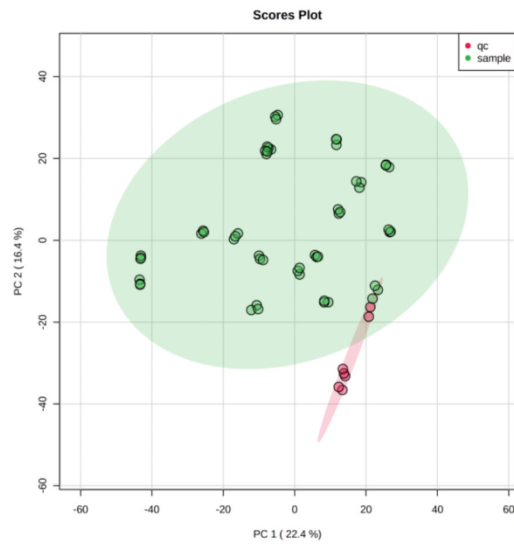
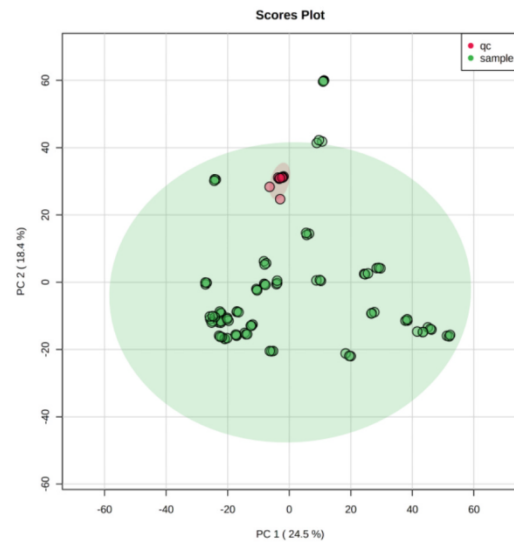


Supplementary Information

(A)



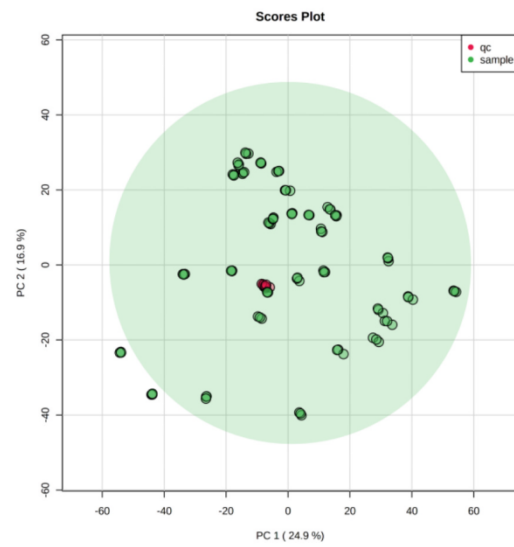
(B)



(C)



(D)



