

Supplementary tables

Supplementary Table 1. List of collaborating centers

1	Sheffield Children's Hospital and NIHR Clinical Research Facility, Sheffield Teaching Hospital, Sheffield
2	Birmingham Children's Hospital, Birmingham
3	Royal Hospital for Sick Children, Yorkhill, Glasgow
4	Great Ormond Street Hospital, London
5	Addenbrooke's Clinical Research Centre, Cambridge
6	Bristol Royal Hospital for Children, Bristol
7	Royal Manchester Children's Hospital, Manchester
8	Oxford Children's Hospital, Oxford
9	Great North Children's Hospital, Newcastle
10	Leeds General Infirmary, Leeds
11	University Hospital Southampton, Southampton
12	The Royal London Hospital, London
13	Nottingham University Hospitals NHS Trust, Nottingham

Supplementary Table 2. Plasma hormone concentrations for patients and controls expressed as median with interquartile range (nmol/l). The statistical difference was explored by the Mann Whitney U test.

	17-hydroxyprogesterone		Androstenedione		Testosterone		11-hydroxyandrostenedione		11-ketotestosterone	
Groups	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls
All	48.2(19.3-218.6)	1.57(0.8-3.0)	6.5(3.1-21.32)	2.3(1.0-3.7)	1.5(0.8-4.9)	0.83(0.3-11.0)	6.2(2.8-17.8)	2.7(1.8-4.7)	2.6(1.0-6.2)	0.9(0.6-1.4)
	$p<0.001$		$p<0.001$		$p=0.143$		$p<0.001$		$p<0.001$	
Boys	83.3(22.2-239.6)	2.2(1.2-3.8)	6.9(2.7-18.1)	1.9(1.1-3.44)	2.4(1.0-11.3)	13.5(2.2-19.4)	8.5(2.4-6.8)	3.18(1.84-9)	3.2(1.4-6.8)	1.0(0.72-1.5)
	$p<0.001$		$p<0.001$		$p=0.01$		$p=0.003$		$p<0.001$	
Girls	36.4(15.9-219.3)	1.1(0.7-2.2)	6.5(3.9-25.4)	2.6(1.0-4.1)	1.3(0.8-3.5)	0.5(0.2-0.9)	5.5(2.8-17.5)	2.6(1.8-4.3)	2.1(0.9-5.4)	0.9(0.6-1.3)
	$p<0.001$		$p<0.001$		$p<0.001$		$p=0.001$		$p<0.001$	
< 12 years	39.2(13.8-163.5)	0.84(0.6-1.3)	4.5(1.2-7.8)	0.9(0.5-1.6)	1.0(0.3-1.4)	0.2(0.1-0.5)	4.0(1.5-9.6)	2.2(1.3-2.8)	2.2(0.6-3.2)	0.6(0.4-0.9)
	$p<0.001$		$p<0.001$		$p=0.008$		$p=0.014$		$p=0.001$	
12-18 years	83.3(23.8-261.2)	2.4(1.5-3.7)	9.2(5.2-27.1)	3.4(2.3-4.6)	3.6(1.4-10.5)	2.9(0.8-17.6)	8.9(4.2-20.2)	4.2(2.0-5.5)	3.5(1.3-8.0)	1.2(0.9-1.6)
	$p<0.001$		$p<0.001$		$p=0.766$		$p<0.001$		$p<0.001$	

Supplementary Table 3. Salivary hormone concentrations for patients and controls expressed as median with interquartile range (pmol/l). The statistical difference was explored by the Mann Whitney U test.

	17-hydroxyprogesterone		Androstenedione		Testosterone		11-hydroxyandrostenedione		11-ketotestosterone	
Groups	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls
All	1452(341-3053)	39(27-74)	412(135-985)	146(62-242)	49(16-143)	34(13-164)	495(225-2214)	238(151-415)	347(161-1026)	167(103-279)
	<i>p</i> <0.001		<i>p</i> <0.001		<i>p</i> =0.681		<i>p</i> <0.001		<i>p</i> <0.001	
Boys	1452(359-3011)	64(33-95)	361(127-838)	168(62-290)	70(23-204)	163(58-249)	555(231-2672)	282(171-539)	432(193-1071)	225(107-338)
	<i>p</i> <0.001		<i>p</i> =0.015		<i>p</i> =0.138		<i>p</i> =0.029		<i>p</i> =0.013	
Girls	1503(291-3815)	30(22-43)	465(127-1238)	137(63-208)	41(15-122)	16(11-27)	443(223-2233)	219(149-399)	299(141-1071)	139(103-192)
	<i>p</i> <0.001		<i>p</i> <0.001		<i>p</i> =0.006		<i>p</i> =0.002		<i>p</i> =0.002	
< 12 years	571(223-2439)	24(18-32)	145(59-424)	60(35-114)	23(8-62)	12(11-22)	329(129-1094)	162(101-239)	195(100-512)	103(71-149)
	<i>p</i> <0.001		<i>p</i> =0.005		<i>p</i> =0.512		<i>p</i> =0.011		<i>p</i> =0.006	
12-18 years	2050(357-3893)	51(35-94)	666(334-1394)	210(139-327)	93(35-198)	71(16-220)	1238(368-2630)	342(223-699)	577(254-1676)	248(167-350)
	<i>p</i> <0.001		<i>p</i> <0.001		<i>p</i> =0.573		<i>p</i> <0.001		<i>p</i> =0.001	

Supplementary Table 4. Partial correlations between plasma and salivary steroids, (only patients treated with hydrocortisone, n=72), controlling for time elapsed from glucocorticoid administration to sample collection and glucocorticoid dose/m².

