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Supplemental information

Sex hormones drive changes in lipoprotein metabolism

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Supplemental Information

Figure S1: Logistic regression analysis between all gender comparisons, Related to Figure 2

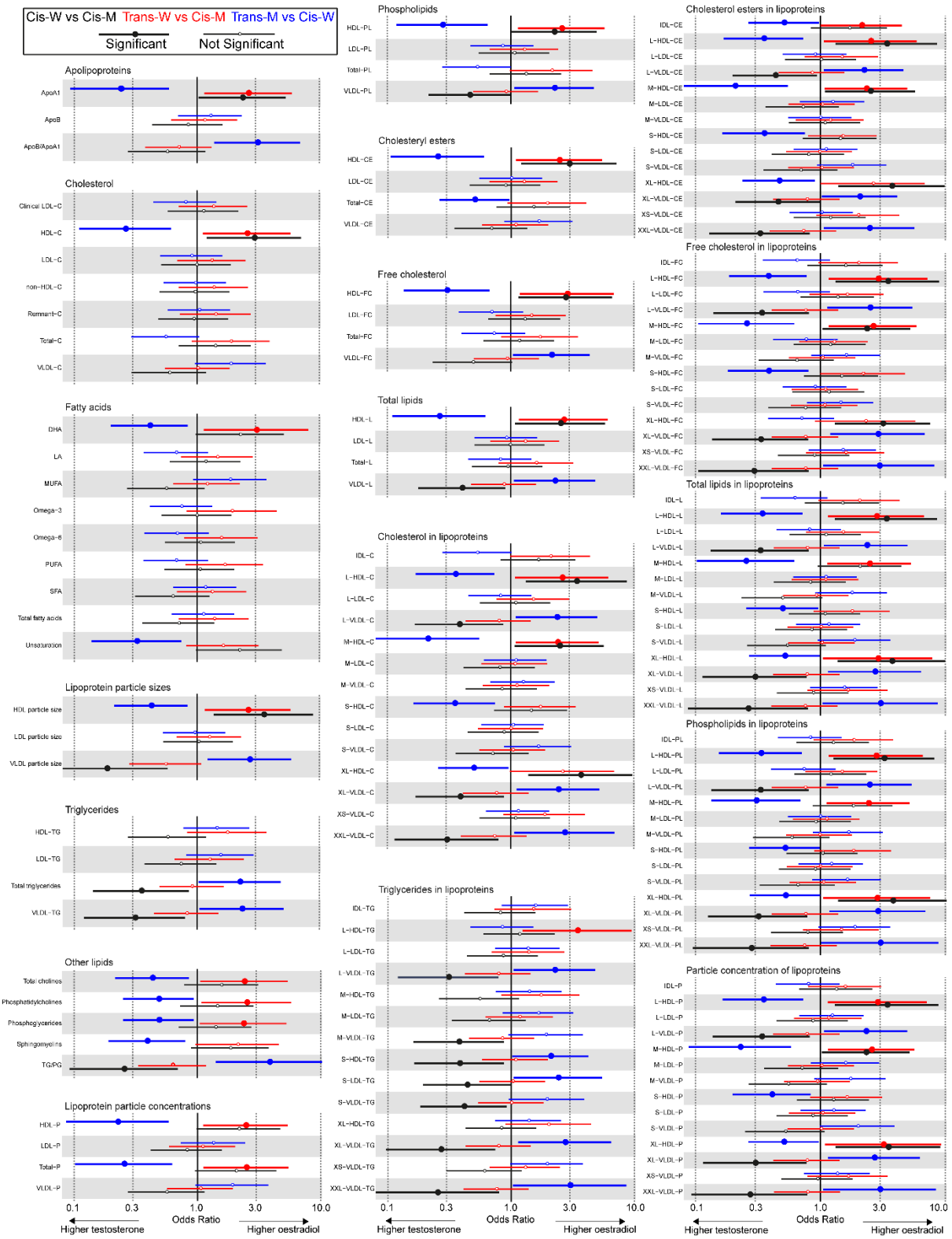

Figure S1: Logistic regression analysis between all gender comparisons, Related to Figure 2. Forest plot displaying odd ratios (OR) and 95% confidence intervals (CIs) of serum metabolites between 3 different young age matched gender comparisons: young post-pubertal cis-gendered men (Cis-M) and women (Cis-W) (n=15 and 17, black); young Cis-M and

transgender individuals undergoing cross-sex-hormone treatment with oestradiol, Trans-W (n=15 and 25, red); and young Cis-W and transgender individuals undergoing cross-sex-hormone treatment with testosterone, Trans-M (n=17 and 26). Measurements include specific fatty acids, cholesterol, triglycerides and phospholipids (mmol/l), apolipoproteins (g/l) and in-depth lipoprotein measurements including particle size (nm), concentration and lipid content (mmol/l). Statistically significant differences are denoted by solid filled and enlarged OR circles and thicker CI bands. Abbreviations: Apo, apolipoprotein; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein; XXL-VLDL, chylomicrons and extremely large VLDL; X-Large, very large; X-small, very small; PG (Phosphoglyceride), DHA, Docosahexaenoic acid; LA, Linoleic acid; PUFA, Polyunsaturated fatty acids; MUFA, Monounsaturated fatty acids; SFA, Saturated fatty acids; TG, triglycerides; PL, phospohlipids, FC, free cholesterol, C, cholesterol, CE, cholesterol esters; P, particle; L, lipids.

Figure S2: Metabolites that overlap between all gender comparisons, Related to Figure 3

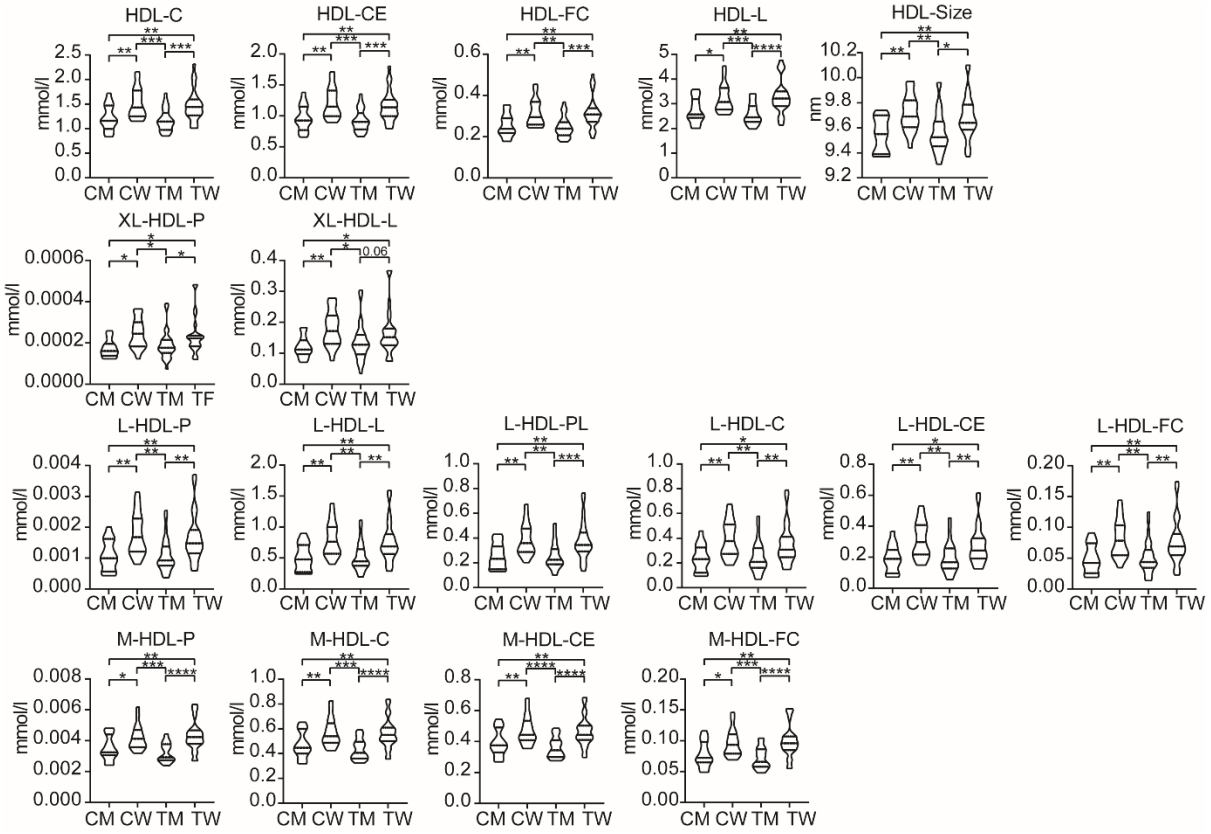

Figure S2: Metabolites that overlap between all gender comparisons, Related to Figure 3. Violin plots comparing levels of metabolites with full overlap (Venn diagram Figure 3A, Table S3) in young post-pubertal cis-men and cis-women (CM, n=15 and CW, n=17) and in age matched young transgender individuals undergoing cross-sex-hormone treatment with oestradiol, trans-women (TF, n=25) or testosterone, trans-men (TM, n=26). One-way ANOVA, *=P<0.05, **=P<0.01, ***=P<0.001, ****=P<0.0001.

Figure S3: Sex differences in lipid metabolism are altered in young post-pubertal patients with autoimmune diseases, Related to Figure 2