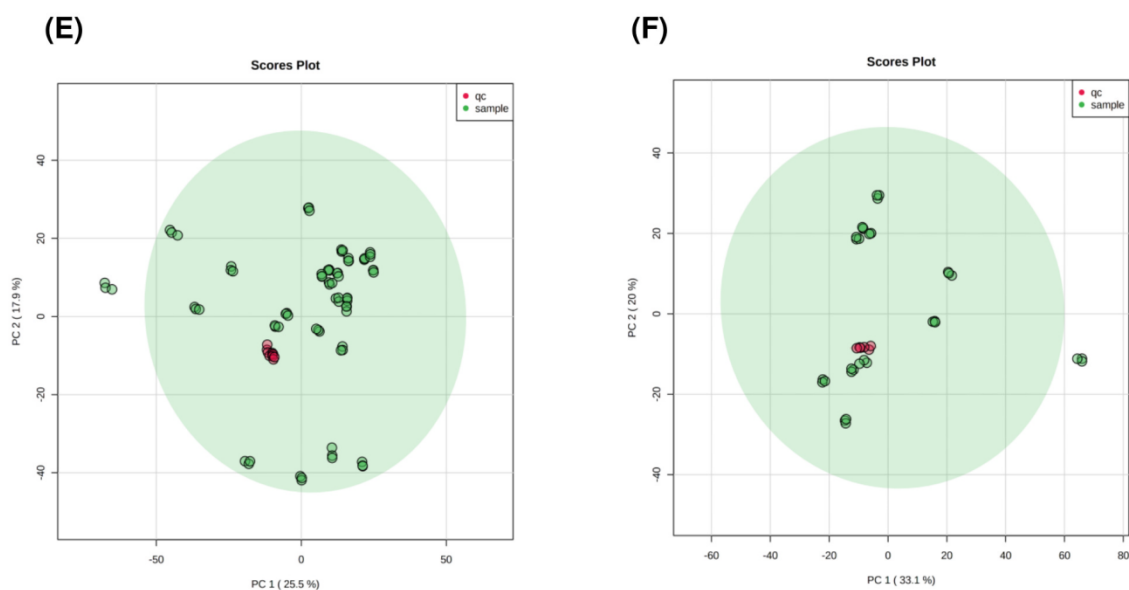
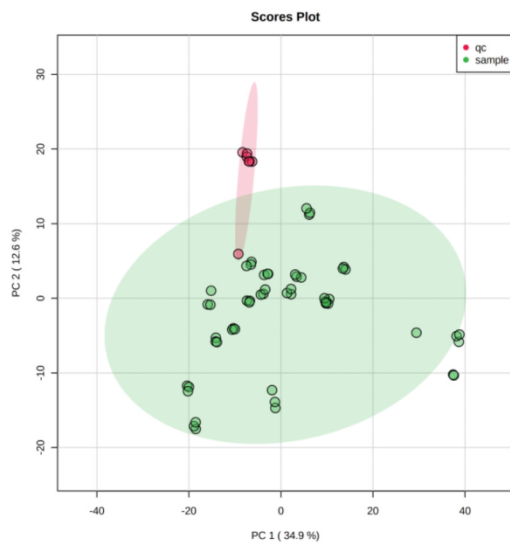
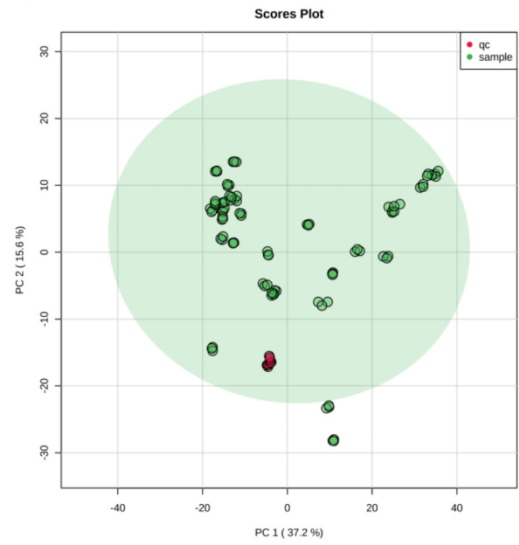


Figure S1. PCA score plot of samples in run 1 – 6 for positive ion mode. Run 1 to 6 (A to F). The QC samples in run 1 were scattered into 2 regions, implying existence of batch effects. QC samples of other runs were tightly clustered together within the respective runs, implying the runs were stable and reliable. Red dot is QC sample; green dot is plasma sample; shade area is the 95% confidence region.

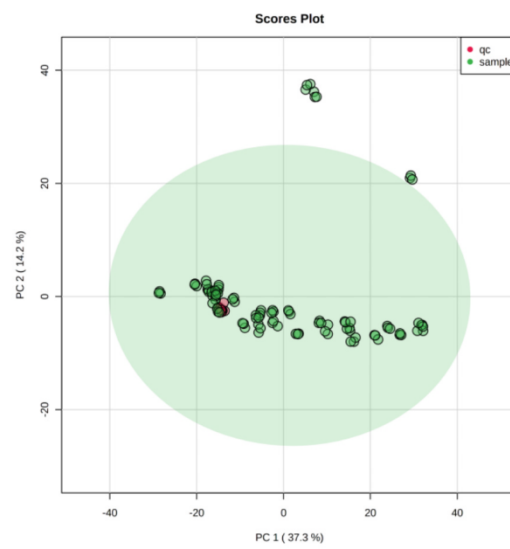
(A)



