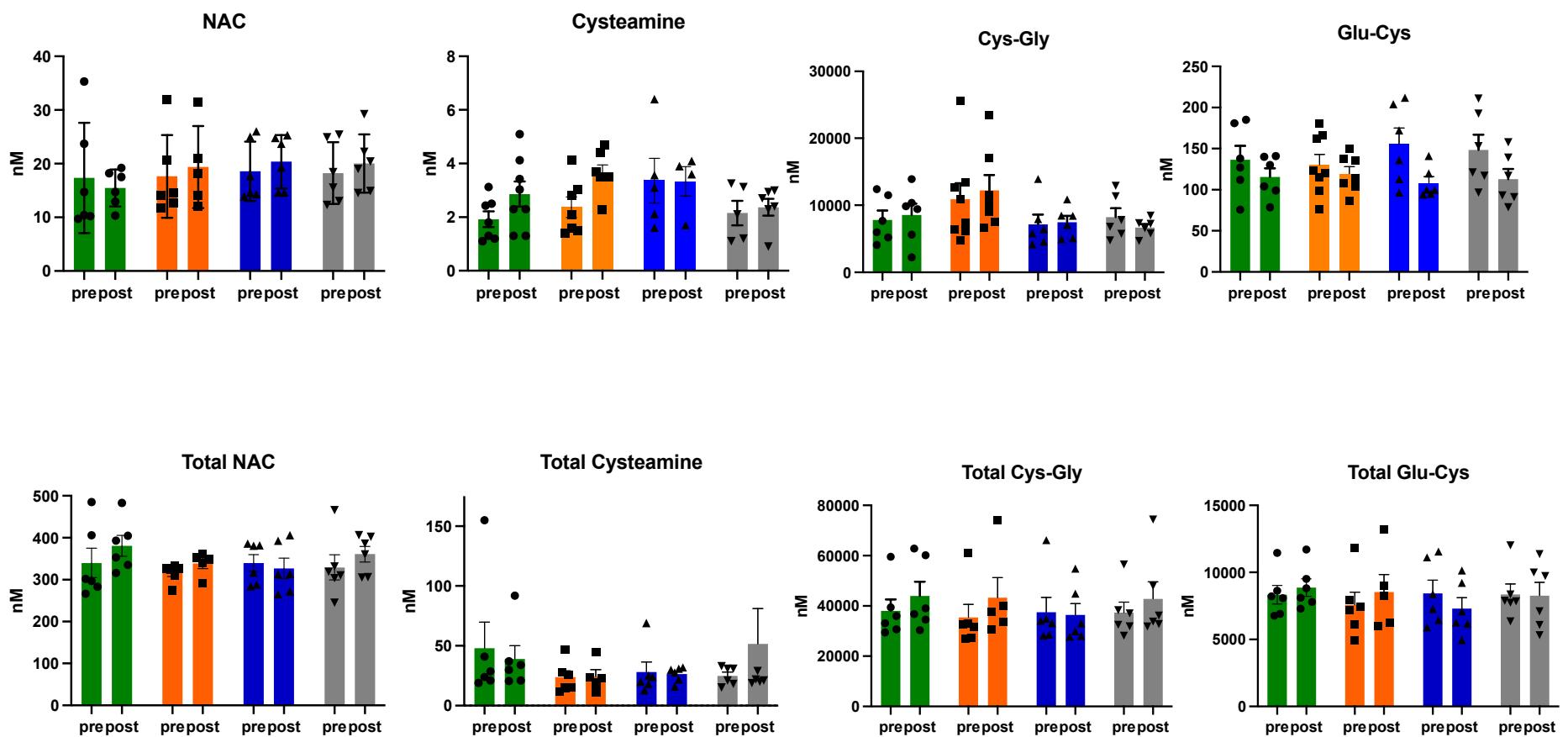


Figure S2 Changes in the pattern of responses of the free and total redox metabolome. Data presented for n=6 before and after acute physiological challenge of a cardiopulmonary exercise test, presented as mean and SEM, with individual data plotted. Data presented in nM. Green bars= baseline, orange bars= week 3, blue bars = week 6 and grey bars =week 12. Abbreviations: NAC; N-acetylcysteine, Cys-Gly; cysteinylglycine; Glu-Cys; L-Glutamyl-L-Cysteine

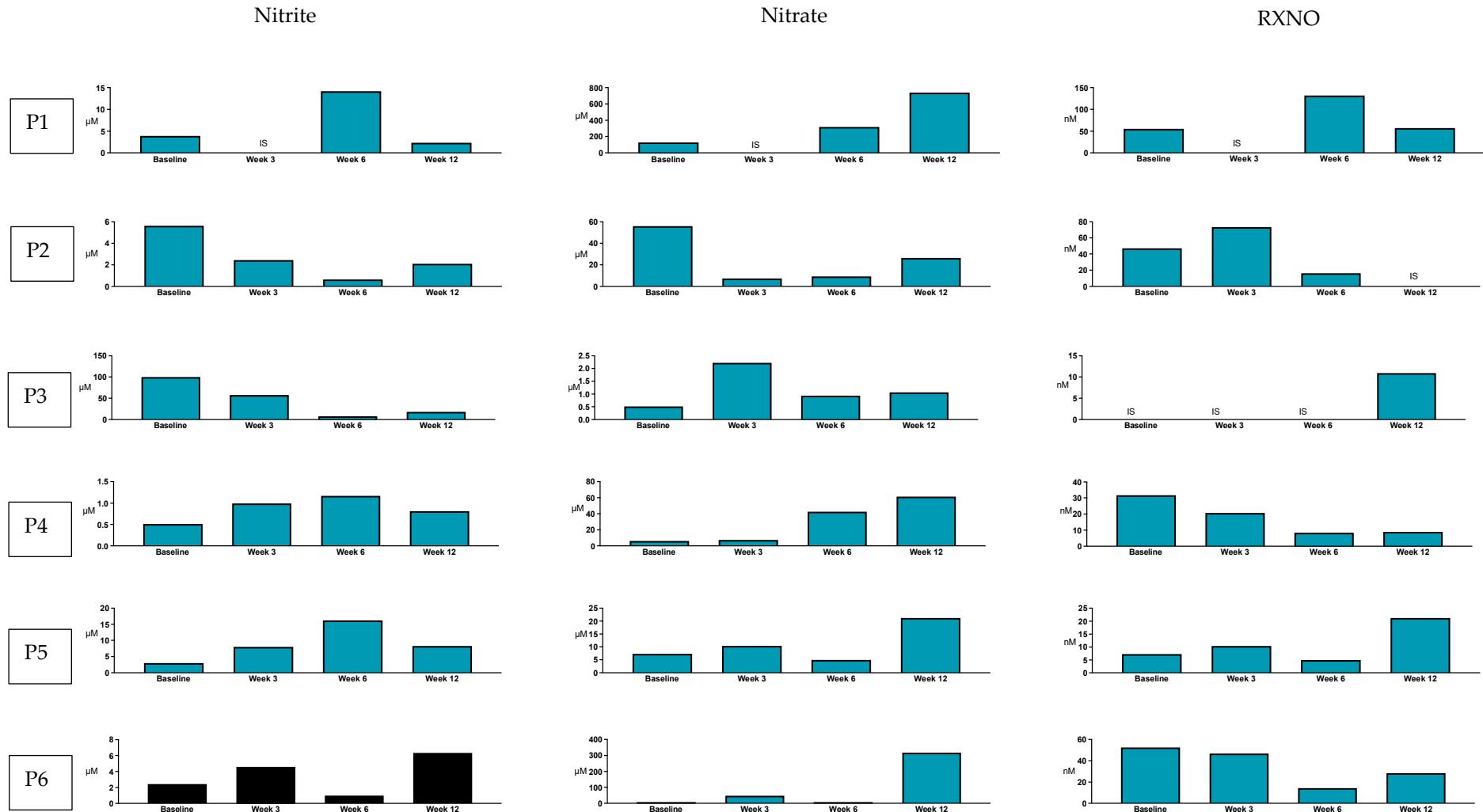
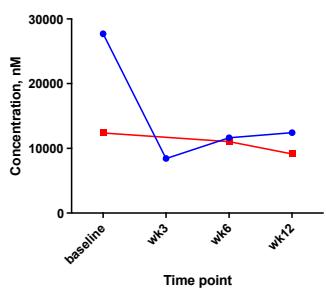
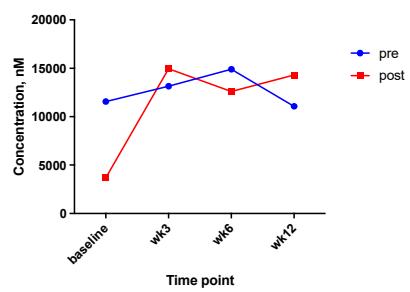


Figure S3. Pattern of airways nitroso-metabolic responses to exercise training, prior to acute exercise challenge, at baseline, week, 3, 6 and post intervention. Data presented for each patient (P1-6), units nitrite and nitrate = μM , RXNO=nM. Blue bar charts = nitrite, turquoise = nitrate and magenta = RXNO .Abbreviations RXNO; other nitrosospecies. IS = insufficient sample to quantify

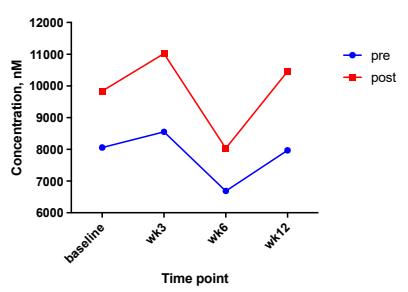
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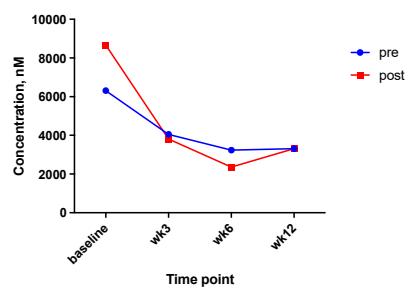
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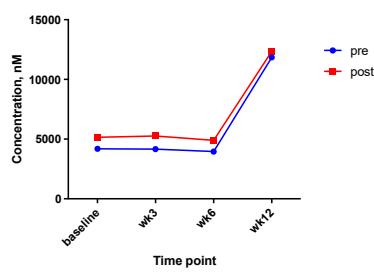
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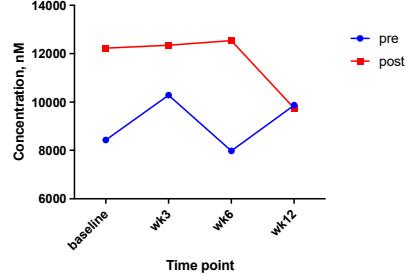
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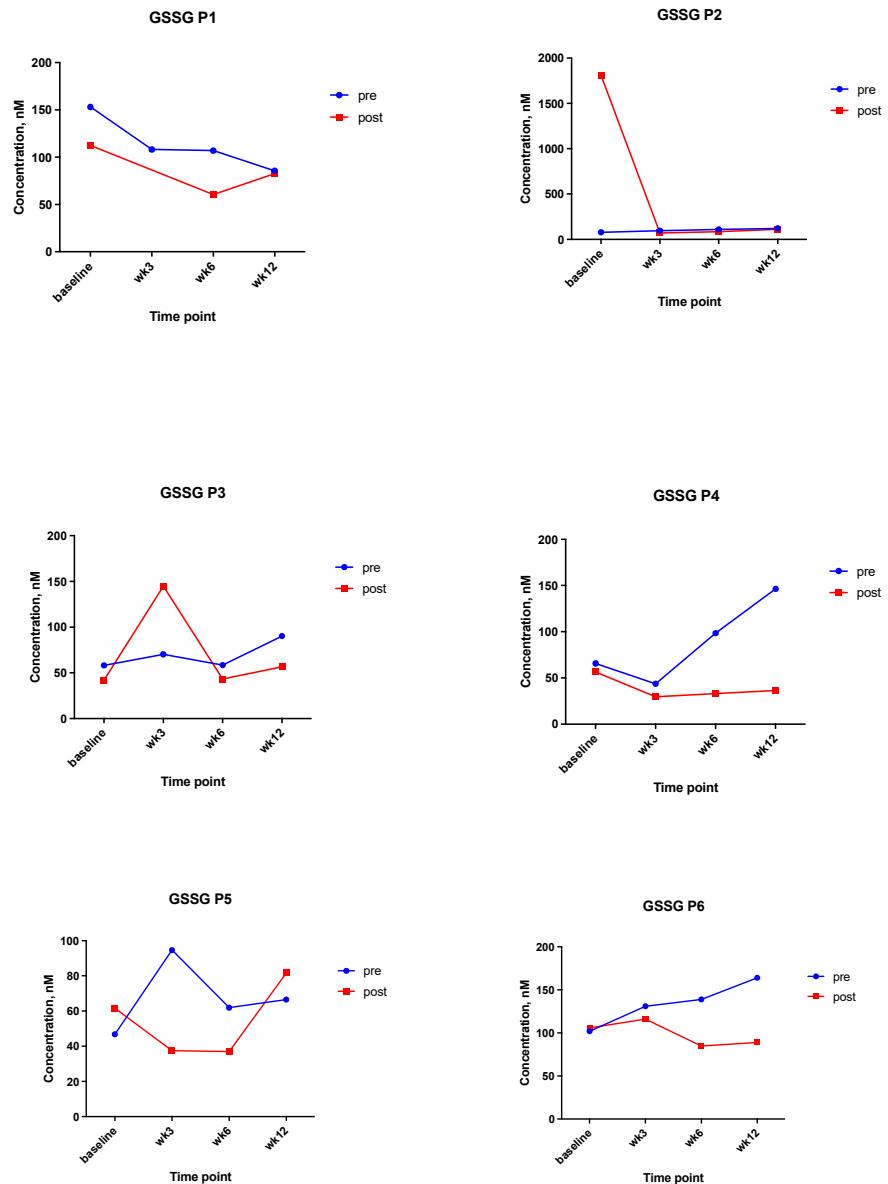