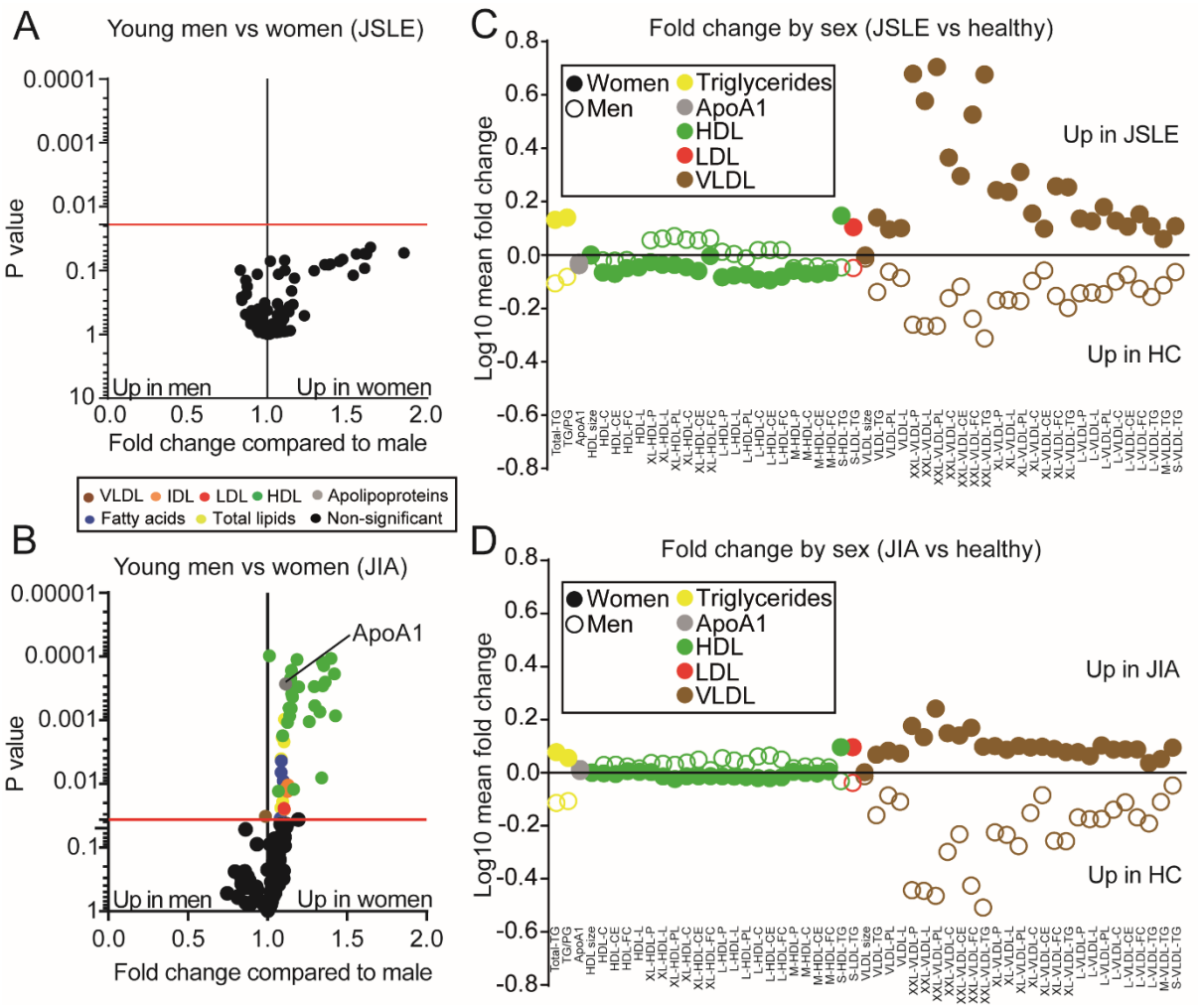

Figure S3: Sex differences in lipid metabolism are altered in young post-pubertal patients with autoimmune diseases, Related to Figure 2. Metabolites were measured in serum by Nightingale Metabolomics (Table S1) from young post-pubertal patients with juvenile-systemic lupus erythematosus (JSLE) and juvenile idiopathic arthritis (JIA). **(A-B)** Volcano plots displaying fold change of all metabolites and Log10 p values from multiple unpaired t-tests comparing **(A)** young men (n=11) and women (n=22) with JSLE, or **(B)** young men (n=48) and women (n=73) with JIA. Bottom y-axis line, p=0.05; top y-axis line, adjusted p value threshold following 6% false discovery rate adjustment for multiple comparisons (Benjamini, Krieger and Yekutieli approach). Coloured dots represent significantly different metabolite groups. **(C-D)** Significant metabolites identified between young post-pubertal healthy men and women (Figure 2B) were compared to age matched young post-pubertal men and women with **(C)** JSLE (men JSLE/HC, n=12/15; women JSLE/HC, n=23/17), or **(D)** JIA (men JIA/HC, n=48/15; women JIA/HC, n=73/17). Data is displayed as log10 mean fold change from healthy. Points are coloured by metabolite group. Points are represented as filled dots for women, hollow dots for men. Abbreviations: VL/I/L/HDL (very low/intermediate/low/high density lipoproteins), Apo (apolipoprotein).

Table S1: List of serum lipid metabolic biomarkers, Related to Figure 2-4

Metabolite group	Metabolite	Metabolite group	Metabolite	Metabolite
Cholesterol (mmol/l)	Total-C	Lipoprotein subclasses (mmol/l)	XXL-VLDL-P	L-LDL-C
	non-HDL-C		XXL-VLDL-L	L-LDL-CE
	Remnant-C		XXL-VLDL-PL	L-LDL-FC
	VLDL-C		XXL-VLDL-C	L-LDL-TG
	Clinical LDL-C		XXL-VLDL-CE	M-LDL-P
	LDL-C		XXL-VLDL-FC	M-LDL-L
	HDL-C		XXL-VLDL-TG	M-LDL-PL
Triglycerides (mmol/l)	Total-TG		XL-VLDL-P	M-LDL-C
	VLDL-TG		XL-VLDL-L	M-LDL-CE
	LDL-TG		XL-VLDL-PL	M-LDL-FC
	HDL-TG		XL-VLDL-C	M-LDL-TG
Phospholipids (mmol/l)	Total-PL		XL-VLDL-CE	S-LDL-P
	VLDL-PL		XL-VLDL-FC	S-LDL-L
	LDL-PL		XL-VLDL-TG	S-LDL-PL
	HDL-PL		L-VLDL-P	S-LDL-C
Cholesteryl esters (mmol/l)	Total-CE		L-VLDL-L	S-LDL-CE
	VLDL-CE		L-VLDL-PL	S-LDL-FC
	LDL-CE		L-VLDL-C	S-LDL-TG
	HDL-CE		L-VLDL-CE	XL-HDL-P
Free cholesterol (mmol/l)	Total-FC		L-VLDL-FC	XL-HDL-L
	VLDL-FC		L-VLDL-TG	XL-HDL-PL
	LDL-FC		M-VLDL-P	XL-HDL-C
	HDL-FC		M-VLDL-L	XL-HDL-CE
Total lipids (mmol/l)	Total-L		M-VLDL-PL	XL-HDL-FC
	VLDL-L		M-VLDL-C	XL-HDL-TG
	LDL-L		M-VLDL-CE	L-HDL-P
	HDL-L		M-VLDL-FC	L-HDL-L
Lipoprotein particle concentrations (mmol/l)	Total-P		M-VLDL-TG	L-HDL-PL
	VLDL-P		S-VLDL-P	L-HDL-C
	LDL-P		S-VLDL-L	L-HDL-CE
	HDL-P		S-VLDL-PL	L-HDL-FC
Lipoprotein particle sizes (nm)	VLDL size		S-VLDL-C	L-HDL-TG
	LDL size		S-VLDL-CE	M-HDL-P
	HDL size		S-VLDL-FC	M-HDL-L
Other lipids (mmol/l)	Phosphoglyceride		S-VLDL-TG	M-HDL-PL
	TG/PG		XS-VLDL-P	M-HDL-C
	Cholines		XS-VLDL-L	M-HDL-CE
	Phosphatidylcholines		XS-VLDL-PL	M-HDL-FC
	Sphingomyelins		XS-VLDL-C	M-HDL-TG
Apolipoproteins (g/l)	ApoB		XS-VLDL-CE	S-HDL-P
	ApoA1		XS-VLDL-FC	S-HDL-L
	ApoB/ApoA1		XS-VLDL-TG	S-HDL-PL
Fatty acids (mmol/l)	Total-FA		IDL-P	S-HDL-C
	Unsaturation		IDL-L	S-HDL-CE
	Omega-3		IDL-PL	S-HDL-FC
	Omega-6		IDL-C	S-HDL-TG
	PUFA		IDL-CE	
	MUFA		IDL-FC	
	SFA		IDL-TG	
	LA		L-LDL-P	
	DHA		L-LDL-L	
			L-LDL-PL	

Table S1: List of serum metabolic biomarkers, Related to Figure 2-4. Nightingale Health metabolomics platform (https://nightingalehealth.com/) was used to measure >140 lipid biomarkers in serum. This service measures blood metabolic biomarkers using nuclear magnetic resonance (NMR) spectroscopy. The platform can simultaneously measure fatty acids, routine lipid measures (mmol/l), apolipoproteins (g/l) and in-depth lipoprotein measurements such as particle size (nm), concentration and lipid content (mmol/l). Abbreviations: Apo, apolipoprotein; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein; XXL-VLDL, chylomicrons and extremely large VLDL; X-Large, very large; X-small, very small; PG (Phosphoglyceride), DHA, Docosahexaenoic acid; LA, Linoleic acid; PUFA, Polyunsaturated fatty acids; MUFA, Monounsaturated fatty acids; SFA, Saturated fatty acids; TG, triglycerides; PL, phospohlipids, FC, free cholesterol, C, cholesterol, CE, cholesterol esters; P, particle; L, lipids.

Table S2: Demographic comparison between pre-pubertal boys and girls, Related to Figure 2A

Demographic	Boys	Girls	P value*
Number	10	10	-
Age, mean (SD)	8.9 (1.66)	8.4 (1.58)	0.85*
Ethnicity, number (%)			
White	6 (60)	5 (50)	1.00^{+}
Asian	3 (30)	4 (40)	1.00^{+}
Black	1 (10)	1 (10)	1.00^{+}
Other	0 (0)	0 (0)	1.00^{+}

Table S2: Demographic comparison between pre-pubertal boys and girls, Related to Figure 2A. *Fisher's exact or $^{+}$unpaired t-test.

Table S3: Metabolites that overlap between gender group comparisons, Related to Figure 3A

Cis-Men vs Cis-Women n=53 (Figure 2B)		Trans-Women vs Cis-Men n=29 (Figure 2C)	Trans-Men vs Cis-Women n=70 (Figure 2D)		Total overlap between all comparisons n=18 (Figure 3A)
HDL-C	S-LDL-TG	HDL-C	HDL-C	XL-VLDL-CE	HDL-C
Total-TG	XL-HDL-P	HDL-PL	Total-TG	XL-VLDL-FC	HDL-CE
VLDL-TG	XL-HDL-L	HDL-CE	VLDL-TG	XL-VLDL-TG	HDL-FC
VLDL-PL	XL-HDL-PL	HDL-FC	VLDL-PL	L-VLDL-P	HDL-L
HDL-CE	XL-HDL-C	HDL-L	HDL-PL	L-VLDL-L	HDL size
HDL-FC	XL-HDL-CE	Total-P	Total-CE	L-VLDL-PL	ApoA1
VLDL-L	XL-HDL-FC	HDL-P	HDL-CE	L-VLDL-C	XL-HDL-P
HDL-L	L-HDL-P	HDL size	VLDL-FC	L-VLDL-CE	XL-HDL-L
VLDL size	L-HDL-L	Phosphoglyc	HDL-FC	L-VLDL-FC	L-HDL-P
HDL size	L-HDL-PL	Cholines	VLDL-L	L-VLDL-TG	L-HDL-L
TG/PG	L-HDL-C	Phosphatidylc	HDL-L	IDL-CE	L-HDL-PL
ApoA1	L-HDL-CE	ApoA1	Total-P	S-LDL-TG	L-HDL-C
XXL-VLDL-P	L-HDL-FC	DHA	HDL-P	XL-HDL-P	L-HDL-CE
XXL-VLDL-L	M-HDL-P	XL-HDL-P	VLDL size	XL-HDL-L	L-HDL-FC
XXL-VLDL-PL	M-HDL-C	XL-HDL-L	HDL size	XL-HDL-C	M-HDL-P
XXL-VLDL-C	M-HDL-CE	XL-HDL-PL	Phosphoglyc	XL-HDL-CE	M-HDL-C
XXL-VLDL-CE	M-HDL-FC	L-HDL-P	TG/PG	L-HDL-P	M-HDL-CE
XXL-VLDL-FC	S-HDL-TG	L-HDL-L	Cholines	L-HDL-L	M-HDL-FC
XXL-VLDL-TG		L-HDL-PL	Phosphatidylc	L-HDL-PL	
XL-VLDL-P		L-HDL-C	Sphingomyelin	L-HDL-C	
XL-VLDL-L		L-HDL-CE	ApoA1	L-HDL-CE	
XL-VLDL-PL		L-HDL-FC	ApoB/ApoA1	L-HDL-FC	
XL-VLDL-C		L-HDL-TG	Unsaturation	M-HDL-P	
XL-VLDL-CE		M-HDL-P	DHA	M-HDL-L	
XL-VLDL-FC		M-HDL-L	XXL-VLDL-P	M-HDL-PL	
XL-VLDL-TG		M-HDL-PL	XXL-VLDL-L	M-HDL-C	
L-VLDL-P		M-HDL-C	XXL-VLDL-PL	M-HDL-CE	
L-VLDL-L		M-HDL-CE	XXL-VLDL-C	M-HDL-FC	
L-VLDL-PL		M-HDL-FC	XXL-VLDL-CE	S-HDL-P	
L-VLDL-C			XXL-VLDL-FC	S-HDL-L	
L-VLDL-CE			XXL-VLDL-TG	S-HDL-C	
L-VLDL-FC			XL-VLDL-P	S-HDL-CE	
L-VLDL-TG			XL-VLDL-L	S-HDL-FC	
M-VLDL-TG			XL-VLDL-PL	S-HDL-TG	
S-VLDL-TG			XL-VLDL-C	XL-VLDL-CE	