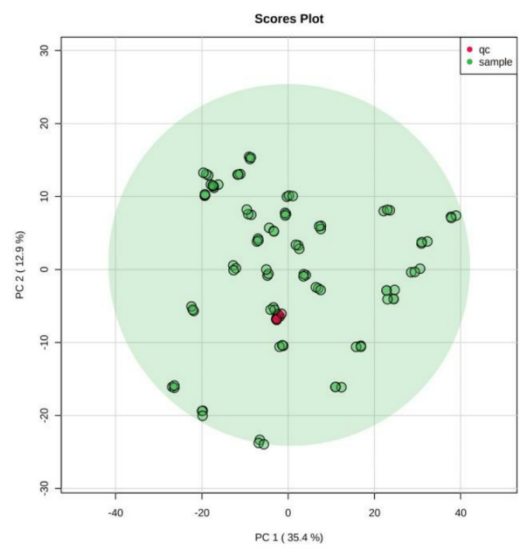
(B)



(C)



(D)



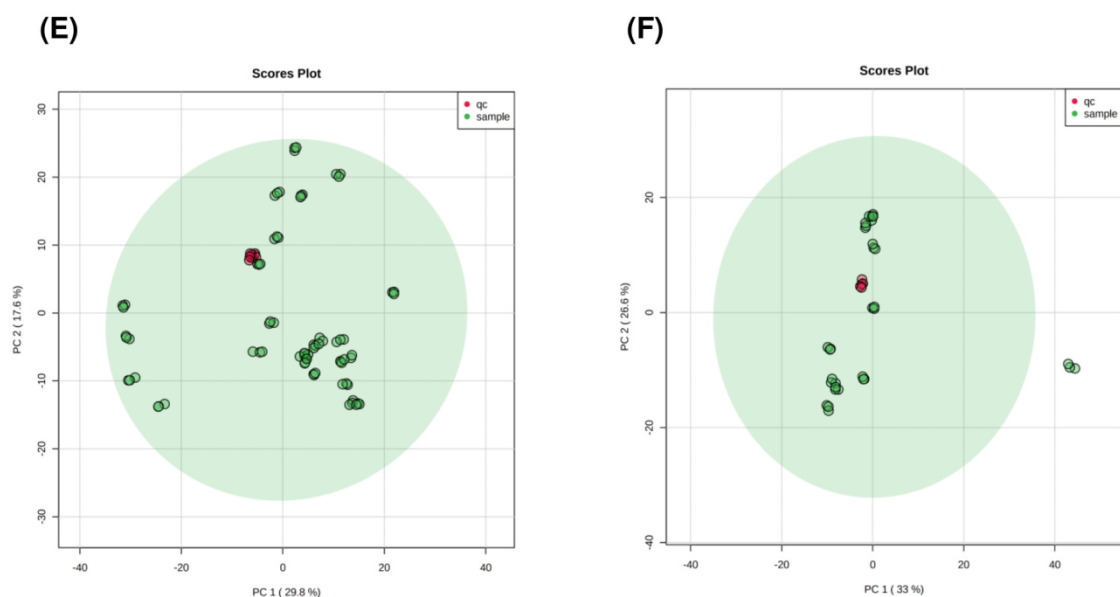


Figure S2. PCA score plot of samples in run 1 – 6 for negative ion mode. Run 1 to 6 (A to F). The QC samples in run 1 were scattered into 2 regions, implying existence of batch effects. QC samples of other runs were tightly clustered together within the respective runs, implying the runs were stable and reliable. Red dot is QC sample; green dot is plasma sample; shade area is the 95% confidence region.

Table S1. Number of total MFs detected, significant MFs, and significant metabolites with level 2 confidence annotation.

Number	Association with gender ^a		Association with age ^b		Association with age in men		Association with age in women	
	+	-	+	-	+	-	+	-
Ion mode								
Total MFs detected	2424	834	2424	834	2424	834	2424	834
Significant MFs (FDR < 0.05)	194	90	1020	325	744	225	692	228
Significant metabolites annotated at level 2	15	8	45	16	27	17	25	13
Total significant metabolites annotated*	23		58 (3)		40 (4)		36 (2)	
Total significant metabolites annotated* with QC CV < 30%	18		26		20		16	

MFs: metabolite features; FDR: false discovery rate; ^a adjusted for age; ^b adjusted for gender; () : number of repeated metabolites in both modes; * after subtracting those repeated metabolites that were detected in both modes; QC CV: coefficient of variation for QC.