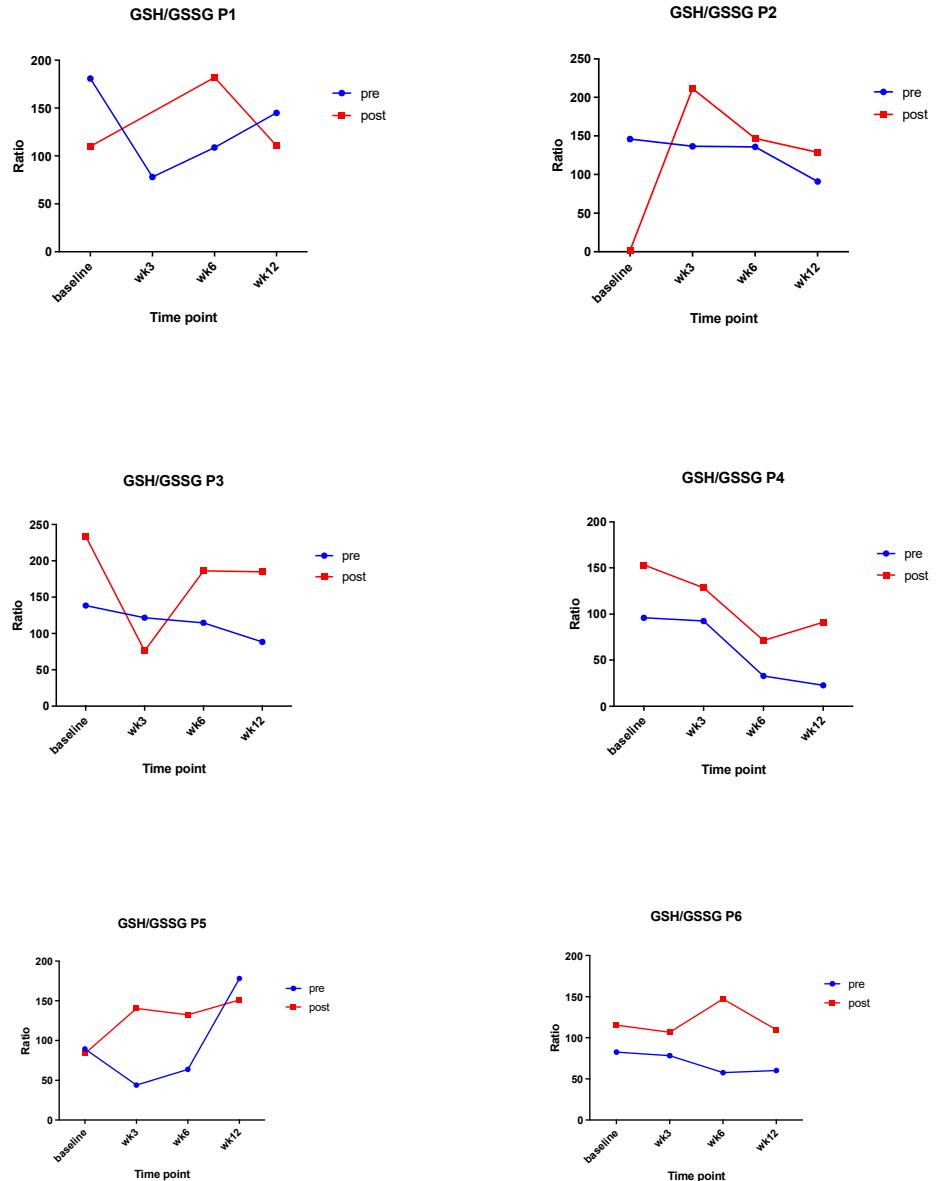
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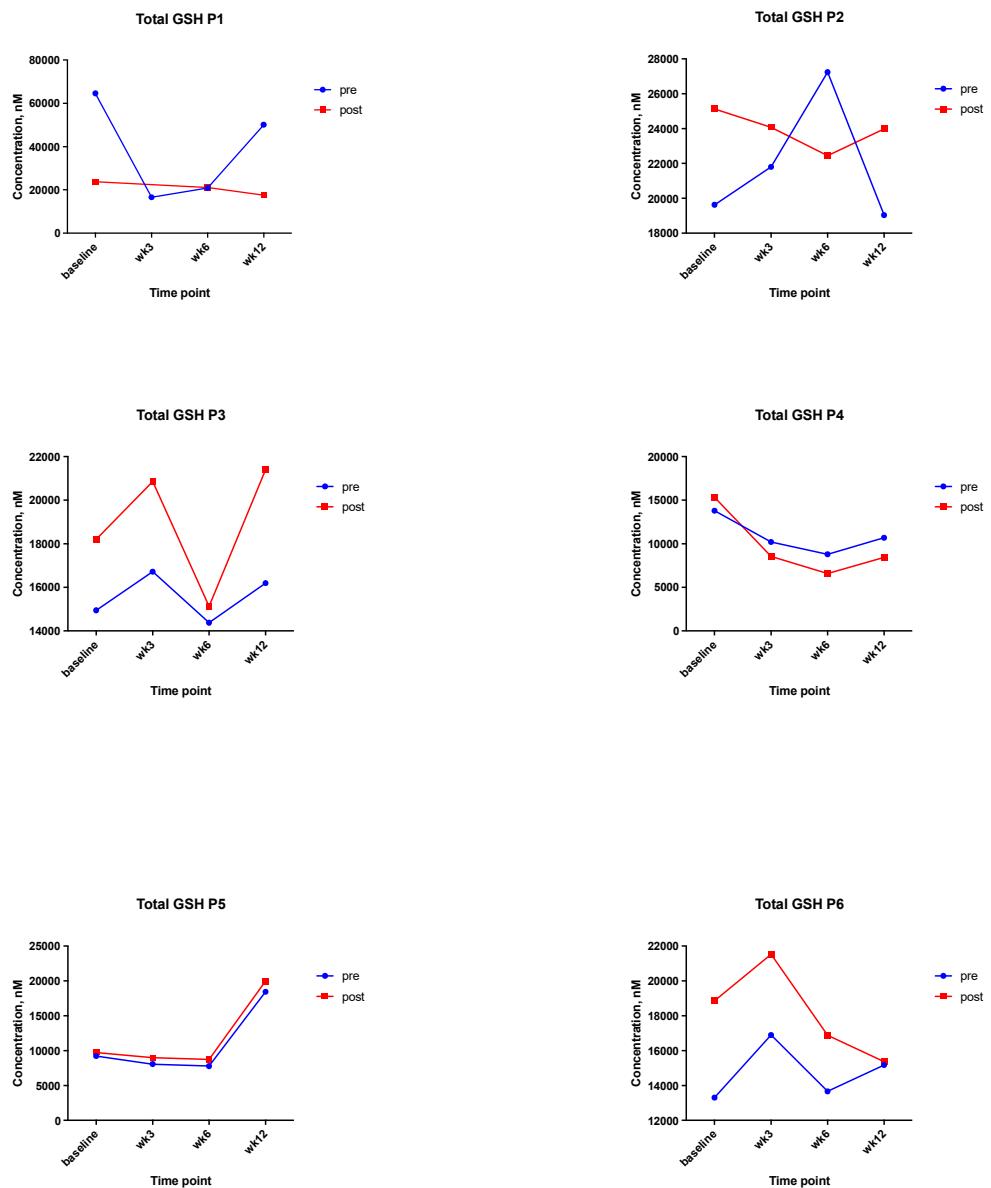


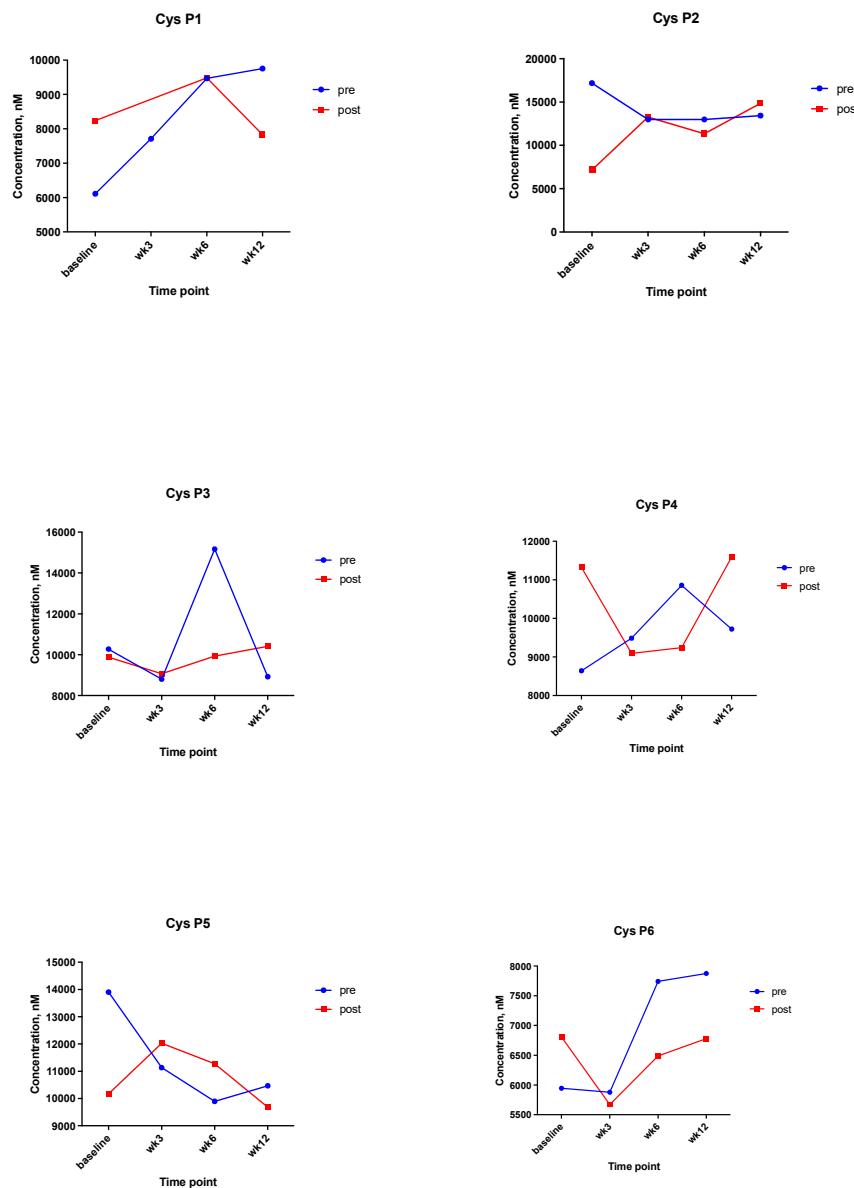
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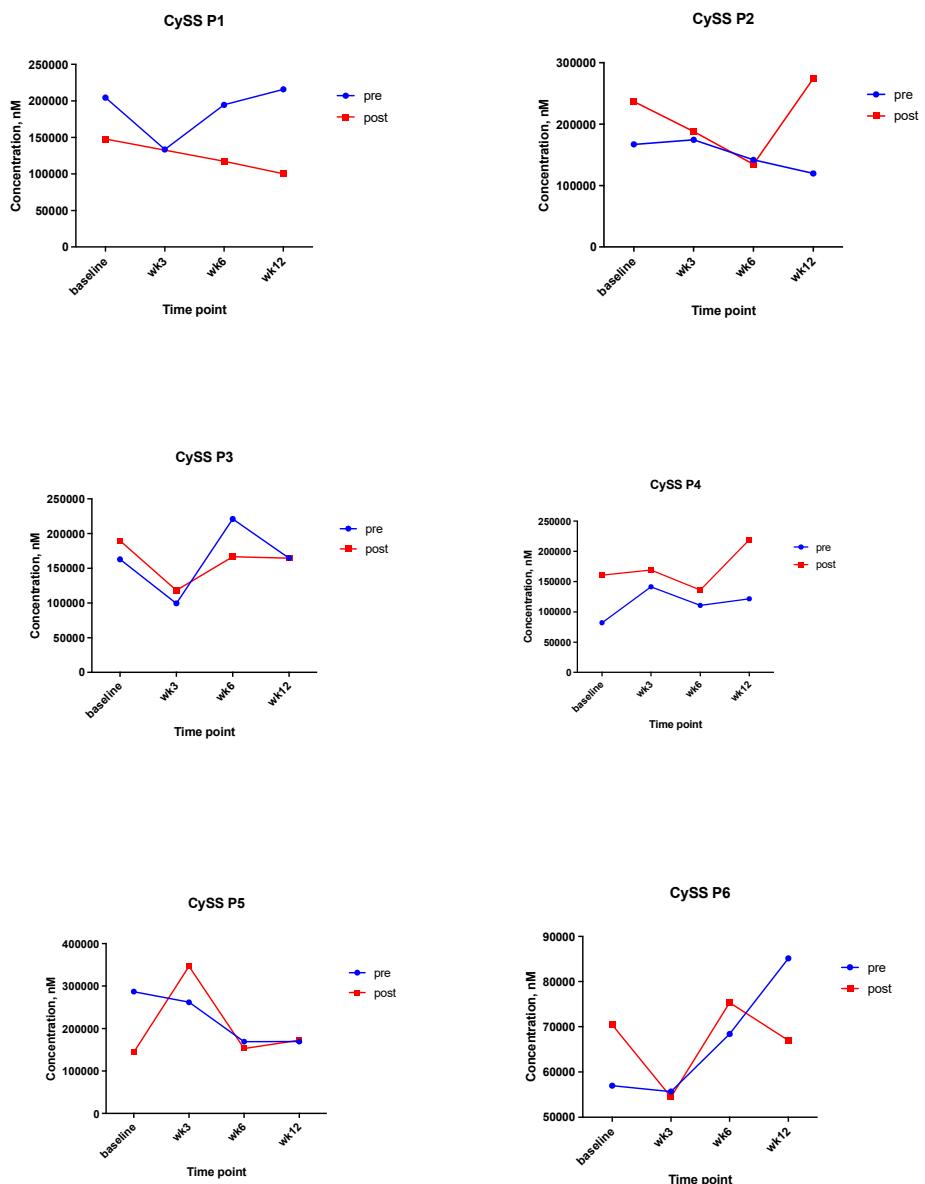