Table S3: Metabolites that overlap between gender group comparisons, Related to Figure 3A. Table displaying the statistically significant metabolites following 6% FDR correction for multiple testing from each young gender comparison from Figure 2B-D, as well as the 18 overlapping metabolites (Venn diagram Figure 3A) that were significantly different between all gender comparisons and validated by logistic regression analysis (Figure S1)**.**

Table S4: Logistic regression of ApoA1 adjusted for ethnicity, Related to Figure 3 and Figure S1

ApoA1				
Cis-Men vs Cis-Women				
Beta	Beta SE	Odds Ratio	Odds Ratio SE	p-value
0.91500005	0.429417099	2.496775376	1.536361716	0.033105988
Cis-Men vs Trans-Women				
Beta	Beta SE	Odds Ratio	Odds Ratio SE	p-value
1.167385677	0.460968551	3.21358031	1.585608984	0.011326441
Cis-Women vs Trans-Men				
Beta	Beta SE	Odds Ratio	Odds Ratio SE	p-value
-1.644784107	0.559258256	0.193054237	1.749374431	0.00327144

Table S4: Logistic regression of ApoA1 adjusted for ethnicity, Related to Figure 3 and Figure S1. Univariate logistic regression analysis, adjusted for ethnicity, displaying the beta values, odds ratios, standard error (SE) and p values of ApoA1 levels from different comparisons of young post-pubertal men (n=15), women (n=17), trans-men (n=26) and trans-women (n=25) Group-1/1A (n=30) and Group-2/2A (n=26).

Table S5: Turners syndrome patient characteristics, Related to Figure 3F

Therapy	Genetic diagnosis
Femoston, 1/10mg; Vitamin D, 1000Umg	Turner variant, deletion of chromosome Xq21.3
Femoston, 1/10mg; Vitamin D, 1000Umg/d; Growth hormone, 1.8mg/d	Turner mosaic, 45,X/46,X,idic(X)(p11.2)
Growth hormone 1.4mg/d; Vitamin D, 400Umg/d	Turner syndrome, 45,X
Estradiol valerate 1mg; Growth hormone 2mg/d; Fluoexetine	Turner syndrome, 45,X
Femoston, 1/10mg; Vitamin D, 1000Umg/d; Growth hormone, 1.6mg/d	Turner variant, 46,X,idic(x)(p22.3)
Ethinylestradiol 0.005mg/d; Growth hormone 1.8mg/d; Vitamin D 1000Umg/d	Turner syndrome, 45,X
Iron supplements	Turner mosaic, 45X/46XX
Growth hormone 1.5mg/d; Vitamin D, 1000Umg/d	Turner mosaic, 45,X/47,XXX
Vitamin D, 500Umg/d	Turner mosaic, 45,X/47,XXX

Table S5: Turners syndrome patient characteristics, Related to Figure 3F. Age, current therapy and genetic diagnosis displayed for patients with Turners syndrome (mean age: 15.6, SD: 2.4) used for the analysis in Figure 3F.

Table S6: Key linking metabolite names with node numbers in network analysis, Related to Figure 4

No.	Metabolite	No.	Metabolite	No.	Metabolite	No.	Metabolite	No.	Metabolite	No.	Metabolite
1	Total-C	**26**	LDL-L	**51**	XL-VLDL-P	**76**	S-VLDL-CE	**101**	M-LDL-L	**126**	L-HDL-FC
2	non-HDL-C	**27**	HDL-L	**52**	XL-VLDL-L	**77**	S-VLDL-FC	**102**	M-LDL-PL	**127**	L-HDL-TG
3	Remnant-C	**28**	Total-P	**53**	XL-VLDL-PL	**78**	S-VLDL-TG	**103**	M-LDL-C	**128**	M-HDL-P
4	VLDL-C	**29**	VLDL-P	**54**	XL-VLDL-C	**79**	XS-VLDL-P	**104**	M-LDL-CE	**129**	M-HDL-L
5	Clinical LDL-C	**30**	LDL-P	**55**	XL-VLDL-CE	**80**	XS-VLDL-L	**105**	M-LDL-FC	**130**	M-HDL-PL
6	LDL-C	**31**	HDL-P	**56**	XL-VLDL-FC	**81**	XS-VLDL-PL	**106**	M-LDL-TG	**131**	M-HDL-C
7	HDL-C	**32**	ApoB	**57**	XL-VLDL-TG	**82**	XS-VLDL-C	**107**	S-LDL-P	**132**	M-HDL-CE
8	Total-TG	**33**	ApoA1	**58**	L-VLDL-P	**83**	XS-VLDL-CE	**108**	S-LDL-L	**133**	M-HDL-FC
9	VLDL-TG	**34**	ApoB/ApoA1	**59**	L-VLDL-L	**84**	XS-VLDL-FC	**109**	S-LDL-PL	**134**	M-HDL-TG
10	LDL-TG	**35**	TotFA	**60**	L-VLDL-PL	**85**	XS-VLDL-TG	**110**	S-LDL-C	**135**	S-HDL-P
11	HDL-TG	**36**	Unsat	**61**	L-VLDL-C	**86**	IDL-P	**111**	S-LDL-CE	**136**	S-HDL-L
12	Total-PL	**37**	Omega-3	**62**	L-VLDL-CE	**87**	IDL-L	**112**	S-LDL-FC	**137**	S-HDL-PL
13	VLDL-PL	**38**	Omega-6	**63**	L-VLDL-FC	**88**	IDL-PL	**113**	S-LDL-TG	**138**	S-HDL-C
14	LDL-PL	**39**	PUFA	**64**	L-VLDL-TG	**89**	IDL-C	**114**	XL-HDL-P	**139**	S-HDL-CE
15	HDL-PL	**40**	MUFA	**65**	M-VLDL-P	**90**	IDL-CE	**115**	XL-HDL-L	**140**	S-HDL-FC
16	Total-CE	**41**	SFA	**66**	M-VLDL-L	**91**	IDL-FC	**116**	XL-HDL-PL	**141**	S-HDL-TG
17	VLDL-CE	**42**	LA	**67**	M-VLDL-PL	**92**	IDL-TG	**117**	XL-HDL-C		
18	LDL-CE	**43**	DHA	**68**	M-VLDL-C	**93**	L-LDL-P	**118**	XL-HDL-CE		
19	HDL-CE	**44**	XXL-VLDL-P	**69**	M-VLDL-CE	**94**	L-LDL-L	**119**	XL-HDL-FC		
20	Total-FC	**45**	XXL-VLDL-L	**70**	M-VLDL-FC	**95**	L-LDL-PL	**120**	XL-HDL-TG		
21	VLDL-FC	**46**	XXL-VLDL-PL	**71**	M-VLDL-TG	**96**	L-LDL-C	**121**	L-HDL-P		
22	LDL-FC	**47**	XXL-VLDL-C	**72**	S-VLDL-P	**97**	L-LDL-CE	**122**	L-HDL-L		
23	HDL-FC	**48**	XXL-VLDL-CE	**73**	S-VLDL-L	**98**	L-LDL-FC	**123**	L-HDL-PL		
24	Total-L	**49**	XXL-VLDL-FC	**74**	S-VLDL-PL	**99**	L-LDL-TG	**124**	L-HDL-C		
25	VLDL-L	**50**	XXL-VLDL-TG	**75**	S-VLDL-C	**100**	M-LDL-P	**125**	L-HDL-CE		

Table S6: Key linking metabolite names with node numbers in network analysis, Related to Figure 4. List of metabolite names matched to network analysis in Figure 4.

Table S7: Demographic and clinical comparison between young post-pubertal men and women with juvenile-systemic lupus erythematosus, Related to Figure 1 and Figure S3

Demographic, n (%)	Men	Women	P value
Number	12	23	-
Age	18 (15-23)	20 (14-25)	0.39
White	3 (25)	10 (43)	0.46*
Asian	6 (50)	7 (30)	0.29*
Black	3 (25)	4 (17)	0.67*
Other	0 (0)	2 (9)	0.54*
Clinical feature, median (IQR)			
Age of disease onset	13 (0-18)	12 (5-18)	0.32
SLEDAI score (NR<4)	2 (0-10)	2 (0-10)	0.62
ESR, mm/hr (NR=1.3-3.5)	6.5 (2-38)	13 (2-127)	0.23
dsDNA, IU/mL (NR=<50)	47 (2-2827)	58 (1-17441)	0.46
C3, g/L (NR=0.9-1.8)	1 (0.33-1.36)	1.11 (0.35-1.64)	0.28
Lymphocyte count, 10^9/L (NR=1·3–3·5)	1.49 (0.68-3.8)	1.63 (0.59-3.08)	0.78
Organ involvement, n (%)			
Neurological	1 (8)	1 (4)	1.00*
Serositis	2 (17)	6 (26)	0.31*
Cutaneous	10 (83)	21 (92)	0.69*
Haematological	5 (42)	9 (39)	1.00*
Musculoskeletal	9 (75)	21 (91)	0.31*
Renal	4 (33)	5 (22)	0.69*
Treatment, n (%)			
Hydroxychloroquine	11 (92)	20 (87)	1.00*
Mycophenolate mofetil	5 (42)	13 (57)	0.49*
Prednisolone	5 (42)	12 (52)	0.72*
Vitamin D	2 (17)	6 (26)	0.19*
Methotrexate	1 (8)	2 (9)	1.00*
Azathioprine	4 (33)	3 (13)	0.20*

Table S7: Demographic and clinical comparison between young post-pubertal men and women with juvenile-systemic lupus erythematosus, Related to Figure 1 and Figure S3. Demographics and common clinical measures and treatments of disease are shown between a cohort of young post-pubertal men and women with juvenile-systemic lupus erythematosus (JSLE). Rituximab treatment was avoided in the cohort due to the known effects on lipids. Fisher's exact test* or unpaired t-test was used. Abbreviations: NR: Normal range, ESR: Erythrocyte sedimentation rate, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, dsDNA: Anti-double-stranded-DNA antibodies, C3: Complement component 3.