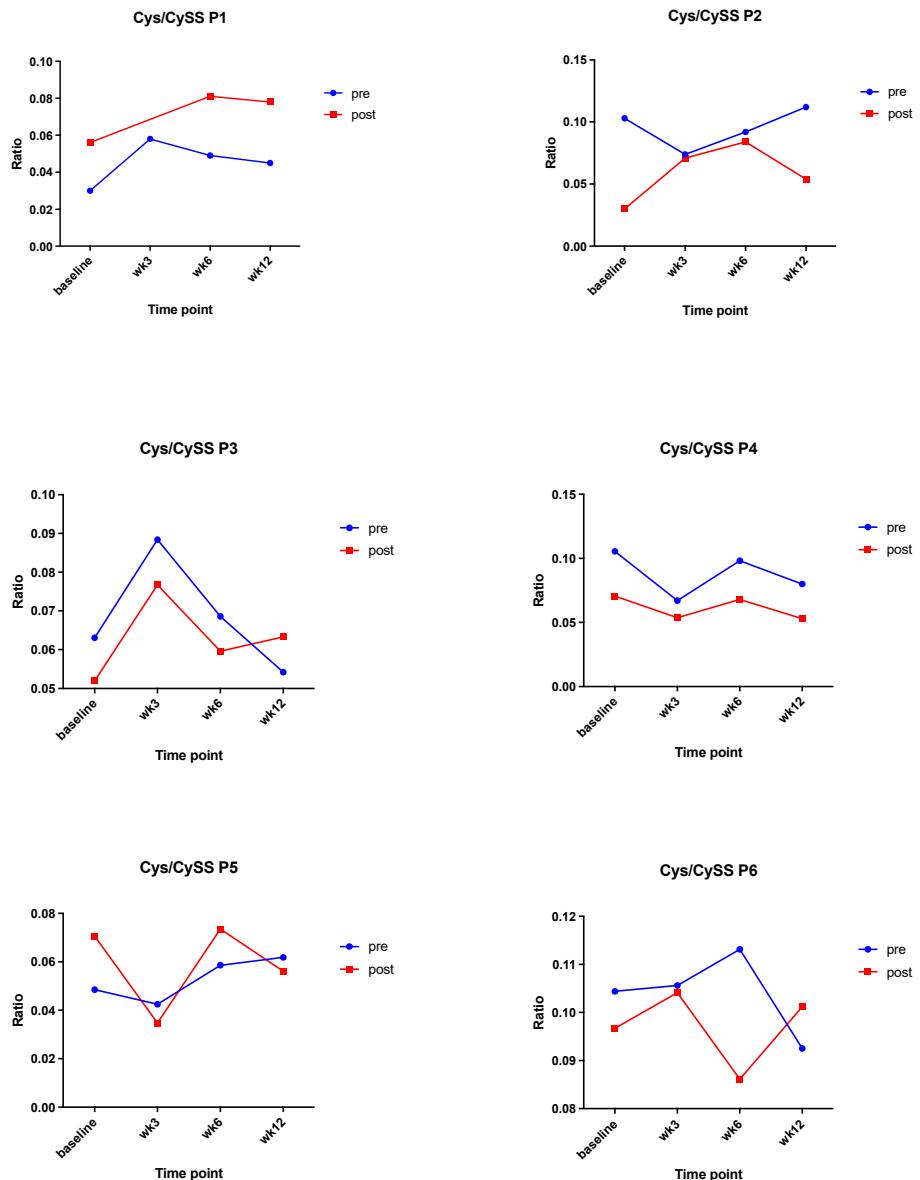


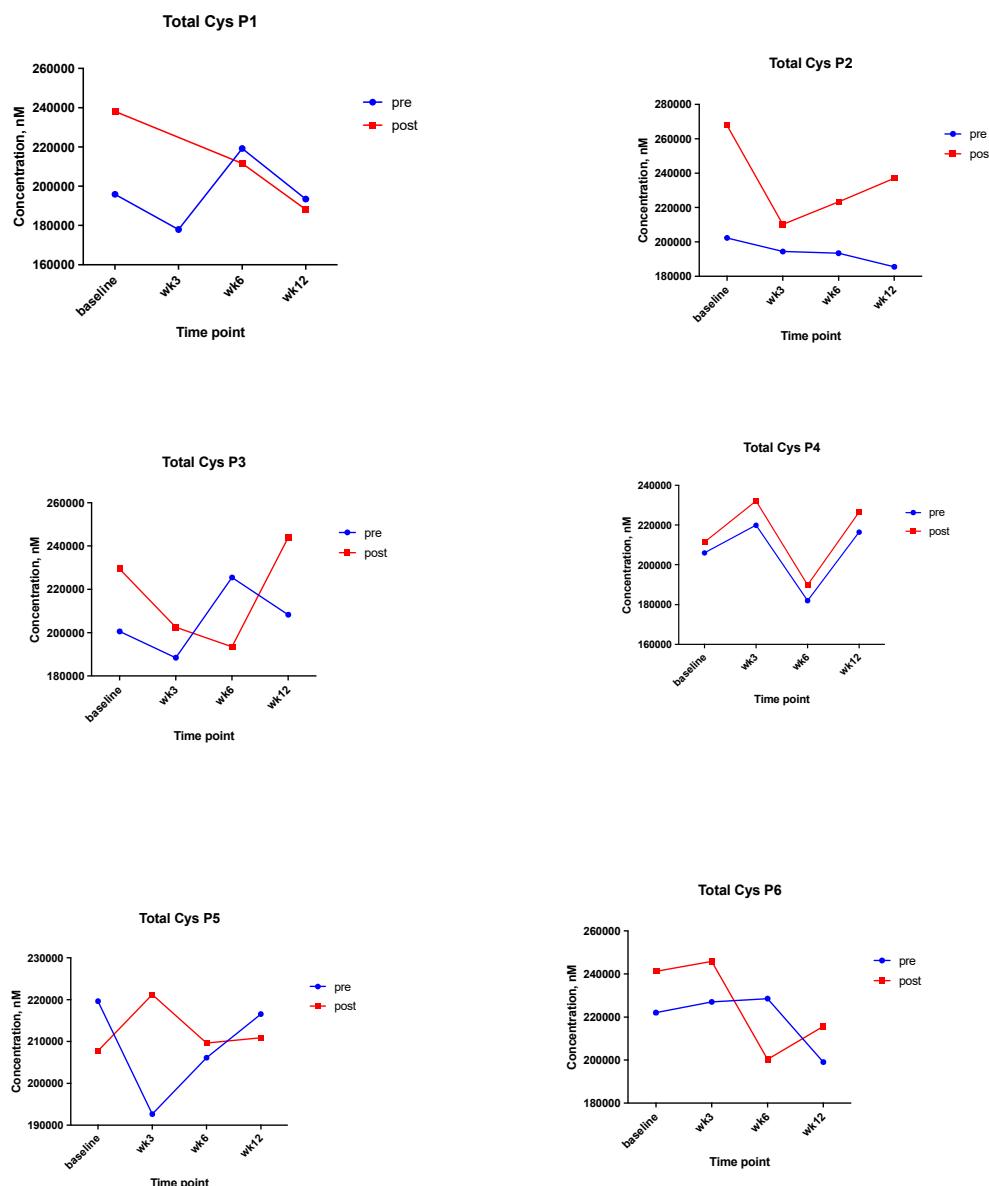


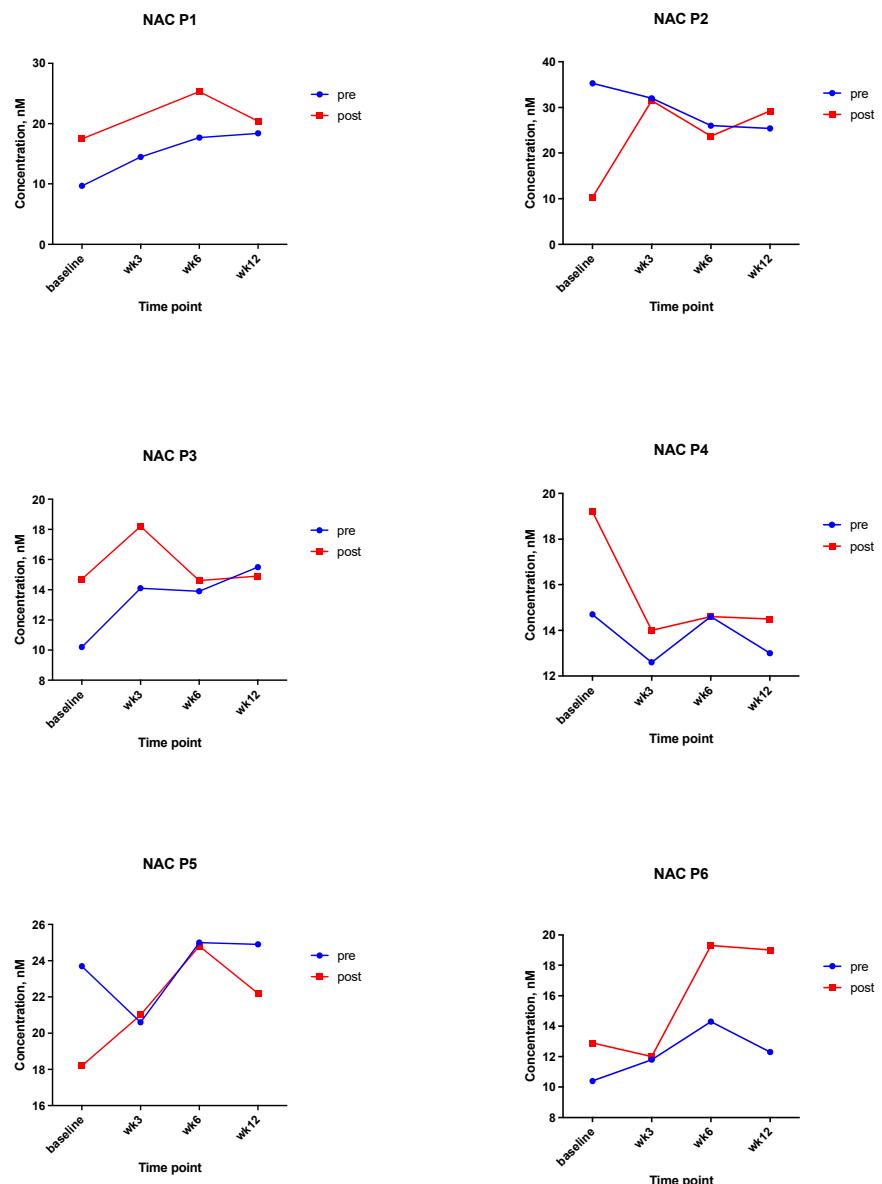


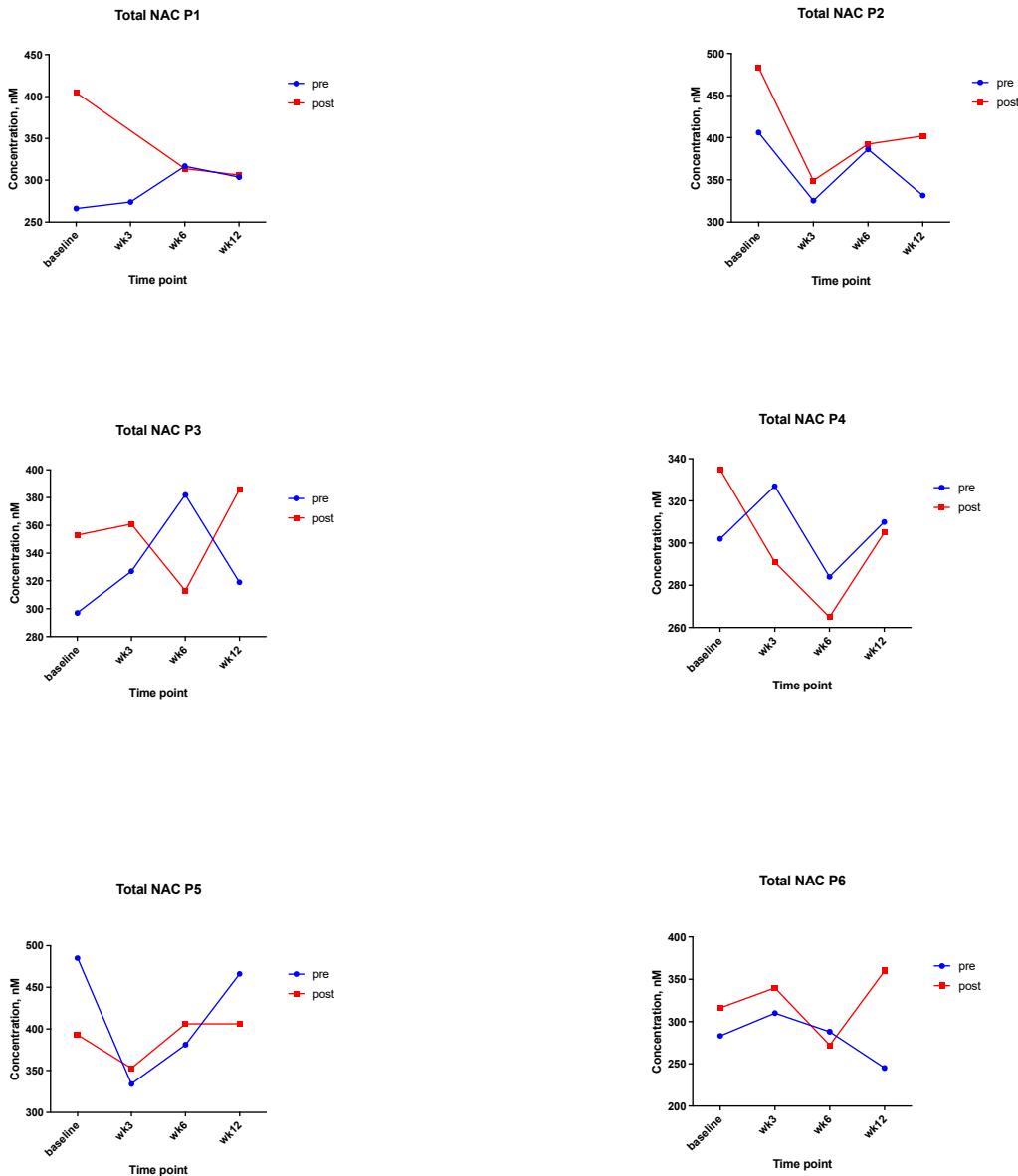


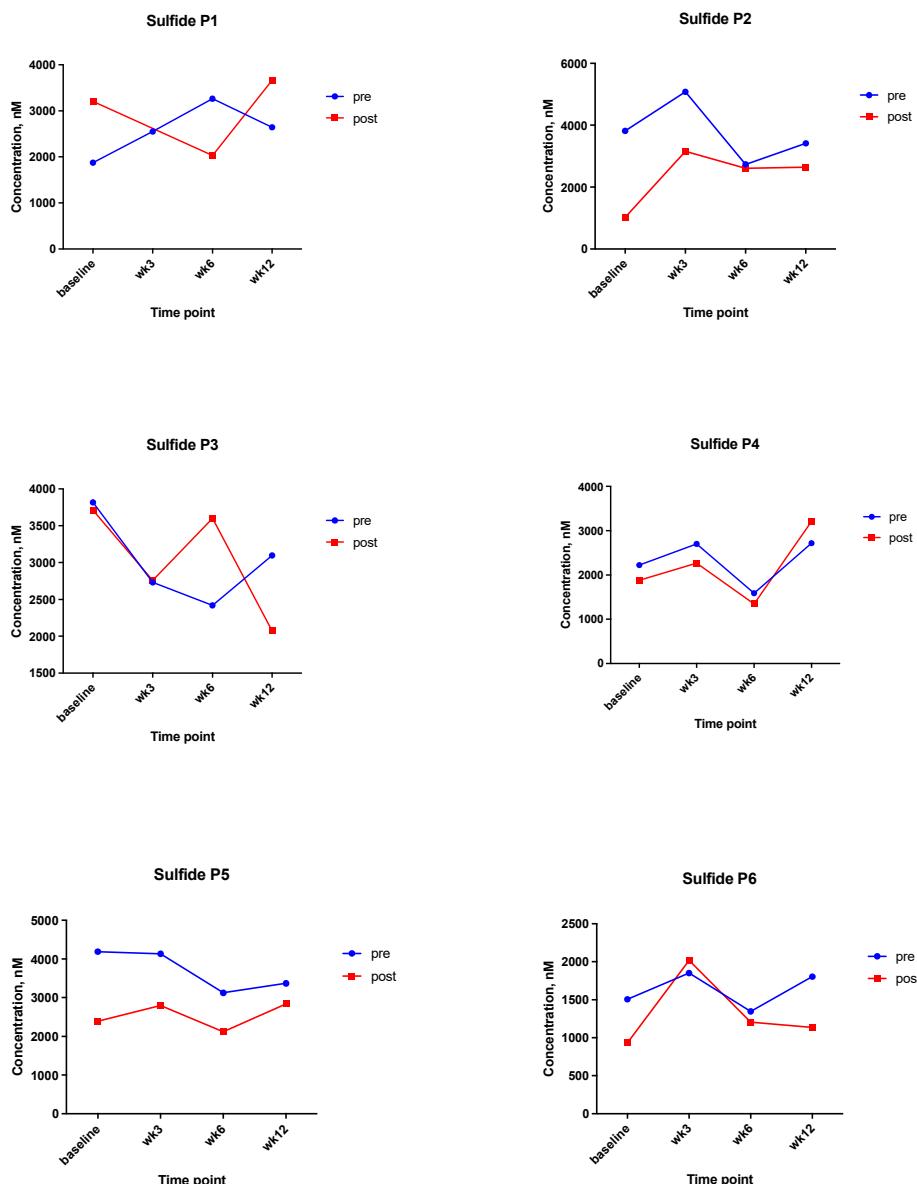


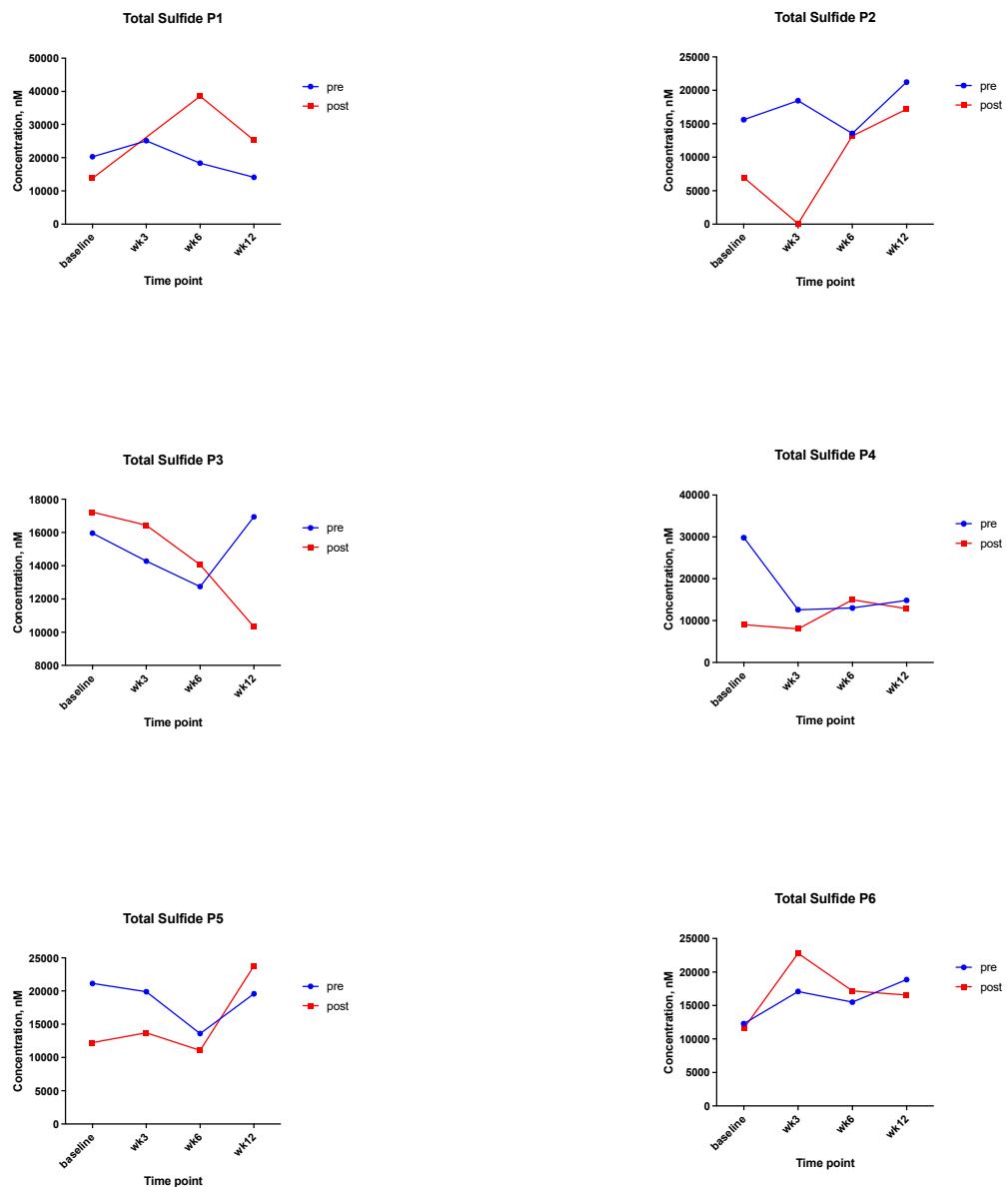




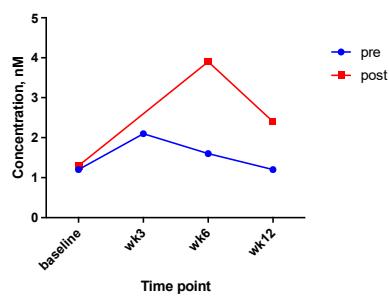




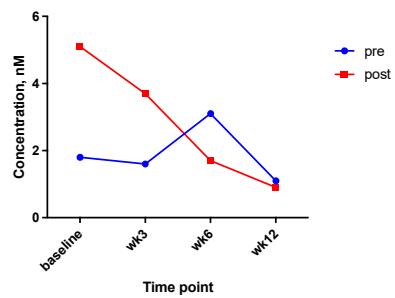




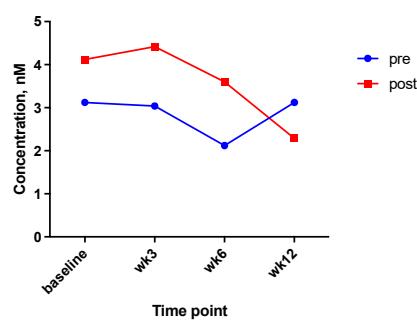
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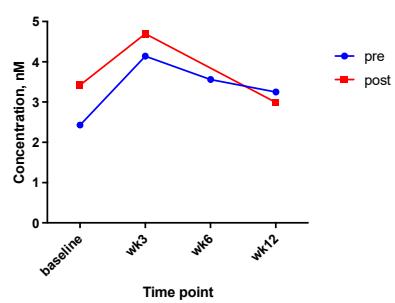
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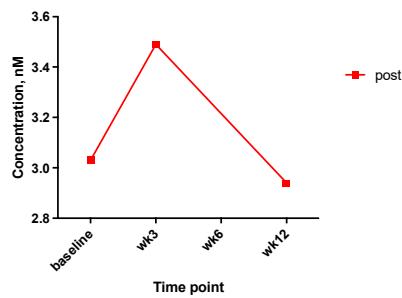
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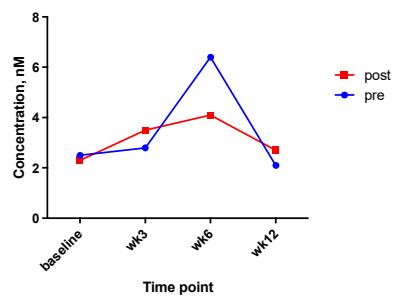
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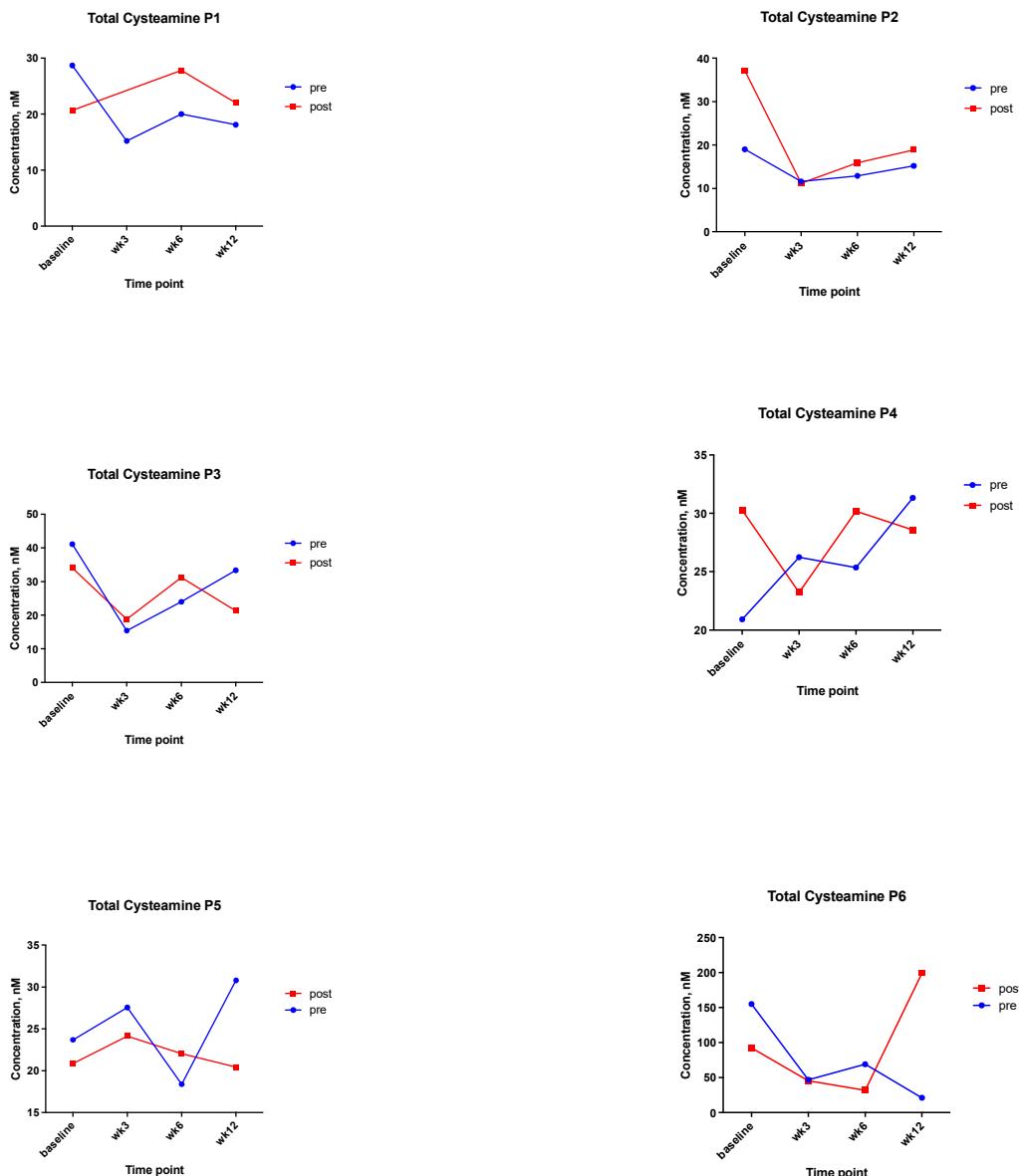


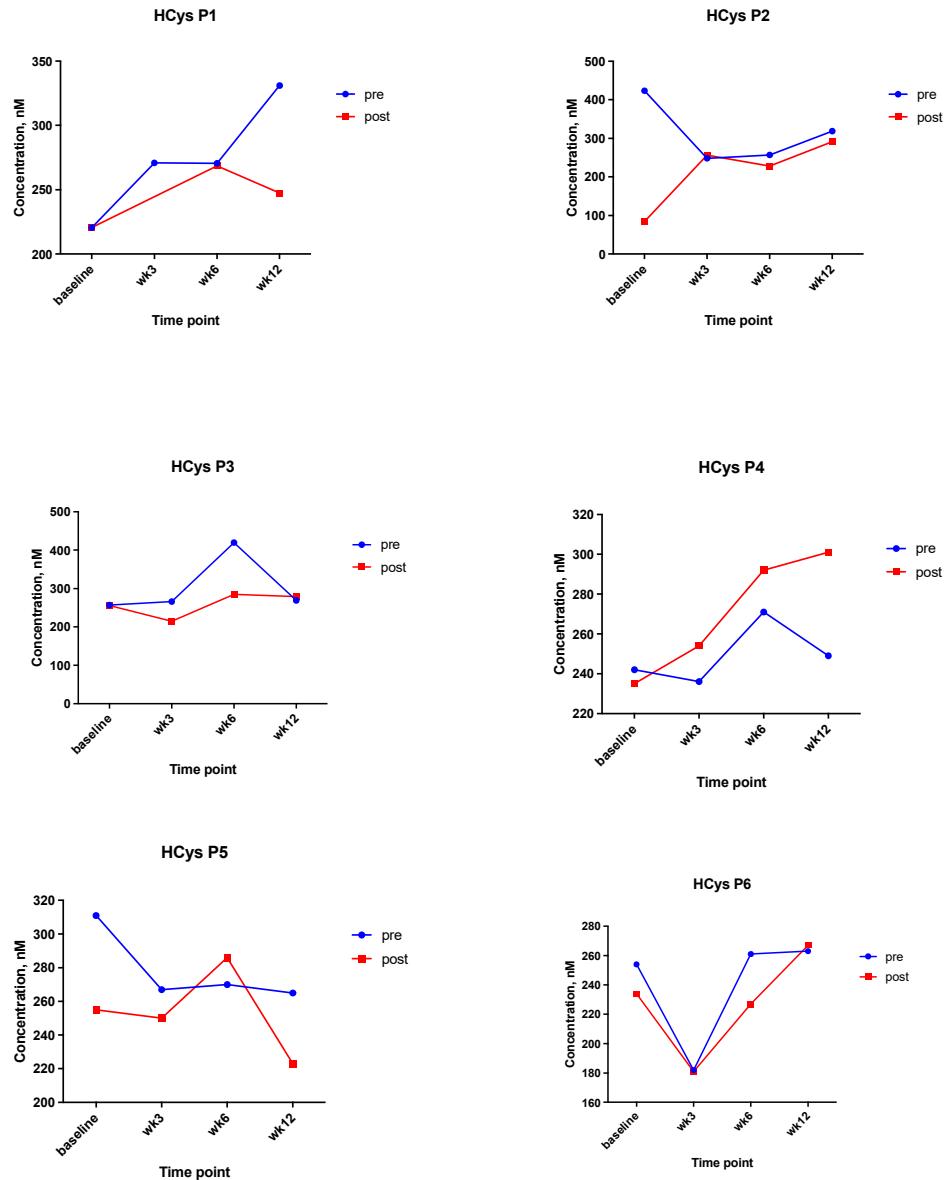
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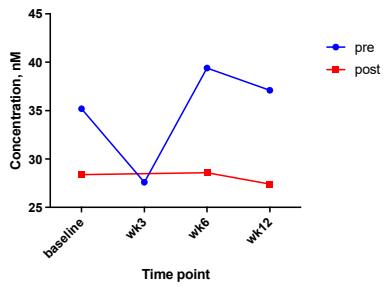