Table S8: Demographic and clinical comparison between young post-pubertal men and women with juvenile idiopathic arthritis, Related to Figure 1 and Figure S3

Demographic, n (%)	Men	Women	P value
Number	48	73	-
Age	18 (16-22)	18 (16-24)	0.74
White	37 (77)	54 (74)	0.83*
Asian	5 (10)	5 (7)	0.52*
Black	2 (4)	5 (7)	0.70*
Other	4 (8)	9 (12)	0.56*
JIA subtype, n (%)			
Extended Oligoarticular Arthritis (EOA)	13 (27)	13 (18)	0.26*
Enthesitis-related arthritis (ERA)	17 (35)	4 (5)	0.0001*
Oligoarthritis (OA)	8 (17)	13 (18)	>0.99*
Polyarticular arthritis (PO)	8 (17)	36 (49)	0.0002*
Psoriatic arthritis (PS)	2 (4)	7 (10)	0.32*
Clinical feature, median (IQR)			
Disease duration, years	9.53 (4.92-2.97)	9.58 (4.14-13.27)	0.88
JADAS score	2 (0-9)	5.65 (1.88-10.55)	0.27
Number of active joints	0 (0-1)	0 (0-2)	0.48
Patient global assessment, VAS	2 (0-5)	3 (0.25-5.6)	0.09
Physician's global assessment, VAS (NR<4)	0 (0-4.5)	1 (0-4)	0.71
CRP, mg/L (NR<5)	0.9 (0.6-3.78)	1.1 (0.6-2.4)	0.12
ESR, mm/hr (NR=1.3-3.5)	2 (2-5.5)	5 (2-14.25)	0.14
Anti-nuclear antibodies+, n (%)	3 (6.25)	18 (24.66)	0.01*
Rheumatoid factor+, n (%)	0 (0)	4 (5.48)	0.15*
HLA-B27+, n (%)	7 (14.58)	2 (2.74)	0.03*
Treatment, n (%)			
Prednisolone	0 (0)	0 (0)	>0.99*
Methotrexate	22 (46)	42 (58)	0.26*
Biologic therapy	0 (0)	0 (0)	>0.99*

Table S8: Demographic and clinical comparison between young post-pubertal men and women with juvenile idiopathic arthritis, Related to Figure 1 and Figure S3. Demographics and common clinical measures and treatments of disease are shown between a cohort of young post-pubertal men and women with juvenile idiopathic arthritis (JIA). Patients on biologic therapy (eg. tocilizumab, anti-TNFα, rituximab etc.) were avoided in the cohorts due to their known effects on lipids. Fisher's exact test* or unpaired t-test was used. Abbreviations: NR: Normal range, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, JADAS: Juvenile Arthritis Disease Activity Score, VAS: Visual Analogue Scale.

Supplemental Data

Table SD1: Metabolites significantly associated with young post-pubertal cis-men and cis-women, Related to Figure 2B

Table SD2: Metabolites significantly altered by hormone treatment in young trans-women, Related to Figure 2C

Table SD3: Metabolites significantly altered by hormone treatment in young trans-men, Related to Figure 2D

Table SD4: List of non-significant p values from the comparison of cis-men vs trans-men and cis-women vs trans-women, Related to Figure 2

Table SD1: Metabolites significantly associated with young post-pubertal cis-men and cis-women, Related to Figure 2B

Metabolite group	Metabolite	Mean (men)	SD (men)	Mean (women)	SD (women)	Fold change (from men)	P value (t-test)
Cholesterol (mmol/l)	Total-C	3.8573	0.8579	4.1247	0.5856	1.0693	0.3065
	non-HDL-C	2.6387	0.8153	2.6047	0.5164	0.9871	0.8876
	Remnant-C	1.1409	0.3971	1.1165	0.2609	0.9786	0.8364
	VLDL-C	0.5232	0.2346	0.4096	0.1622	0.7829	0.1181
	Clinical LDL-C	2.0653	0.6826	2.1359	0.4249	1.0342	0.7247
	LDL-C	1.4971	0.4271	1.4912	0.2685	0.9961	0.9626
	HDL-C	1.2189	0.2620	1.5188	0.3117	1.2461	0.0065
Triglycerides (mmol/l)	Total-TG	1.2637	0.5867	0.7899	0.3362	0.6251	0.0079
	VLDL-TG	0.9639	0.5106	0.5219	0.2903	0.5415	0.0047
	LDL-TG	0.1183	0.0336	0.1090	0.0202	0.9217	0.3467
	HDL-TG	0.1069	0.0381	0.0868	0.0299	0.8124	0.1061
Phospholipids (mmol/l)	Total-PL	2.5013	0.4305	2.6159	0.3327	1.0458	0.4033
	VLDL-PL	0.3783	0.1782	0.2570	0.1156	0.6793	0.0278
	LDL-PL	0.5233	0.1353	0.5305	0.0842	1.0138	0.8561
	HDL-PL	1.3867	0.2613	1.6029	0.2732	1.1560	0.0298
Cholesteryl esters (mmol/l)	Total-CE	2.8307	0.6127	3.0641	0.4319	1.0825	0.2183
	VLDL-CE	0.2990	0.1327	0.2521	0.0932	0.8432	0.2522
	LDL-CE	1.1041	0.3194	1.0705	0.2039	0.9696	0.7226
	HDL-CE	0.9649	0.2101	1.2059	0.2489	1.2499	0.0063
Free cholesterol (mmol/l)	Total-FC	1.0257	0.2511	1.0606	0.1600	1.0340	0.6383
	VLDL-FC	0.2241	0.1049	0.1573	0.0697	0.7019	0.0401
	LDL-FC	0.3943	0.1114	0.4198	0.0681	1.0646	0.4351
	HDL-FC	0.2541	0.0552	0.3142	0.0654	1.2368	0.0091
Total lipids (mmol/l)	Total-L	7.6233	1.6180	7.5300	1.1029	0.9878	0.8485
	VLDL-L	1.8638	0.8787	1.1874	0.5555	0.6371	0.0132
	LDL-L	2.1400	0.5864	2.1294	0.3645	0.9951	0.9509
	HDL-L	2.7113	0.5133	3.2100	0.5770	1.1839	0.0155
Lipoprotein particle concentrations (mmol/l)	Total-P	0.0158	0.0021	0.0174	0.0023	1.1028	0.0454
	VLDL-P	0.0001	0.0000	0.0001	0.0000	0.7955	0.085
	LDL-P	0.0010	0.0003	0.0010	0.0002	0.9477	0.5257
	HDL-P	0.0145	0.0021	0.0161	0.0022	1.1164	0.0349
Lipoprotein particle sizes (nm)	VLDL size	39.5400	1.3168	37.7353	1.1297	0.9544	0.0002
	LDL size	23.8800	0.0862	23.8824	0.0951	1.0001	0.9423
	HDL size	9.5427	0.1360	9.7165	0.1482	1.0182	0.0017
Other lipids (mmol/l)	PG	2.0320	0.3469	2.1494	0.3075	1.0578	0.3181
	TG/PG	0.6153	0.2457	0.3648	0.1384	0.5928	0.0011
	Cholines	2.3167	0.3520	2.4759	0.3189	1.0687	0.1895
	Phosphatidylcho	1.9180	0.3251	2.0388	0.2929	1.0630	0.2774
	Sphingomyelins	0.4077	0.0604	0.4422	0.0463	1.0845	0.0783
Apolipoproteins (g/l)	ApoB	0.6958	0.1976	0.6640	0.1235	0.9543	0.5843
	ApoA1	1.3467	0.2014	1.5265	0.2214	1.1335	0.0233
	ApoB/ApoA1	0.5277	0.1727	0.4433	0.1042	0.8400	0.0999
Fatty acids (mmol/l)	Total-FA	10.8300	2.4677	10.0488	1.6107	0.9279	0.2919
	Unsaturation	1.2720	0.0655	1.3188	0.0531	1.0368	0.0332
	Omega-3	0.3593	0.0983	0.3578	0.1290	0.9958	0.971
	Omega-6	4.1287	0.6732	4.1665	0.5693	1.0092	0.8645
	PUFA	4.4873	0.7466	4.5247	0.6547	1.0083	0.8811
	MUFA	2.7093	0.8727	2.2794	0.4737	0.8413	0.0885
	SFA	3.6227	0.9593	3.2335	0.5712	0.8926	0.1676
	LA	3.4193	0.6324	3.5241	0.5940	1.0306	0.6325
	DHA	0.1962	0.0314	0.2298	0.0509	1.1711	0.0349
Lipoprotein subclasses (mmol/l)	XXL-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.1957	0.0041
	XXL-VLDL-L	0.1859	0.1824	0.0400	0.0680	0.2150	0.0045
	XXL-VLDL-PL	0.0241	0.0249	0.0041	0.0090	0.1704	0.0042
	XXL-VLDL-C	0.0422	0.0344	0.0138	0.0151	0.3260	0.0043
	XXL-VLDL-CE	0.0257	0.0194	0.0100	0.0093	0.3900	0.0058
	XXL-VLDL-FC	0.0165	0.0155	0.0038	0.0062	0.2273	0.004
	XXL-VLDL-TG	0.1198	0.1245	0.0222	0.0450	0.1850	0.0051
	XL-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.4028	0.0034
	XL-VLDL-L	0.2089	0.1404	0.0832	0.0793	0.3984	0.0035
	XL-VLDL-PL	0.0352	0.0262	0.0124	0.0142	0.3507	0.0039
	XL-VLDL-C	0.0472	0.0287	0.0244	0.0179	0.5171	0.0103
	XL-VLDL-CE	0.0266	0.0146	0.0163	0.0100	0.6148	0.0264
	XL-VLDL-FC	0.0206	0.0144	0.0081	0.0081	0.3911	0.0044
	XL-VLDL-TG	0.1266	0.0878	0.0465	0.0481	0.3669	0.0028
	L-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.5131	0.0055
	L-VLDL-L	0.3621	0.1984	0.1832	0.1279	0.5061	0.0046
	L-VLDL-PL	0.0689	0.0414	0.0320	0.0258	0.4640	0.0045
	L-VLDL-C	0.0884	0.0490	0.0475	0.0336	0.5368	0.0091
	L-VLDL-CE	0.0429	0.0234	0.0250	0.0171	0.5836	0.0186
	L-VLDL-FC	0.0456	0.0260	0.0224	0.0166	0.4913	0.0048
	L-VLDL-TG	0.2048	0.1105	0.1040	0.0700	0.5079	0.004
	M-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.7611	0.0772
	M-VLDL-L	0.5295	0.2196	0.3860	0.1602	0.7289	0.0415
	M-VLDL-PL	0.1055	0.0485	0.0814	0.0340	0.7717	0.111
	M-VLDL-C	0.1188	0.0610	0.1089	0.0417	0.9169	0.5931
	M-VLDL-CE	0.0587	0.0345	0.0609	0.0219	1.0379	0.8269
	M-VLDL-FC	0.0600	0.0287	0.0481	0.0205	0.8005	0.1805
	M-VLDL-TG	0.3055	0.1315	0.1957	0.0899	0.6406	0.0092
	S-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.7778	0.0577
	S-VLDL-L	0.3415	0.1215	0.2707	0.0902	0.7928	0.0691
	S-VLDL-PL	0.0771	0.0283	0.0657	0.0207	0.8522	0.1993
	S-VLDL-C	0.1119	0.0455	0.0970	0.0332	0.8673	0.2963
	S-VLDL-CE	0.0672	0.0280	0.0572	0.0211	0.8520	0.2615
	S-VLDL-FC	0.0446	0.0176	0.0399	0.0125	0.8930	0.3788
	S-VLDL-TG	0.1524	0.0577	0.1079	0.0392	0.7078	0.015
	XS-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.9804	0.8403