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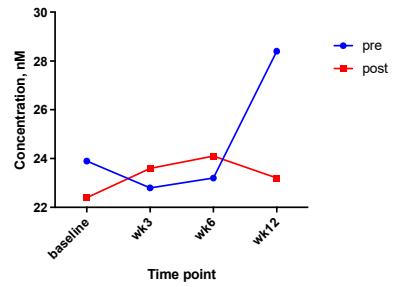




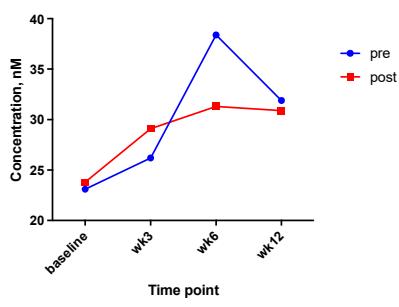
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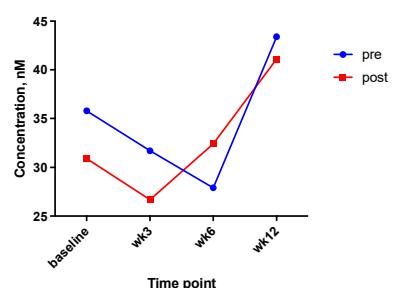
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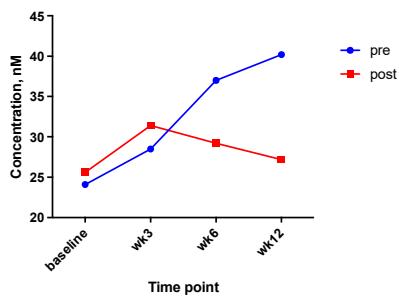
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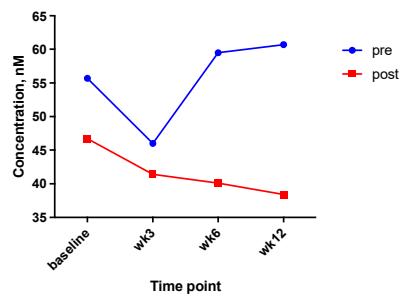
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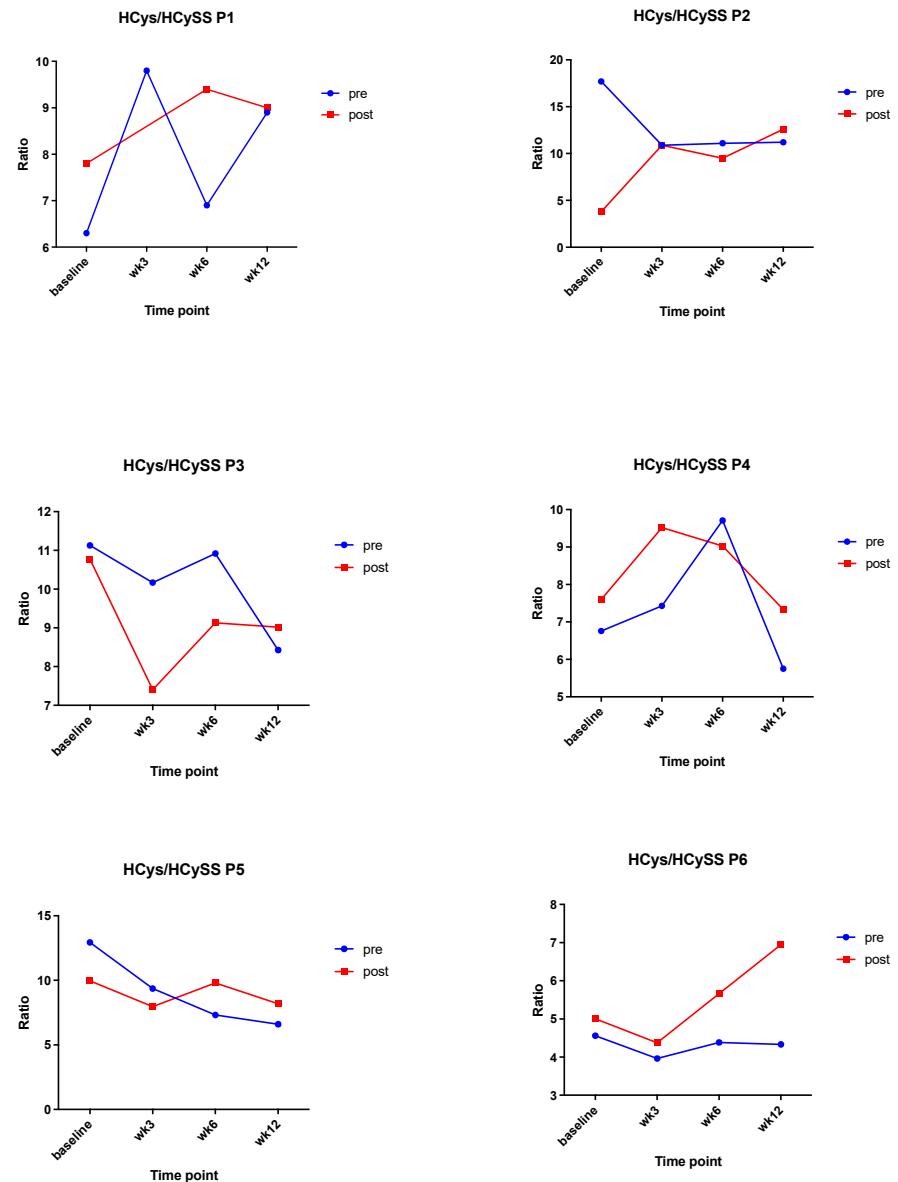