	XS-VLDL-L	0.2359	0.0803	0.2250	0.0574	0.9537	0.658
	XS-VLDL-PL	0.0674	0.0247	0.0615	0.0184	0.9127	0.4475
	XS-VLDL-C	0.1147	0.0430	0.1179	0.0283	1.0277	0.8042
	XS-VLDL-CE	0.0779	0.0304	0.0826	0.0191	1.0606	0.5978
	XS-VLDL-FC	0.0367	0.0131	0.0352	0.0094	0.9579	0.7009
	XS-VLDL-TG	0.0539	0.0172	0.0457	0.0126	0.8472	0.1305
	IDL-P	0.0002	0.0001	0.0002	0.0000	1.0708	0.3936
	IDL-L	0.9091	0.2695	1.0041	0.1655	1.1046	0.2325
	IDL-PL	0.2138	0.0637	0.2263	0.0359	1.0584	0.4932
	IDL-C	0.6180	0.1918	0.7058	0.1231	1.1420	0.1294
	IDL-CE	0.4629	0.1452	0.5323	0.0972	1.1500	0.1186
	IDL-FC	0.1550	0.0474	0.1735	0.0264	1.1194	0.1763
	IDL-TG	0.0768	0.0215	0.0725	0.0143	0.9447	0.511
	L-LDL-P	0.0006	0.0002	0.0006	0.0001	0.9610	0.6355
	L-LDL-L	1.3267	0.3641	1.3562	0.2299	1.0222	0.7833
	L-LDL-PL	0.2969	0.0774	0.3094	0.0484	1.0421	0.5838
	L-LDL-C	0.9521	0.2707	0.9728	0.1748	1.0217	0.7973
	L-LDL-CE	0.7097	0.2008	0.7104	0.1336	1.0009	0.9918
	L-LDL-FC	0.2425	0.0711	0.2618	0.0424	1.0793	0.3534
	L-LDL-TG	0.0773	0.0212	0.0742	0.0132	0.9599	0.6185
	M-LDL-P	0.0003	0.0001	0.0002	0.0000	0.9018	0.2851
	M-LDL-L	0.5553	0.1644	0.5264	0.1004	0.9478	0.5466
	M-LDL-PL	0.1458	0.0399	0.1423	0.0256	0.9756	0.7637
	M-LDL-C	0.3821	0.1179	0.3596	0.0722	0.9412	0.5149
	M-LDL-CE	0.2767	0.0912	0.2498	0.0545	0.9028	0.3124
	M-LDL-FC	0.1052	0.0295	0.1098	0.0191	1.0434	0.6026
	M-LDL-TG	0.0275	0.0081	0.0245	0.0048	0.8909	0.2066
	S-LDL-P	0.0001	0.0000	0.0001	0.0000	0.9636	0.6348
	S-LDL-L	0.2576	0.0673	0.2474	0.0385	0.9602	0.5956
	S-LDL-PL	0.0807	0.0195	0.0788	0.0109	0.9773	0.7411
	S-LDL-C	0.1636	0.0447	0.1582	0.0260	0.9671	0.6758
	S-LDL-CE	0.1169	0.0338	0.1101	0.0192	0.9415	0.4807
	S-LDL-FC	0.0467	0.0115	0.0482	0.0072	1.0316	0.6624
	S-LDL-TG	0.0135	0.0049	0.0103	0.0026	0.7630	0.0255
	XL-HDL-P	0.0002	0.0000	0.0002	0.0001	1.4029	0.0028
	XL-HDL-L	0.1203	0.0341	0.1787	0.0581	1.4853	0.0019
	XL-HDL-PL	0.0517	0.0185	0.0836	0.0319	1.6161	0.0019
	XL-HDL-C	0.0637	0.0160	0.0905	0.0258	1.4215	0.0016
	XL-HDL-CE	0.0455	0.0136	0.0683	0.0219	1.5003	0.0016
	XL-HDL-FC	0.0182	0.0030	0.0223	0.0041	1.2272	0.0029
	XL-HDL-TG	0.0049	0.0020	0.0045	0.0015	0.9229	0.5539
	L-HDL-P	0.0011	0.0005	0.0018	0.0007	1.6394	0.0031
	L-HDL-L	0.5121	0.2136	0.7974	0.2810	1.5572	0.0032
	L-HDL-PL	0.2559	0.1035	0.3864	0.1310	1.5102	0.0042
	L-HDL-C	0.2389	0.1103	0.3928	0.1485	1.6438	0.0026
	L-HDL-CE	0.1899	0.0880	0.3116	0.1174	1.6412	0.0026
	L-HDL-FC	0.0490	0.0231	0.0812	0.0313	1.6559	0.0027
	L-HDL-TG	0.0172	0.0085	0.0185	0.0078	1.0747	0.6577
	M-HDL-P	0.0035	0.0008	0.0042	0.0008	1.1942	0.0253
	M-HDL-L	0.9523	0.1985	1.0960	0.1928	1.1509	0.0466
	M-HDL-PL	0.4443	0.0898	0.4972	0.0807	1.1189	0.0898
	M-HDL-C	0.4677	0.1078	0.5686	0.1152	1.2159	0.0162
	M-HDL-CE	0.3903	0.0876	0.4729	0.0934	1.2115	0.0154
	M-HDL-FC	0.0774	0.0211	0.0959	0.0222	1.2377	0.0229
	M-HDL-TG	0.0392	0.0157	0.0303	0.0129	0.7725	0.0882
	S-HDL-P	0.0097	0.0009	0.0099	0.0009	1.0239	0.488
	S-HDL-L	1.1283	0.1176	1.1372	0.1081	1.0079	0.825
	S-HDL-PL	0.6335	0.0720	0.6358	0.0644	1.0036	0.925
	S-HDL-C	0.4488	0.0451	0.4672	0.0456	1.0411	0.2606
	S-HDL-CE	0.3394	0.0331	0.3523	0.0337	1.0380	0.2846
	S-HDL-FC	0.1095	0.0138	0.1150	0.0131	1.0504	0.2554
	S-HDL-TG	0.0456	0.0139	0.0335	0.0106	0.7352	0.0094

Table SD1: Metabolites significantly associated with young post-pubertal cis-men and cis-women, Related to Figure 2B. Mean, standard deviations and p values (multiple unpaired t-tests) from metabolite comparisons (Figure 2B) between young post-pubertal men (n=15) and women (n=17). Statistically significant p values following 6% false discovery rate adjustment for multiple comparisons (Benjamini, Krieger and Yekutieli approach) are highlighted in red. Abbreviations: Apo, apolipoprotein; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein; XXL-VLDL, chylomicrons and extremely large VLDL; X-Large, very large; X-small, very small; PG (Phosphoglyceride), DHA, Docosahexaenoic acid; LA, Linoleic acid; PUFA, Polyunsaturated fatty acids; MUFA, Monounsaturated fatty acids; SFA, Saturated fatty acids; TG, triglycerides; PL, phospohlipids, FC, free cholesterol, C, cholesterol, CE, cholesterol esters; P, particle; L, lipids.

Table SD2: Metabolites significantly altered by hormone treatment in young trans-women, Related to Figure 2C

Metabolite group	Metabolite	Mean (men)	SD (men)	Mean (Trans-women)	SD (Trans-women)	Fold change (from men)	P value (t-test)
Cholesterol (mmol/l)	Total-C	3.8573	0.8579	4.3500	0.7797	1.1277	0.0701
	non-HDL-C	2.6387	0.8153	2.8732	0.6785	1.0889	0.3327
	Remnant-C	1.1409	0.3971	1.2659	0.3284	1.1095	0.2882
	VLDL-C	0.5232	0.2346	0.5248	0.1994	1.0031	0.9813
	Clinical LDL-C	2.0653	0.6826	2.2528	0.5342	1.0908	0.3394
	LDL-C	1.4971	0.4271	1.6064	0.3589	1.0730	0.3905
	HDL-C	1.2189	0.2620	1.4764	0.3253	1.2113	0.0133
Triglycerides (mmol/l)	Total-TG	1.2637	0.5867	1.2017	0.5294	0.9509	0.7325
	VLDL-TG	0.9639	0.5106	0.8593	0.4445	0.8915	0.4997
	LDL-TG	0.1183	0.0336	0.1264	0.0340	1.0686	0.4678
	HDL-TG	0.1069	0.0381	0.1305	0.0482	1.2212	0.114
Phospholipids (mmol/l)	Total-PL	2.5013	0.4305	2.8240	0.4770	1.1290	0.0383
	VLDL-PL	0.3783	0.1782	0.3606	0.1542	0.9534	0.7431
	LDL-PL	0.5233	0.1353	0.5542	0.1078	1.0589	0.4314
	HDL-PL	1.3867	0.2613	1.6632	0.3425	1.1994	0.0106
Cholesteryl esters (mmol/l)	Total-CE	2.8307	0.6127	3.1992	0.5559	1.1302	0.0581
	VLDL-CE	0.2990	0.1327	0.3087	0.1108	1.0324	0.8052
	LDL-CE	1.1041	0.3194	1.1751	0.2780	1.0644	0.4638
	HDL-CE	0.9649	0.2101	1.1581	0.2479	1.2002	0.016
Free cholesterol (mmol/l)	Total-FC	1.0257	0.2511	1.1492	0.2262	1.1204	0.1168
	VLDL-FC	0.2241	0.1049	0.2162	0.0901	0.9648	0.8026
	LDL-FC	0.3943	0.1114	0.4315	0.0838	1.0943	0.2378
	HDL-FC	0.2541	0.0552	0.3180	0.0784	1.2518	0.0086
Total lipids (mmol/l)	Total-L	7.6233	1.6180	8.3768	1.6226	1.0988	0.1628
	VLDL-L	1.8638	0.8787	1.7448	0.7741	0.9362	0.6571
	LDL-L	2.1400	0.5864	2.2868	0.4953	1.0686	0.4023
	HDL-L	2.7113	0.5133	3.2692	0.6805	1.2058	0.0094
Lipoprotein particle concentrations (mmol/l)	Total-P	0.0158	0.0021	0.0177	0.0024	1.1223	0.0135
	VLDL-P	0.0001	0.0000	0.0001	0.0000	1.0182	0.8787
	LDL-P	0.0010	0.0003	0.0010	0.0002	1.0232	0.7751
	HDL-P	0.0145	0.0021	0.0163	0.0023	1.1297	0.0136
Lipoprotein particle sizes (nm)	VLDL size	39.5400	1.3168	38.7600	1.2024	0.9803	0.0628
	LDL size	23.8800	0.0862	23.9040	0.1020	1.0010	0.4509
	HDL size	9.5427	0.1360	9.6896	0.1810	1.0154	0.01
Other lipids (mmol/l)	PG	2.0320	0.3469	2.3364	0.4302	1.1498	0.0257
	TG/PG	0.6153	0.2457	0.5097	0.1755	0.8284	0.1215
	Cholines	2.3167	0.3520	2.6248	0.4251	1.1330	0.0235
	Phosphatidylcho	1.9180	0.3251	2.2296	0.4252	1.1625	0.0196
	Sphingomyelins	0.4077	0.0604	0.4494	0.0618	1.1023	0.044
Apolipoproteins (g/l)	ApoB	0.6958	0.1976	0.7210	0.1576	1.0362	0.6588
	ApoA1	1.3467	0.2014	1.5564	0.2575	1.1557	0.0104
	ApoB/ApoA1	0.5277	0.1727	0.4740	0.1169	0.8983	0.2478
Fatty acids (mmol/l)	Total-FA	10.8300	2.4677	11.6440	2.5102	1.0752	0.3241
	Unsaturation	1.2720	0.0655	1.3000	0.0512	1.0220	0.1402
	Omega-3	0.3593	0.0983	0.4478	0.1923	1.2464	0.1068
	Omega-6	4.1287	0.6732	4.4120	0.6066	1.0686	0.1779
	PUFA	4.4873	0.7466	4.8604	0.7773	1.0831	0.1442
	MUFA	2.7093	0.8727	2.8680	0.7768	1.0586	0.5539
	SFA	3.6227	0.9593	3.9156	1.0546	1.0809	0.385
	LA	3.4193	0.6324	3.6440	0.5609	1.0657	0.2496
	DHA	0.1962	0.0314	0.2349	0.0576	1.1971	0.022
Lipoprotein subclasses (mmol/l)	XXL-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.7665	0.4041
	XXL-VLDL-L	0.1859	0.1824	0.1363	0.1297	0.7330	0.3215
	XXL-VLDL-PL	0.0241	0.0249	0.0171	0.0174	0.7091	0.3009
	XXL-VLDL-C	0.0422	0.0344	0.0323	0.0249	0.7648	0.2977
	XXL-VLDL-CE	0.0257	0.0194	0.0199	0.0140	0.7746	0.2811
	XXL-VLDL-FC	0.0165	0.0155	0.0124	0.0112	0.7510	0.338
	XXL-VLDL-TG	0.1198	0.1245	0.0870	0.0899	0.7261	0.3402
	XL-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.8251	0.3847
	XL-VLDL-L	0.2089	0.1404	0.1721	0.1206	0.8236	0.3843
	XL-VLDL-PL	0.0352	0.0262	0.0280	0.0212	0.7938	0.3423
	XL-VLDL-C	0.0472	0.0287	0.0395	0.0233	0.8365	0.3583
	XL-VLDL-CE	0.0266	0.0146	0.0229	0.0121	0.8601	0.3903
	XL-VLDL-FC	0.0206	0.0144	0.0166	0.0114	0.8063	0.3382
	XL-VLDL-TG	0.1266	0.0878	0.1045	0.0775	0.8259	0.4125
	L-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.8526	0.3825
	L-VLDL-L	0.3621	0.1984	0.3103	0.1757	0.8569	0.3949
	L-VLDL-PL	0.0689	0.0414	0.0569	0.0355	0.8250	0.3342
	L-VLDL-C	0.0884	0.0490	0.0770	0.0438	0.8703	0.4475
	L-VLDL-CE	0.0429	0.0234	0.0388	0.0219	0.9052	0.5828
	L-VLDL-FC	0.0456	0.0260	0.0382	0.0222	0.8371	0.3429
	L-VLDL-TG	0.2048	0.1105	0.1764	0.0985	0.8610	0.4032
	M-VLDL-P	0.0000	0.0000	0.0000	0.0000	0.9701	0.8182
	M-VLDL-L	0.5295	0.2196	0.5103	0.1996	0.9636	0.7776
	M-VLDL-PL	0.1055	0.0485	0.1043	0.0424	0.9891	0.9378
	M-VLDL-C	0.1188	0.0610	0.1247	0.0467	1.0496	0.7329
	M-VLDL-CE	0.0587	0.0345	0.0638	0.0235	1.0868	0.5815
	M-VLDL-FC	0.0600	0.0287	0.0609	0.0247	1.0139	0.9228
	M-VLDL-TG	0.3055	0.1315	0.2812	0.1202	0.9207	0.5547
	S-VLDL-P	0.0000	0.0000	0.0000	0.0000	1.0011	0.9923
	S-VLDL-L	0.3415	0.1215	0.3439	0.1169	1.0071	0.9506
	S-VLDL-PL	0.0771	0.0283	0.0784	0.0258	1.0171	0.8808
	S-VLDL-C	0.1119	0.0455	0.1133	0.0391	1.0129	0.9157
	S-VLDL-CE	0.0672	0.0280	0.0675	0.0245	1.0054	0.9661
	S-VLDL-FC	0.0446	0.0176	0.0458	0.0148	1.0260	0.824
	S-VLDL-TG	0.1524	0.0577	0.1520	0.0574	0.9976	0.9842
	XS-VLDL-P	0.0000	0.0000	0.0000	0.0000	1.1483	0.1596