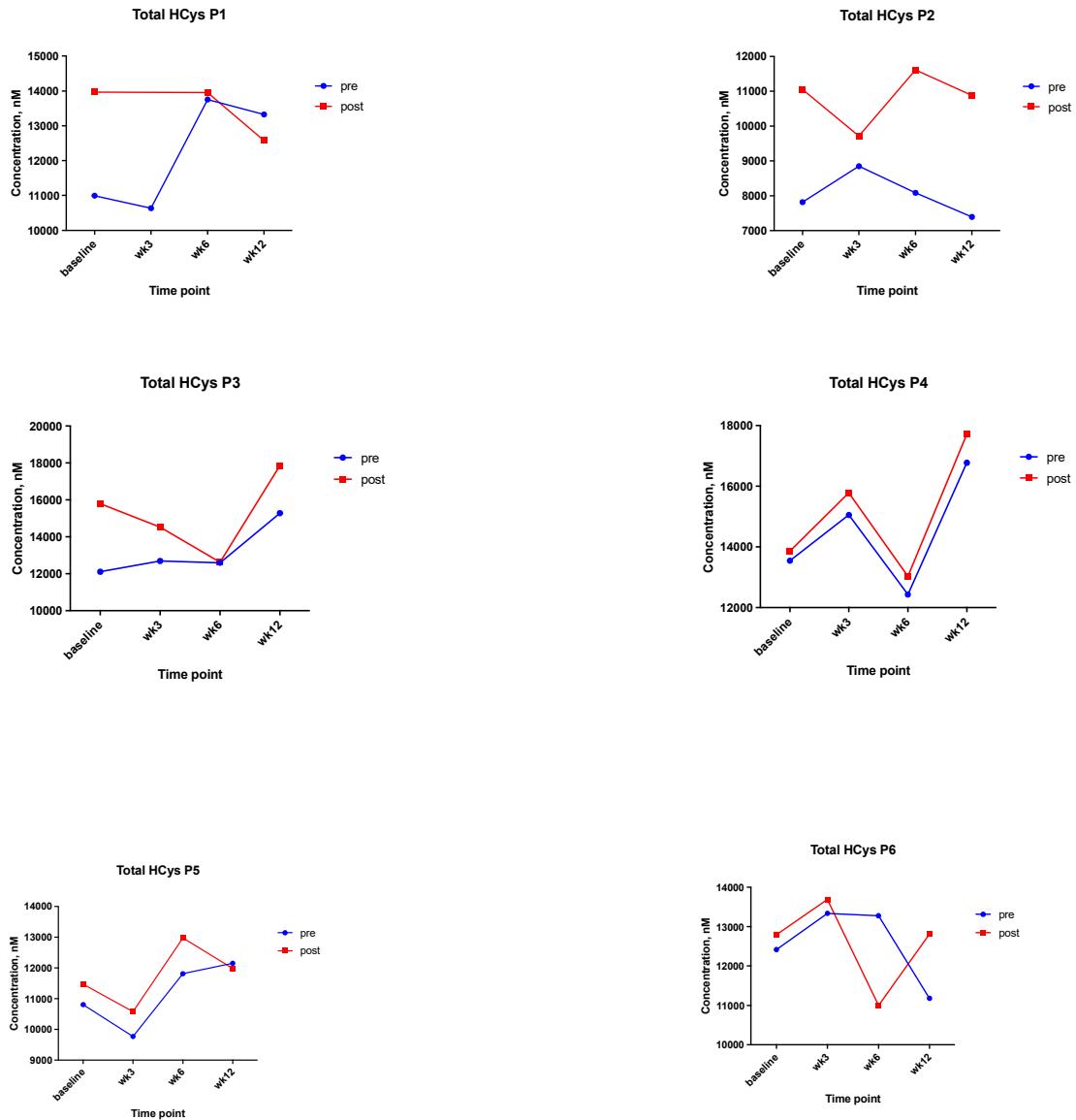
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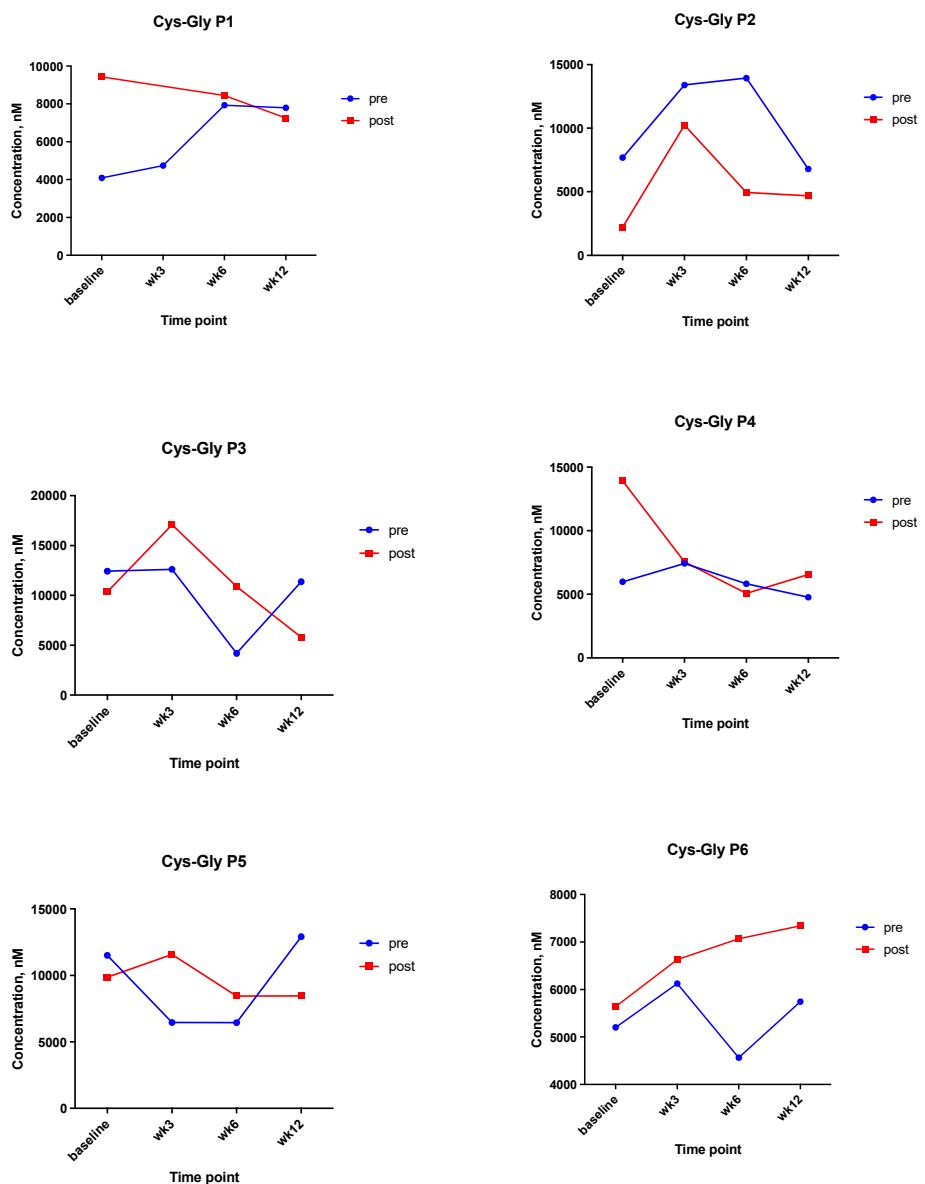


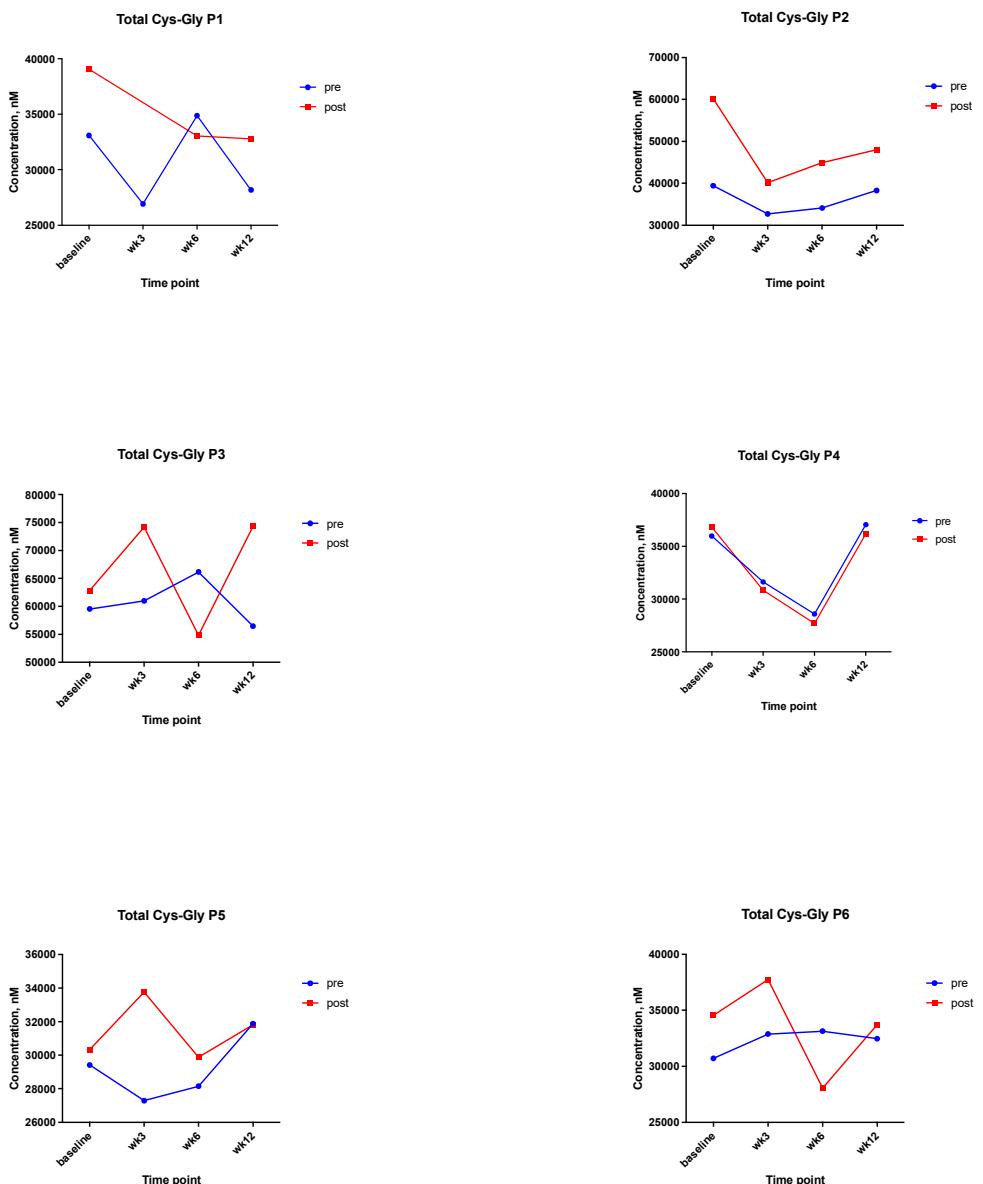
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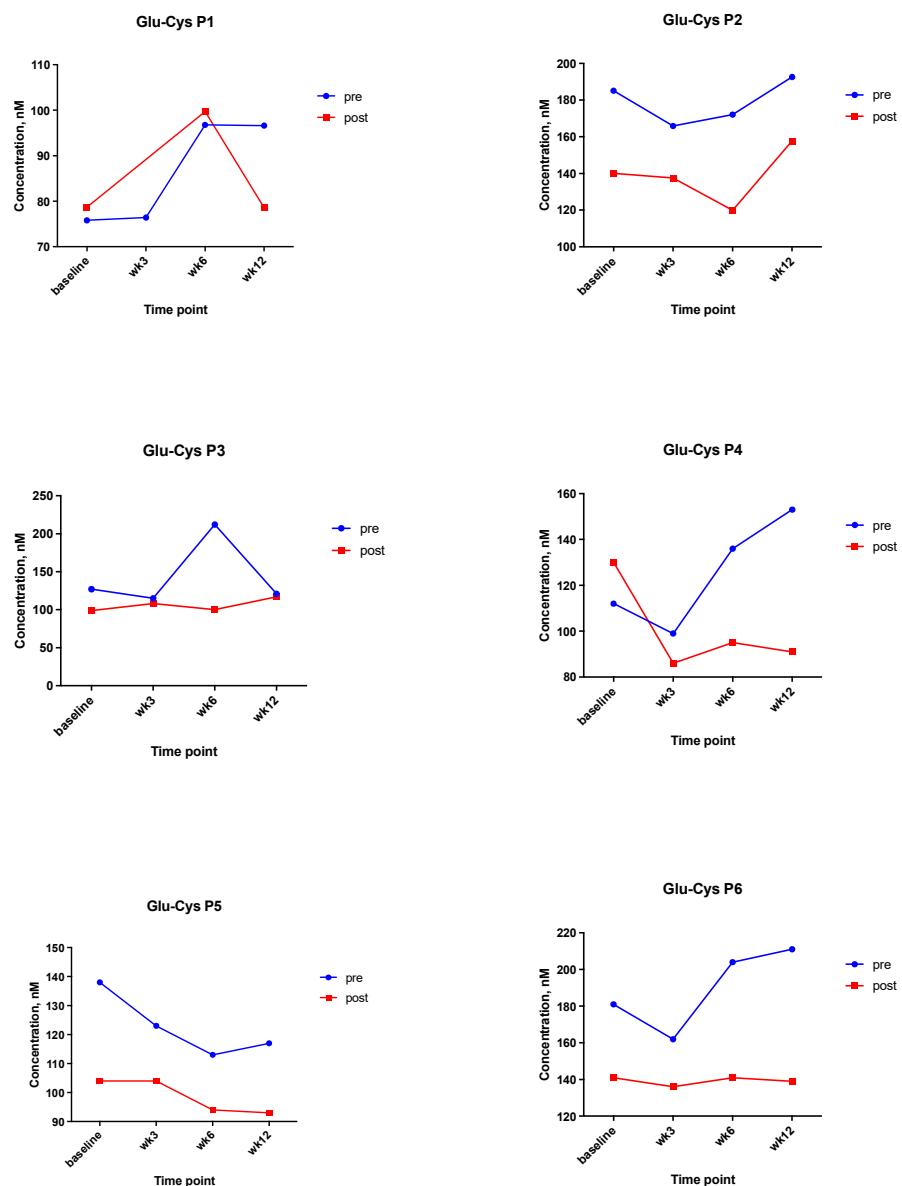