	XS-VLDL-L	0.2359	0.0803	0.2726	0.0777	1.1552	0.1623
	XS-VLDL-PL	0.0674	0.0247	0.0760	0.0229	1.1283	0.2688
	XS-VLDL-C	0.1147	0.0430	0.1380	0.0391	1.2036	0.0861
	XS-VLDL-CE	0.0779	0.0304	0.0958	0.0268	1.2291	0.0596
	XS-VLDL-FC	0.0367	0.0131	0.0423	0.0126	1.1512	0.1913
	XS-VLDL-TG	0.0539	0.0172	0.0585	0.0178	1.0847	0.4318
	IDL-P	0.0002	0.0001	0.0003	0.0000	1.1080	0.1734
	IDL-L	0.9091	0.2695	1.0729	0.2270	1.1802	0.0463
	IDL-PL	0.2138	0.0637	0.2463	0.0513	1.1519	0.0849
	IDL-C	0.6180	0.1918	0.7411	0.1593	1.1992	0.0346
	IDL-CE	0.4629	0.1452	0.5574	0.1206	1.2043	0.0322
	IDL-FC	0.1550	0.0474	0.1837	0.0397	1.1855	0.0461
	IDL-TG	0.0768	0.0215	0.0853	0.0226	1.1108	0.2473
	L-LDL-P	0.0006	0.0002	0.0006	0.0001	1.0343	0.6592
	L-LDL-L	1.3267	0.3641	1.4608	0.3013	1.1011	0.2154
	L-LDL-PL	0.2969	0.0774	0.3239	0.0621	1.0911	0.2317
	L-LDL-C	0.9521	0.2707	1.0529	0.2224	1.1058	0.2089
	L-LDL-CE	0.7097	0.2008	0.7810	0.1707	1.1004	0.2392
	L-LDL-FC	0.2425	0.0711	0.2722	0.0537	1.1222	0.1433
	L-LDL-TG	0.0773	0.0212	0.0840	0.0218	1.0875	0.3439
	M-LDL-P	0.0003	0.0001	0.0003	0.0001	1.0028	0.9782
	M-LDL-L	0.5553	0.1644	0.5693	0.1494	1.0252	0.784
	M-LDL-PL	0.1458	0.0399	0.1498	0.0325	1.0275	0.731
	M-LDL-C	0.3821	0.1179	0.3907	0.1108	1.0225	0.8174
	M-LDL-CE	0.2767	0.0912	0.2789	0.0897	1.0080	0.9405
	M-LDL-FC	0.1052	0.0295	0.1118	0.0230	1.0627	0.4353
	M-LDL-TG	0.0275	0.0081	0.0288	0.0082	1.0468	0.6327
	S-LDL-P	0.0001	0.0000	0.0001	0.0000	1.0075	0.9219
	S-LDL-L	0.2576	0.0673	0.2576	0.0541	0.9998	0.9984
	S-LDL-PL	0.0807	0.0195	0.0804	0.0149	0.9964	0.9575
	S-LDL-C	0.1636	0.0447	0.1635	0.0358	0.9994	0.9942
	S-LDL-CE	0.1169	0.0338	0.1160	0.0274	0.9924	0.928
	S-LDL-FC	0.0467	0.0115	0.0476	0.0091	1.0184	0.7945
	S-LDL-TG	0.0135	0.0049	0.0136	0.0046	1.0076	0.9471
	XL-HDL-P	0.0002	0.0000	0.0002	0.0001	1.3577	0.0201
	XL-HDL-L	0.1203	0.0341	0.1681	0.0744	1.3973	0.0249
	XL-HDL-PL	0.0517	0.0185	0.0785	0.0416	1.5176	0.0242
	XL-HDL-C	0.0637	0.0160	0.0831	0.0317	1.3043	0.034
	XL-HDL-CE	0.0455	0.0136	0.0616	0.0258	1.3531	0.032
	XL-HDL-FC	0.0182	0.0030	0.0215	0.0061	1.1837	0.0544
	XL-HDL-TG	0.0049	0.0020	0.0065	0.0029	1.3302	0.0701
	L-HDL-P	0.0011	0.0005	0.0017	0.0008	1.5463	0.0129
	L-HDL-L	0.5121	0.2136	0.7625	0.3258	1.4891	0.0117
	L-HDL-PL	0.2559	0.1035	0.3779	0.1563	1.4769	0.0107
	L-HDL-C	0.2389	0.1103	0.3564	0.1623	1.4916	0.0179
	L-HDL-CE	0.1899	0.0880	0.2789	0.1253	1.4689	0.0208
	L-HDL-FC	0.0490	0.0231	0.0774	0.0373	1.5786	0.0116
	L-HDL-TG	0.0172	0.0085	0.0287	0.0147	1.6681	0.009
	M-HDL-P	0.0035	0.0008	0.0043	0.0010	1.2268	0.0102
	M-HDL-L	0.9523	0.1985	1.1407	0.2296	1.1979	0.012
	M-HDL-PL	0.4443	0.0898	0.5280	0.1024	1.1883	0.0127
	M-HDL-C	0.4677	0.1078	0.5643	0.1198	1.2066	0.0145
	M-HDL-CE	0.3903	0.0876	0.4652	0.0944	1.1918	0.0171
	M-HDL-FC	0.0774	0.0211	0.0991	0.0258	1.2793	0.0093
	M-HDL-TG	0.0392	0.0157	0.0486	0.0192	1.2406	0.1173
	S-HDL-P	0.0097	0.0009	0.0101	0.0008	1.0451	0.1366
	S-HDL-L	1.1283	0.1176	1.1979	0.1238	1.0617	0.0877
	S-HDL-PL	0.6335	0.0720	0.6789	0.0793	1.0716	0.0779
	S-HDL-C	0.4488	0.0451	0.4719	0.0373	1.0515	0.0876
	S-HDL-CE	0.3394	0.0331	0.3517	0.0247	1.0362	0.1884
	S-HDL-FC	0.1095	0.0138	0.1200	0.0153	1.0959	0.0354
	S-HDL-TG	0.0456	0.0139	0.0467	0.0148	1.0246	0.8133

Table SD2: Metabolites significantly altered by hormone treatment in young trans-women, Related to Figure 2C. Mean, standard deviations and p values (multiple unpaired t-tests) from metabolite comparisons (Figure 2C) between young post-pubertal men (n=15) and trans-women (n=25). Statistically significant p values following 6% false discovery rate adjustment for multiple comparisons (Benjamini, Krieger and Yekutieli approach) are highlighted in red. Abbreviations: Apo, apolipoprotein; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein; XXL-VLDL, chylomicrons and extremely large VLDL; X-Large, very large; X-small, very small; PG (Phosphoglyceride), DHA, Docosahexaenoic acid; LA, Linoleic acid; PUFA, Polyunsaturated fatty acids; MUFA, Monounsaturated fatty acids; SFA, Saturated fatty acids; TG, triglycerides; PL, phospohlipids, FC, free cholesterol, C, cholesterol, CE, cholesterol esters; P, particle; L, lipids.

Table SD3: Metabolites significantly altered by hormone treatment in young trans-men, Related to Figure 2D

Metabolite group	Metabolite	Mean (women)	SD (women)	Mean (Trans-men)	SD (Trans-men)	Fold change (from women)	P value (t-test)
Cholesterol (mmol/l)	Total-C	4.1247	0.5856	3.7562	0.5842	0.9106	0.0499
	non-HDL-C	2.6047	0.5164	2.5846	0.4650	0.9923	0.8951
	Remnant-C	1.1165	0.2609	1.1256	0.2172	1.0082	0.9018
	VLDL-C	0.4096	0.1622	0.5034	0.1355	1.2290	0.0465
	Clinical LDL-C	2.1359	0.4249	2.0342	0.4175	0.9524	0.4427
	LDL-C	1.4912	0.2685	1.4602	0.2609	0.9792	0.7089
	HDL-C	1.5188	0.3117	1.1715	0.2289	0.7713	0.0001
Triglycerides (mmol/l)	Total-TG	0.7899	0.3362	1.1312	0.5387	1.4321	0.025
	VLDL-TG	0.5219	0.2903	0.8335	0.4779	1.5970	0.0206
	LDL-TG	0.1090	0.0202	0.1185	0.0212	1.0866	0.1541
	HDL-TG	0.0868	0.0299	0.1005	0.0391	1.1570	0.2289
Phospholipids (mmol/l)	Total-PL	2.6159	0.3327	2.3996	0.3137	0.9173	0.0368
	VLDL-PL	0.2570	0.1156	0.3514	0.1279	1.3675	0.0184
	LDL-PL	0.5305	0.0842	0.5160	0.0815	0.9727	0.5768
	HDL-PL	1.6029	0.2732	1.3135	0.2120	0.8194	0.0003
Cholesteryl esters (mmol/l)	Total-CE	3.0641	0.4319	2.7523	0.4306	0.8982	0.0255
	VLDL-CE	0.2521	0.0932	0.2944	0.0699	1.1678	0.0968
	LDL-CE	1.0705	0.2039	1.0688	0.1918	0.9984	0.9777
	HDL-CE	1.2059	0.2489	0.9254	0.1807	0.7674	0.0001
Free cholesterol (mmol/l)	Total-FC	1.0606	0.1600	1.0058	0.1578	0.9483	0.2748
	VLDL-FC	0.1573	0.0697	0.2090	0.0705	1.3287	0.0231
	LDL-FC	0.4198	0.0681	0.3915	0.0755	0.9324	0.2183
	HDL-FC	0.3142	0.0654	0.2464	0.0508	0.7842	0.0004
Total lipids (mmol/l)	Total-L	7.5300	1.1029	7.2869	1.1234	0.9677	0.4887
	VLDL-L	1.1874	0.5555	1.6886	0.7170	1.4221	0.0191
	LDL-L	2.1294	0.3645	2.0958	0.3517	0.9842	0.7639
	HDL-L	3.2100	0.5770	2.5850	0.4275	0.8053	0.0002
Lipoprotein particle concentrations (mmol/l)	Total-P	0.0174	0.0023	0.0149	0.0017	0.8563	0.0002
	VLDL-P	0.0001	0.0000	0.0001	0.0000	1.2112	0.0457
	LDL-P	0.0010	0.0002	0.0010	0.0002	1.0511	0.334
	HDL-P	0.0161	0.0022	0.0136	0.0017	0.8410	0.0001
Lipoprotein particle sizes (nm)	VLDL size	37.7353	1.1297	38.9885	1.5034	1.0332	0.0055
	LDL size	23.8824	0.0951	23.8769	0.1032	0.9998	0.8628
	HDL size	9.7165	0.1482	9.5692	0.1706	0.9848	0.0058
Other lipids (mmol/l)	PG	2.1494	0.3075	1.9300	0.2750	0.8979	0.019
	TG/PG	0.3648	0.1384	0.5785	0.2412	1.5861	0.002
	Cholines	2.4759	0.3189	2.2185	0.2732	0.8960	0.0072
	Phosphatidylcho	2.0388	0.2929	1.8269	0.2665	0.8961	0.0186
	Sphingomyelins	0.4422	0.0463	0.3962	0.0480	0.8959	0.0033
Apolipoproteins (g/l)	ApoB	0.6640	0.1235	0.6938	0.1047	1.0448	0.4008
	ApoA1	1.5265	0.2214	1.2792	0.1603	0.8380	0.0001
	ApoB/ApoA1	0.4433	0.1042	0.5478	0.0941	1.2359	0.0014
Fatty acids (mmol/l)	Total-FA	10.0488	1.6107	10.2650	1.8989	1.0215	0.7009
	Unsaturation	1.3188	0.0531	1.2542	0.0675	0.9510	0.0019
	Omega-3	0.3578	0.1290	0.3163	0.1254	0.8841	0.3008
	Omega-6	4.1665	0.5693	3.9496	0.4963	0.9480	0.1936
	PUFA	4.5247	0.6547	4.2662	0.5711	0.9429	0.1782
	MUFA	2.2794	0.4737	2.6608	0.7131	1.1673	0.0594
	SFA	3.2335	0.5712	3.3435	0.7713	1.0340	0.6173
	LA	3.5241	0.5940	3.2938	0.4925	0.9347	0.1746
	DHA	0.2298	0.0509	0.1874	0.0432	0.8157	0.0055
Lipoprotein subclasses (mmol/l)	XXL-VLDL-P	0.0000	0.0000	0.0000	0.0000	4.0991	0.0171
	XXL-VLDL-L	0.0400	0.0680	0.1476	0.1693	3.6922	0.0171
	XXL-VLDL-PL	0.0041	0.0090	0.0183	0.0234	4.4699	0.0219
	XXL-VLDL-C	0.0138	0.0151	0.0331	0.0298	2.4077	0.0176
	XXL-VLDL-CE	0.0100	0.0093	0.0204	0.0160	2.0402	0.0198
	XXL-VLDL-FC	0.0038	0.0062	0.0127	0.0141	3.3853	0.0182
	XXL-VLDL-TG	0.0222	0.0450	0.0961	0.1175	4.3383	0.0177
	XL-VLDL-P	0.0000	0.0000	0.0000	0.0000	2.0880	0.0102
	XL-VLDL-L	0.0832	0.0793	0.1766	0.1261	2.1214	0.0096
	XL-VLDL-PL	0.0124	0.0142	0.0295	0.0224	2.3827	0.008
	XL-VLDL-C	0.0244	0.0179	0.0409	0.0215	1.6737	0.0124
	XL-VLDL-CE	0.0163	0.0100	0.0235	0.0100	1.4355	0.0279
	XL-VLDL-FC	0.0081	0.0081	0.0174	0.0119	2.1583	0.007
	XL-VLDL-TG	0.0465	0.0481	0.1062	0.0828	2.2866	0.0104
	L-VLDL-P	0.0000	0.0000	0.0000	0.0000	1.6559	0.0187
	L-VLDL-L	0.1832	0.1279	0.3085	0.1792	1.6834	0.0168
	L-VLDL-PL	0.0320	0.0258	0.0583	0.0363	1.8245	0.0131
	L-VLDL-C	0.0475	0.0336	0.0778	0.0405	1.6385	0.0143
	L-VLDL-CE	0.0250	0.0171	0.0388	0.0189	1.5494	0.0198
	L-VLDL-FC	0.0224	0.0166	0.0390	0.0221	1.7398	0.0117
	L-VLDL-TG	0.1040	0.0700	0.1723	0.1038	1.6569	0.0221
	M-VLDL-P	0.0000	0.0000	0.0000	0.0000	1.2185	0.0848
	M-VLDL-L	0.3860	0.1602	0.4809	0.1686	1.2459	0.073
	M-VLDL-PL	0.0814	0.0340	0.0987	0.0323	1.2120	0.1014
	M-VLDL-C	0.1089	0.0417	0.1179	0.0343	1.0823	0.4464
	M-VLDL-CE	0.0609	0.0219	0.0607	0.0204	0.9961	0.9713
	M-VLDL-FC	0.0481	0.0205	0.0572	0.0180	1.1904	0.1301
	M-VLDL-TG	0.1957	0.0899	0.2644	0.1204	1.3512	0.0509
	S-VLDL-P	0.0000	0.0000	0.0000	0.0000	1.2431	0.0364
	S-VLDL-L	0.2707	0.0902	0.3278	0.0921	1.2108	0.0518
	S-VLDL-PL	0.0657	0.0207	0.0755	0.0184	1.1485	0.1131
	S-VLDL-C	0.0970	0.0332	0.1123	0.0253	1.1578	0.094
	S-VLDL-CE	0.0572	0.0211	0.0680	0.0152	1.1891	0.057
	S-VLDL-FC	0.0399	0.0125	0.0442	0.0103	1.1081	0.2247
	S-VLDL-TG	0.1079	0.0392	0.1401	0.0573	1.2990	0.0492
	XS-VLDL-P	0.0000	0.0000	0.0000	0.0000	1.0609	0.3139
	XS-VLDL-L	0.2250	0.0574	0.2468	0.0413	1.0969	0.1547

	XS-VLDL-PL	0.0615	0.0184	0.0711	0.0122	1.1562	0.0454
	XS-VLDL-C	0.1179	0.0283	0.1215	0.0241	1.0308	0.6553
	XS-VLDL-CE	0.0826	0.0191	0.0829	0.0178	1.0032	0.9628
	XS-VLDL-FC	0.0352	0.0094	0.0385	0.0067	1.0947	0.183
	XS-VLDL-TG	0.0457	0.0126	0.0543	0.0132	1.1886	0.0393
	IDL-P	0.0002	0.0000	0.0002	0.0000	0.9551	0.415
	IDL-L	1.0041	0.1655	0.9192	0.1686	0.9155	0.1116
	IDL-PL	0.2263	0.0359	0.2184	0.0372	0.9652	0.4957
	IDL-C	0.7058	0.1231	0.6213	0.1291	0.8803	0.0387
	IDL-CE	0.5323	0.0972	0.4625	0.0967	0.8688	0.0259
	IDL-FC	0.1735	0.0264	0.1588	0.0335	0.9157	0.1371
	IDL-TG	0.0725	0.0143	0.0788	0.0127	1.0862	0.1411
	L-LDL-P	0.0006	0.0001	0.0006	0.0001	1.0369	0.4847
	L-LDL-L	1.3562	0.2299	1.3059	0.2267	0.9629	0.4829
	L-LDL-PL	0.3094	0.0484	0.2930	0.0476	0.9471	0.2804
	L-LDL-C	0.9728	0.1748	0.9350	0.1742	0.9611	0.4911
	L-LDL-CE	0.7104	0.1336	0.6950	0.1288	0.9783	0.7077
	L-LDL-FC	0.2618	0.0424	0.2403	0.0483	0.9182	0.1439
	L-LDL-TG	0.0742	0.0132	0.0782	0.0121	1.0546	0.3068
	M-LDL-P	0.0002	0.0000	0.0003	0.0001	1.0976	0.1411
	M-LDL-L	0.5264	0.1004	0.5356	0.0988	1.0175	0.7677
	M-LDL-PL	0.1423	0.0256	0.1418	0.0249	0.9969	0.9563
	M-LDL-C	0.3596	0.0722	0.3663	0.0705	1.0188	0.7624
	M-LDL-CE	0.2498	0.0545	0.2624	0.0546	1.0505	0.4624
	M-LDL-FC	0.1098	0.0191	0.1039	0.0200	0.9468	0.3457
	M-LDL-TG	0.0245	0.0048	0.0272	0.0057	1.1107	0.1144
	S-LDL-P	0.0001	0.0000	0.0001	0.0000	1.0400	0.4329
	S-LDL-L	0.2474	0.0385	0.2532	0.0386	1.0238	0.6276
	S-LDL-PL	0.0788	0.0109	0.0811	0.0116	1.0288	0.5233
	S-LDL-C	0.1582	0.0260	0.1592	0.0256	1.0063	0.9021
	S-LDL-CE	0.1101	0.0192	0.1120	0.0185	1.0171	0.7507
	S-LDL-FC	0.0482	0.0072	0.0472	0.0083	0.9806	0.7071
	S-LDL-TG	0.0103	0.0026	0.0130	0.0041	1.2635	0.0211
	XL-HDL-P	0.0002	0.0001	0.0002	0.0001	0.7831	0.0236
	XL-HDL-L	0.1787	0.0581	0.1358	0.0616	0.7602	0.028
	XL-HDL-PL	0.0836	0.0319	0.0604	0.0340	0.7227	0.0305
	XL-HDL-C	0.0905	0.0258	0.0705	0.0281	0.7783	0.0229
	XL-HDL-CE	0.0683	0.0219	0.0502	0.0223	0.7352	0.0124
	XL-HDL-FC	0.0223	0.0041	0.0203	0.0059	0.9088	0.2237
	XL-HDL-TG	0.0045	0.0015	0.0051	0.0018	1.1269	0.2926
	L-HDL-P	0.0018	0.0007	0.0011	0.0006	0.6198	0.001
	L-HDL-L	0.7974	0.2810	0.5185	0.2318	0.6502	0.001
	L-HDL-PL	0.3864	0.1310	0.2548	0.1066	0.6595	0.0008
	L-HDL-C	0.3928	0.1485	0.2466	0.1258	0.6278	0.0012
	L-HDL-CE	0.3116	0.1174	0.1951	0.0982	0.6260	0.0011
	L-HDL-FC	0.0812	0.0313	0.0515	0.0278	0.6344	0.0023
	L-HDL-TG	0.0185	0.0078	0.0170	0.0080	0.9176	0.5422
	M-HDL-P	0.0042	0.0008	0.0032	0.0006	0.7718	0.0001
	M-HDL-L	1.0960	0.1928	0.8802	0.1517	0.8031	0.0002
	M-HDL-PL	0.4972	0.0807	0.4116	0.0703	0.8279	0.0007
	M-HDL-C	0.5686	0.1152	0.4333	0.0822	0.7620	0.0001
	M-HDL-CE	0.4729	0.0934	0.3622	0.0658	0.7659	0.0001
	M-HDL-FC	0.0959	0.0222	0.0712	0.0169	0.7428	0.0002
	M-HDL-TG	0.0303	0.0129	0.0355	0.0165	1.1718	0.2789
	S-HDL-P	0.0099	0.0009	0.0091	0.0010	0.9131	0.0059
	S-HDL-L	1.1372	0.1081	1.0508	0.1234	0.9240	0.0235
	S-HDL-PL	0.6358	0.0644	0.5868	0.0743	0.9229	0.0317
	S-HDL-C	0.4672	0.0456	0.4210	0.0438	0.9011	0.0019
	S-HDL-CE	0.3523	0.0337	0.3175	0.0336	0.9013	0.0019
	S-HDL-FC	0.1150	0.0131	0.1034	0.0113	0.8992	0.0037
	S-HDL-TG	0.0335	0.0106	0.0430	0.0147	1.2810	0.0281