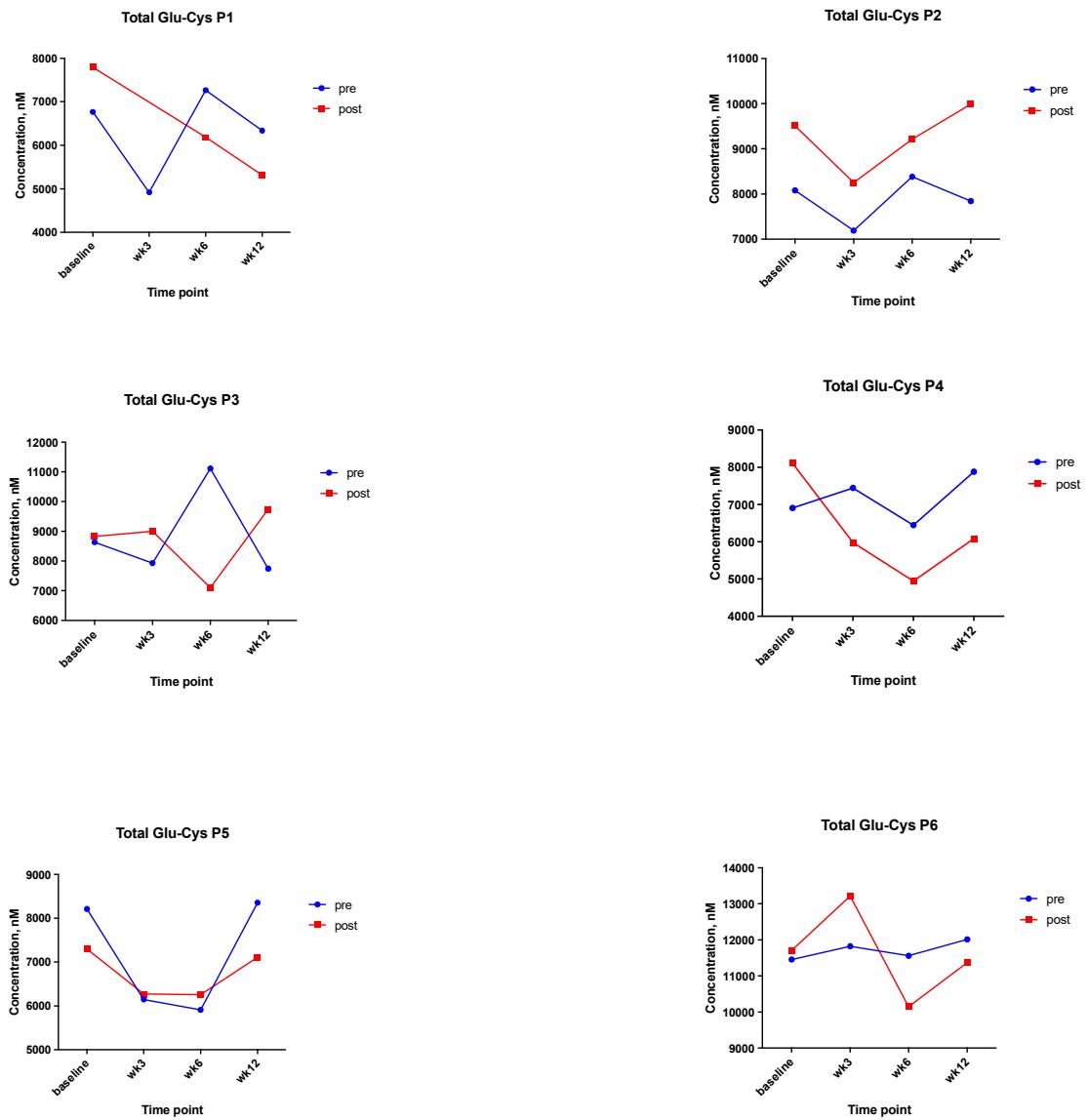


Figure S4 Individual responses of the free and total thiol metabolome to exercise. Data presented for individual patients (n=6). Red line = pre acute exercise challenge, blue line = post acute exercise challenge. Abbreviations GSH: reduced glutathione; GSSG: oxidised glutathione; cys:cysteine, cyss: cystine, hcys: homocysteine, hcyss:homocystine NAC; N-acetylcysteine, Cys-Gly; cysteinylglycine; Glu-Cys; L-Glutamyl-L-Cysteine

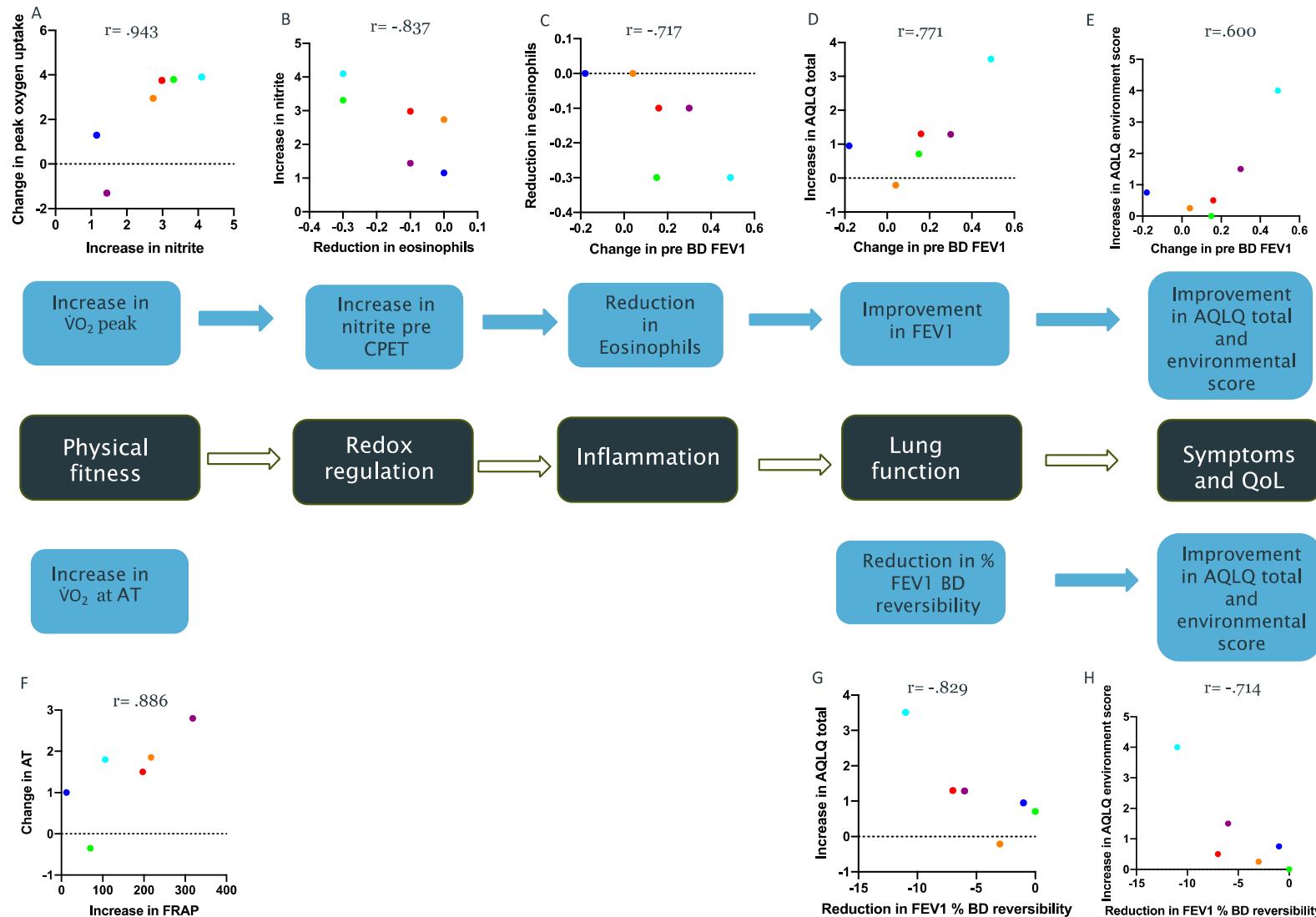
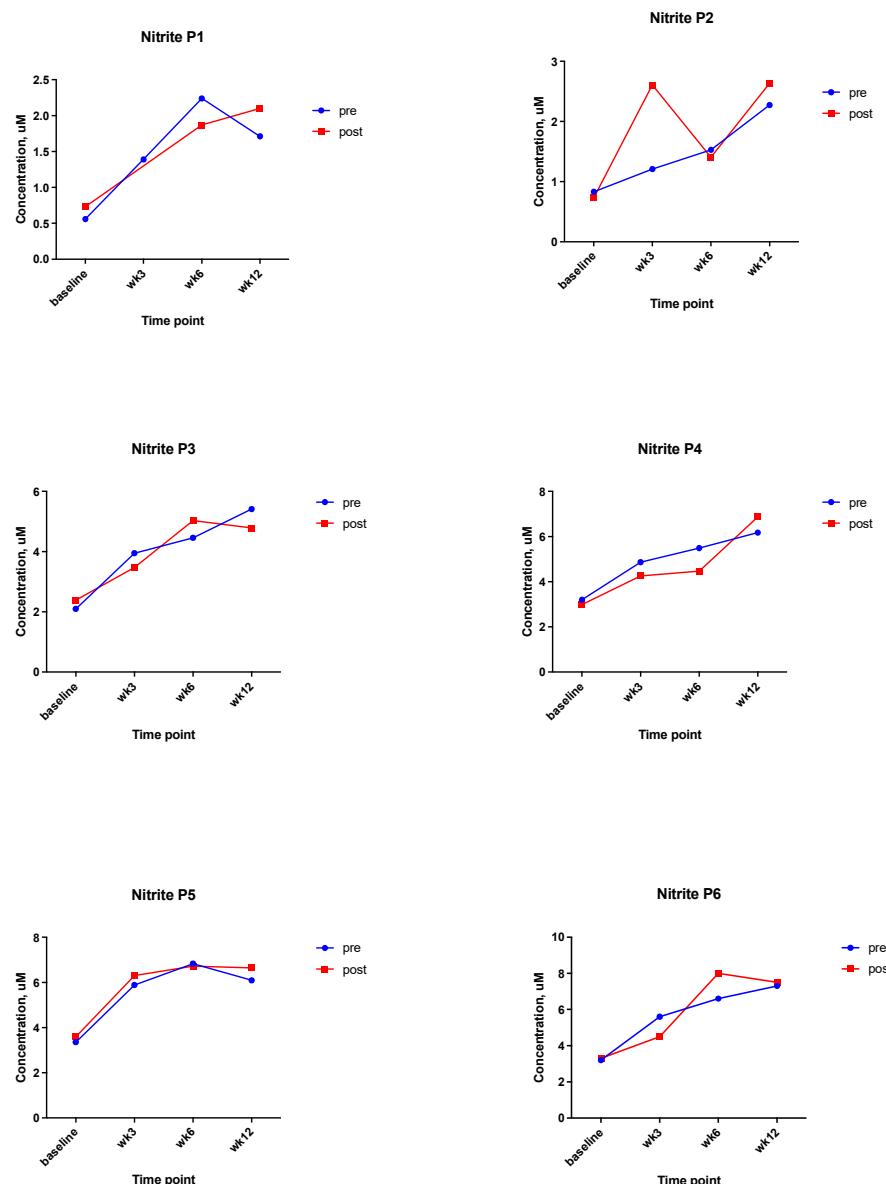
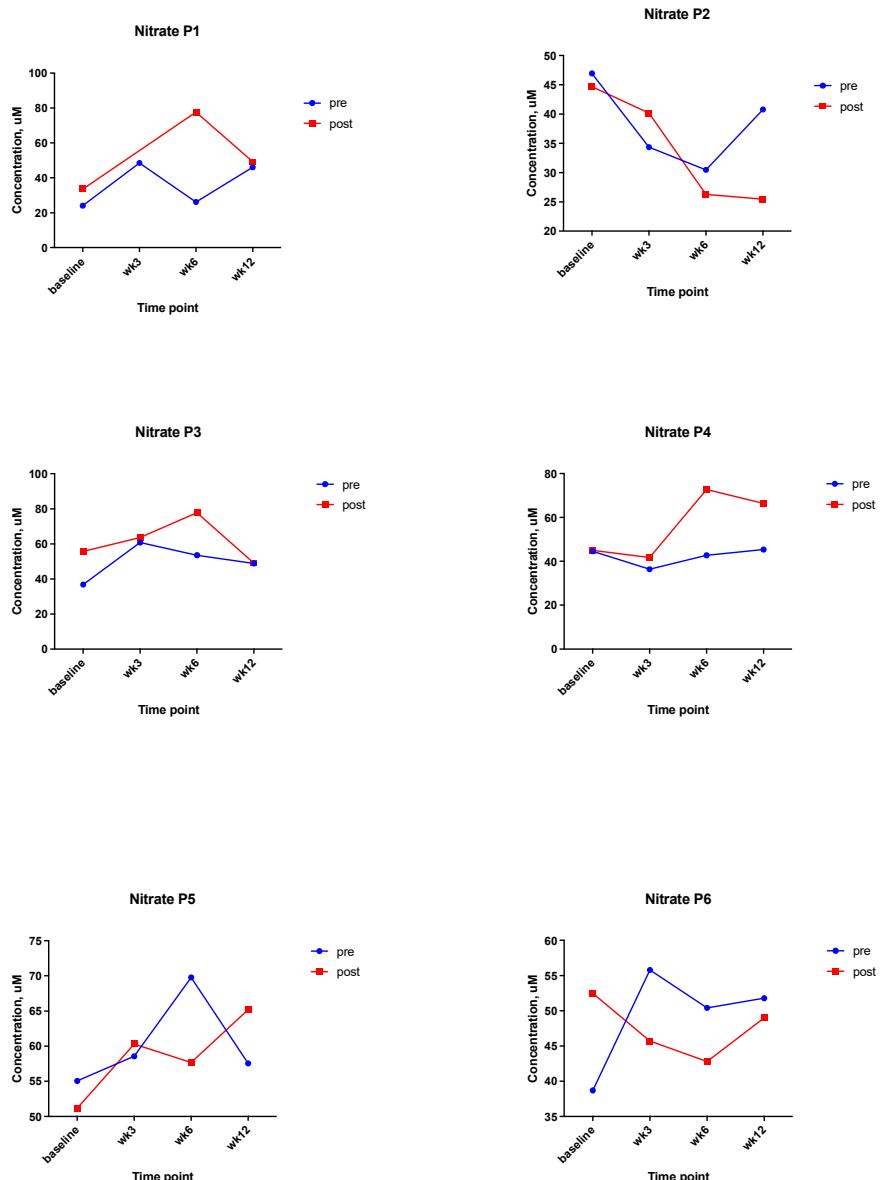
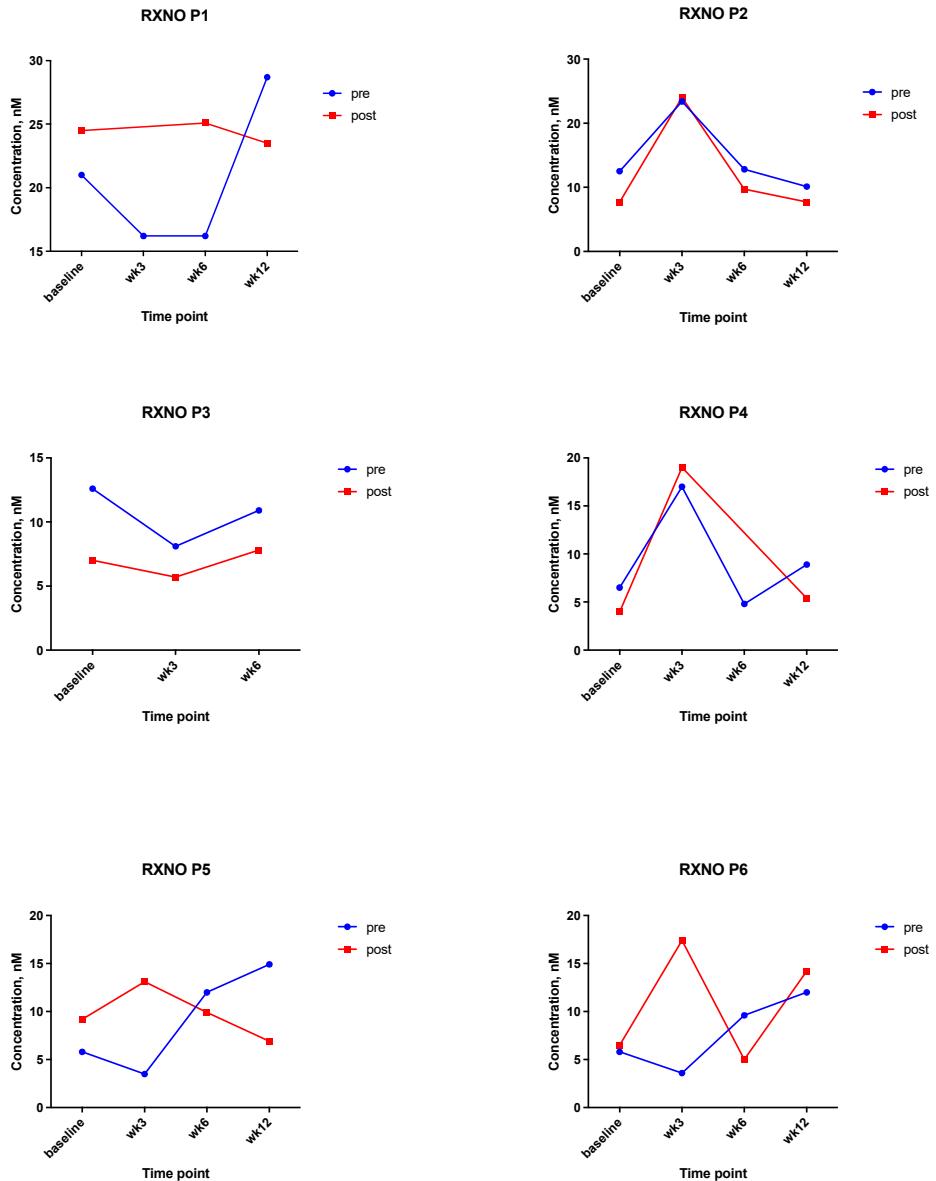


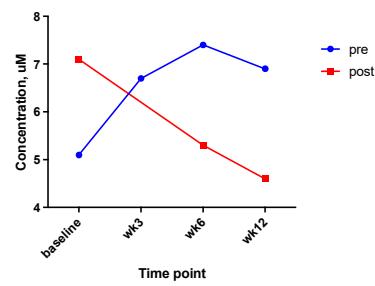
Figure S5. Significant associations (Spearman's Test) between physical fitness and clinical asthma symptoms. On the top row, A) a greater increase in maximum oxygen uptake is associated with a greater increase in pre CPET nitrite from baseline ($r=.943$). B) A greater increase in pre CPET nitrite is significantly associated with a greater reduction in eosinophil levels ($r=-.837$). C) A greater reduction in eosinophils is associated with a greater increase in pre-BD FEV1 ($r=-.717$), and D) greater increase in FEV1 correlates with a greater increase in AQLQ total score ($r=.771$) and E) AQLQ environmental score ($r=.600$). On the bottom row, F) a greater increase in oxygen uptake at AT is associated with a larger increase in FRAP. G and H) A greater reduction in FEV1% BD reversibility negatively correlates with a greater increase in AQLQ total and environmental scores ($r=-.829$ and $-.714$). To link the two rows, a greater reduction in airways hyper-reactivity as assessed by reduction in %FEV1 BD reversibility negatively correlates with a greater increase in FEV1 in litres ($r=-.771$; data not shown) Abbreviations: AT; anaerobic threshold, CPET; cardiopulmonary exercise test; BD; bronchodilator, FEV1; forced expiratory volume in 1 second, FRAP; ferric reducing antioxidant capacity of plasma. An r value of > 0.7 is considered a strong correlation, 0.4-0.7 a moderate correlation.



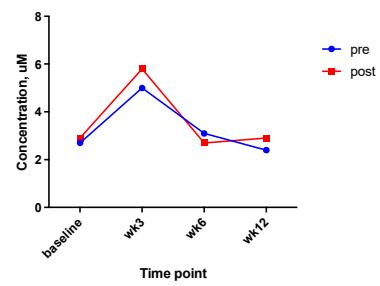




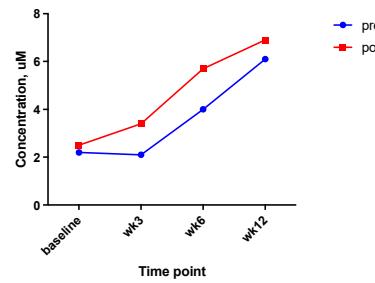
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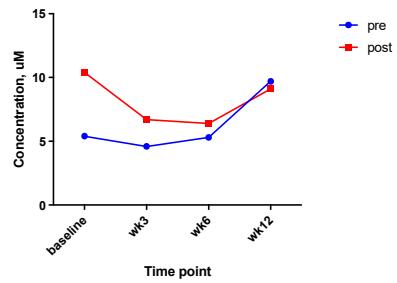
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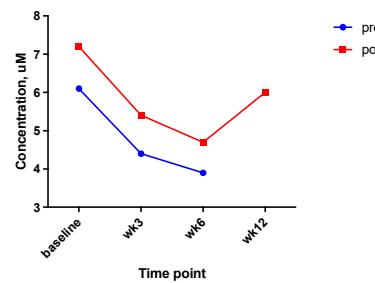
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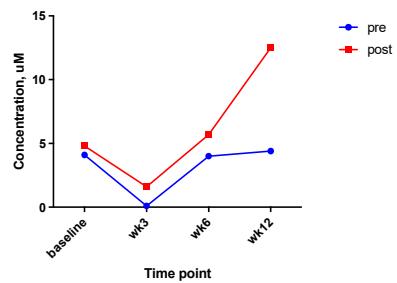
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TBARS P5



TBARS P6



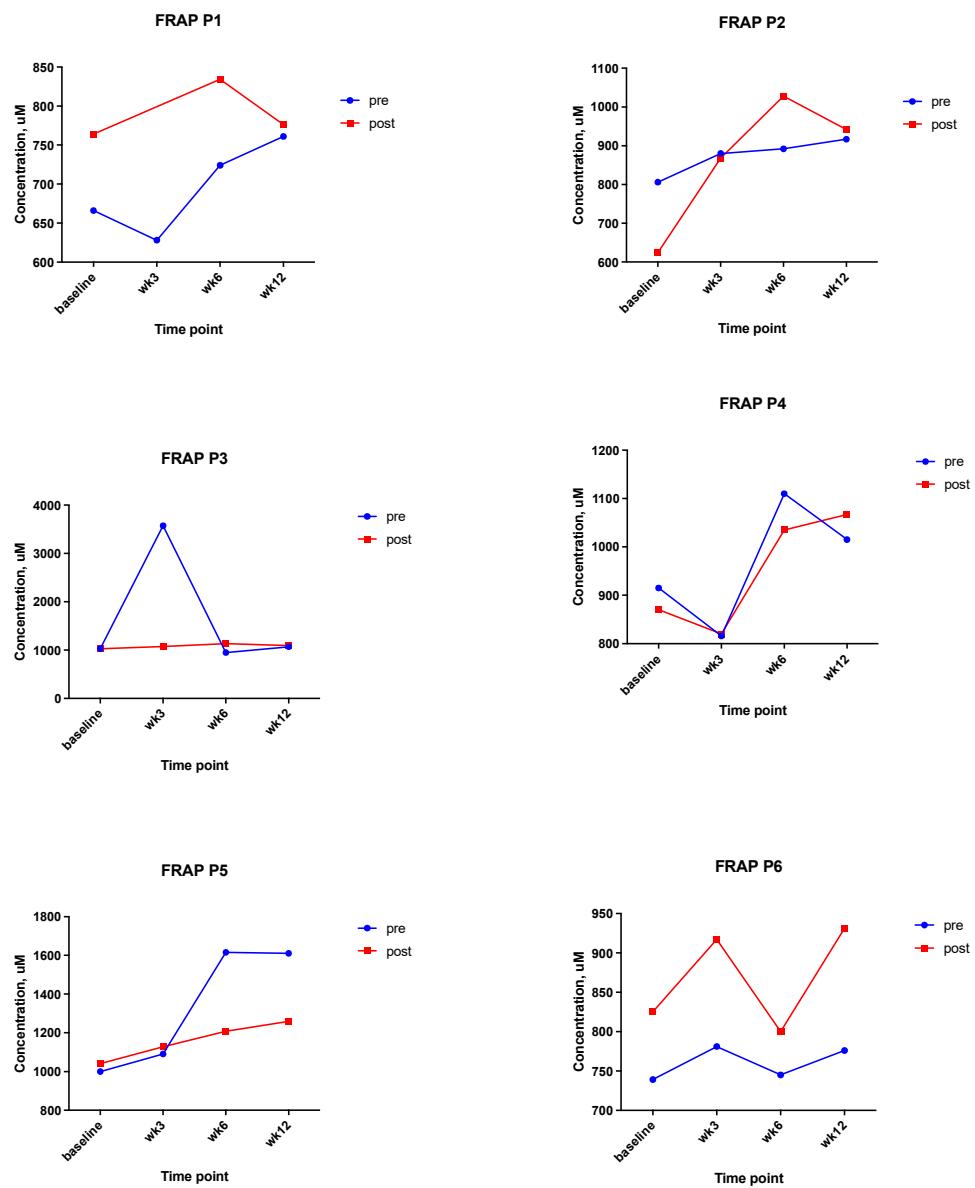


Figure S6 Individual responses of nitrospecies, TBARS and FRAP to exercise.
Data presented for individual patients (n=6). Red line = pre acute exercise challenge, blue line = post acute exercise challenge. Abbreviations; RXNO; other nitrosospecies; TBARS; thiobarbituric acid reactive substances, FRAP; Ferric reducing antioxidant capacity of plasma