Table SD3: Metabolites significantly altered by hormone treatment in young trans-men, Related to Figure 2D. Mean, standard deviations and p values (multiple unpaired t-tests) from metabolite comparisons (Figure 2D) between young post-pubertal women (n=17) and trans-men (n=26). Statistically significant p values following 6% false discovery rate adjustment for multiple comparisons (Benjamini, Krieger and Yekutieli approach) are highlighted in red. Abbreviations: Apo, apolipoprotein; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein; XXL-VLDL, chylomicrons and extremely large VLDL; X-Large, very large; X-small, very small; PG (Phosphoglyceride), DHA, Docosahexaenoic acid; LA, Linoleic acid; PUFA, Polyunsaturated fatty acids; MUFA, Monounsaturated fatty acids; SFA, Saturated fatty acids; TG, triglycerides; PL, phospohlipids, FC, free cholesterol, C, cholesterol, CE, cholesterol esters; P, particle; L, lipids.

Table SD4: List of non-significant p values from the comparison of cis-men vs trans-men and cis-women vs trans-women, Related to Figure 2.

Metabolite group	Metabolite	Cis-men vs Trans-men (adjusted p value)	Cis-women vs Trans-women (adjusted p value)
Cholesterol (mmol/l)	Total-C	0.4933	0.4933
	non-HDL-C	0.3480	0.3480
	Remnant-C	0.2818	0.2818
	VLDL-C	0.1720	0.1720
	Clinical LDL-C	0.6282	0.6282
	LDL-C	0.4469	0.4469
	HDL-C	0.7754	0.7754
Triglycerides (mmol/l)	Total-TG	0.0800	0.0800
	VLDL-TG	0.0800	0.0800
	LDL-TG	0.1907	0.1907
	HDL-TG	0.0800	0.0800
Phospholipids (mmol/l)	Total-PL	0.2832	0.2832
	VLDL-PL	0.1030	0.1030
	LDL-PL	0.6282	0.6282
	HDL-PL	0.6865	0.6865
Cholesteryl esters (mmol/l)	Total-CE	0.5967	0.5967
	VLDL-CE	0.2278	0.2278
	LDL-CE	0.3716	0.3716
	HDL-CE	0.6859	0.6859
Free cholesterol (mmol/l)	Total-FC	0.3473	0.3473
	VLDL-FC	0.1150	0.1150
	LDL-FC	0.7637	0.7637
	HDL-FC	0.8818	0.8818
Total lipids (mmol/l)	Total-L	0.1907	0.1907
	VLDL-L	0.0802	0.0802
	LDL-L	0.4469	0.4469
	HDL-L	0.8100	0.8100
Lipoprotein particle concentrations (mmol/l)	Total-P	0.7754	0.7754
	VLDL-P	0.1205	0.1205
	LDL-P	0.4259	0.4259
	HDL-P	0.8217	0.8217
Lipoprotein particle sizes (nm)	VLDL size	0.0800	0.0800
	LDL size	0.6487	0.6487
	HDL size	0.7512	0.7512
Other lipids (mmol/l)	PG	0.2871	0.2871
	TG/PG	0.0800	0.0800
	Cholines	0.4126	0.4126
	Phosphatidylcho	0.2663	0.2663
	Sphingomyelins	0.7754	0.7754
Apolipoproteins (g/l)	ApoB	0.4105	0.4105
	ApoA1	0.7762	0.7762
	ApoB/ApoA1	0.5834	0.5834
Fatty acids (mmol/l)	Total-FA	0.1077	0.1077
	Unsaturation	0.4391	0.4391
	Omega-3	0.2393	0.2393
	Omega-6	0.3716	0.3716
	PUFA	0.3276	0.3276
	MUFA	0.0800	0.0800
	SFA	0.0891	0.0891
	LA	0.6541	0.6541
	DHA	0.8100	0.8100
Lipoprotein subclasses (mmol/l)	XXL-VLDL-P	0.0800	0.0800
	XXL-VLDL-L	0.0800	0.0800
	XXL-VLDL-PL	0.0800	0.0800
	XXL-VLDL-C	0.0800	0.0800
	XXL-VLDL-CE	0.0802	0.0802
	XXL-VLDL-FC	0.0800	0.0800
	XXL-VLDL-TG	0.0800	0.0800
	XL-VLDL-P	0.0800	0.0800
	XL-VLDL-L	0.0800	0.0800
	XL-VLDL-PL	0.0800	0.0800
	XL-VLDL-C	0.1172	0.1172
	XL-VLDL-CE	0.1982	0.1982
	XL-VLDL-FC	0.0800	0.0800
	XL-VLDL-TG	0.0800	0.0800
	L-VLDL-P	0.0817	0.0817
	L-VLDL-L	0.0802	0.0802
	L-VLDL-PL	0.0818	0.0818
	L-VLDL-C	0.1030	0.1030
	L-VLDL-CE	0.1234	0.1234
	L-VLDL-FC	0.0817	0.0817
	L-VLDL-TG	0.0802	0.0802
	M-VLDL-P	0.1838	0.1838
	M-VLDL-L	0.1280	0.1280
	M-VLDL-PL	0.1907	0.1907
	M-VLDL-C	0.4469	0.4469
	M-VLDL-CE	0.7754	0.7754
	M-VLDL-FC	0.2199	0.2199
	M-VLDL-TG	0.0817	0.0817
	S-VLDL-P	0.1205	0.1205
	S-VLDL-L	0.1234	0.1234
	S-VLDL-PL	0.2388	0.2388
	S-VLDL-C	0.3462	0.3462
	S-VLDL-CE	0.3462	0.3462
	S-VLDL-FC	0.3575	0.3575
	S-VLDL-TG	0.0800	0.0800
	XS-VLDL-P	0.1849	0.1849
	XS-VLDL-L	0.1269	0.1269

	XS-VLDL-PL	0.1234	0.1234
	XS-VLDL-C	0.1982	0.1982
	XS-VLDL-CE	0.2251	0.2251
	XS-VLDL-FC	0.1720	0.1720
	XS-VLDL-TG	0.0802	0.0802
	IDL-P	0.7120	0.7120
	IDL-L	0.4716	0.4716
	IDL-PL	0.3473	0.3473
	IDL-C	0.6259	0.6259
	IDL-CE	0.6397	0.6397
	IDL-FC	0.5483	0.5483
	IDL-TG	0.1491	0.1491
	L-LDL-P	0.4250	0.4250
	L-LDL-L	0.4191	0.4191
	L-LDL-PL	0.6112	0.6112
	L-LDL-C	0.4105	0.4105
	L-LDL-CE	0.3408	0.3408
	L-LDL-FC	0.6541	0.6541
	L-LDL-TG	0.2452	0.2452
	M-LDL-P	0.4126	0.4126
	M-LDL-L	0.4861	0.4861
	M-LDL-PL	0.6112	0.6112
	M-LDL-C	0.4933	0.4933
	M-LDL-CE	0.4246	0.4246
	M-LDL-FC	0.8100	0.8100
	M-LDL-TG	0.1833	0.1833
	S-LDL-P	0.6397	0.6397
	S-LDL-L	0.6541	0.6541
	S-LDL-PL	0.7842	0.7842
	S-LDL-C	0.7452	0.7452
	S-LDL-CE	0.6259	0.6259
	S-LDL-FC	0.8378	0.8378
	S-LDL-TG	0.0800	0.0800
	XL-HDL-P	0.8100	0.8100
	XL-HDL-L	0.7570	0.7570
	XL-HDL-PL	0.7754	0.7754
	XL-HDL-C	0.6112	0.6112
	XL-HDL-CE	0.5834	0.5834
	XL-HDL-FC	0.7649	0.7649
	XL-HDL-TG	0.0802	0.0802
	L-HDL-P	0.7754	0.7754
	L-HDL-L	0.7842	0.7842
	L-HDL-PL	0.8717	0.8717
	L-HDL-C	0.6303	0.6303
	L-HDL-CE	0.5951	0.5951
	L-HDL-FC	0.7910	0.7910
	L-HDL-TG	0.0802	0.0802
	M-HDL-P	0.7754	0.7754
	M-HDL-L	0.6541	0.6541
	M-HDL-PL	0.4861	0.4861
	M-HDL-C	0.9130	0.9130
	M-HDL-CE	0.8239	0.8239
	M-HDL-FC	0.7754	0.7754
	M-HDL-TG	0.0800	0.0800
	S-HDL-P	0.6303	0.6303
	S-HDL-L	0.2538	0.2538
	S-HDL-PL	0.1907	0.1907
	S-HDL-C	0.7842	0.7842
	S-HDL-CE	0.9459	0.9459
	S-HDL-FC	0.4560	0.4560
	S-HDL-TG	0.0800	0.0800

Table SD4: List of non-significant p values from the comparison of cis-men vs trans-men and cis-women vs trans-women, Related to Figure 2. List of adjusted p values following 6% false discovery rate correction (Benjamini, Krieger and Yekutieli approach) from multiple unpaired t-tests of metabolite comparisons between young post-pubertal cis-men (n=15) and trans-men (n=26), or cis-women (n=17) and trans-women (n=25). Abbreviations: Apo, apolipoprotein; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein; XXL-VLDL, chylomicrons and extremely large VLDL; X-Large, very large; X-small, very small; PG (Phosphoglyceride), DHA, Docosahexaenoic acid; LA, Linoleic acid; PUFA, Polyunsaturated fatty acids; MUFA, Monounsaturated fatty acids; SFA, Saturated fatty acids; TG, triglycerides; PL, phospholipids, FC, free cholesterol, C, cholesterol, CE, cholesterol esters; P, particle; L, lipids.