Spearman correlations	17OHP	A4	T	11OHA4	11KT
Without controlling for covariates	$r_s = 0.871$ $p < 0.001$	$r_s = 0.931$ $p < 0.001$	$r_s = 0.867$ $p < 0.001$	$r_s = 0.876$ $p < 0.001$	$r_s = 0.944$ $p < 0.001$
Controlling for time and dose/m ²	$r_s = 0.809$ $p < 0.001$	$r_s = 0.909$ $p < 0.001$	$r_s = 0.897$ $p < 0.001$	$r_s = 0.875$ $p < 0.001$	$r_s = 0.915$ $p < 0.001$

Supplementary Table 5. Results of Spearman correlations between plasma and salivary concentrations for steroid hormones in patients subgroups of age and gender. (17OHP: 17-hydroxyprogesterone, A4: androstenedione, T: testosterone, 11OHA4: 11-hydroxyandrostenedione, 11KT: 11-ketotestosterone)

	17OHP		A4		T		11OHA4		11KT	
	r_s	p	r_s	p	r_s	p	r_s	p	r_s	p
<12years	0.923	<0.001	0.918	<0.001	0.796	<0.001	0.857	<0.001	0.913	<0.001
12-18years	0.861	<0.001	0.894	<0.001	0.824	<0.001	0.859	<0.001	0.962	<0.001
Boys	0.863	<0.001	0.932	<0.001	0.786	<0.001	0.899	<0.001	0.932	<0.001
Girls	0.882	<0.001	0.919	<0.001	0.923	<0.001	0.870	<0.001	0.940	<0.001

Supplementary Table 6. Results of Spearman correlations between plasma and salivary concentrations for steroid hormones in controls subgroups of age and gender. (17OHP: 17-hydroxyprogesterone, A4: androstenedione, T: testosterone, 11OHA4: 11-hydroxyandrostenedione, 11KT: 11-ketotestosterone)

	17OHP		A4		T		11OHA4		11KT	
	r_s	p	r_s	p	r_s	p	r_s	p	r_s	p
<12years	0.082	0.771	0.962	<0.001	-0.03	0.934	0.770	<0.001	0.834	<0.001
12-18years	0.748	<0.001	0.779	<0.001	0.838	<0.001	0.840	<0.001	0.733	<0.001
Boys	0.782	<0.001	0.961	<0.001	0.749	<0.001	0.870	<0.001	0.830	<0.001
Girls	0.419	0.037	0.941	<0.001	0.261	0.266	0.799	<0.001	0.790	<0.001

Supplementary Table 7. Concentrations of plasma cortisol, salivary cortisol and cortisone in patients and controls expressed as median with interquartile range (nmol/l). The statistical difference was explored by the Mann Whitney U test.

Plasma cortisol		Salivary cortisol		Salivary cortisone	
Patients	Controls	Patients	Controls	Patients	Controls
287.3 (146.4- 419.9)	258.6 (196.5 – 317.8)	14.5 (6.7-78.9)	5.7 (3 – 8)	24.6 (16.5 – 45.4)	27.3 (20.4– 34.8)
$p=0.538$		$p<0.001$		$p=0.765$	

Supplementary Table 8. Results of Spearman correlations between plasma androgens and cortisol, salivary cortisol and cortisone in patients with CAH.

	Plasma Cortisol	Salivary Cortisol	Salivary Cortisone
Plasma 17-Hydroxyprogesterone	$r_s = 0.346$ $p = 0.006$	$r_s = 0.097$ $p = 0.489$	$r_s = 0.228$ $p = 0.100$
Plasma Androstenedione	$r_s = 0.302$ $p = 0.017$	$r_s = 0.114$ $p = 0.416$	$r_s = 0.142$ $p = 0.312$
Plasma Testosterone	$r_s = 0.227$ $p = 0.079$	$r_s = 0.256$ $p = 0.067$	$r_s = 0.321$ $p = 0.020$
Plasma 11-OHAndrostenedione	$r_s = 0.642$ $p < 0.001$	$r_s = 0.416$ $p = 0.002$	$r_s = 0.390$ $p = 0.004$
Plasma 11-Ketotestosterone	$r_s = 0.116$ $p = 0.370$	$r_s = 0.114$ $p = 0.418$	$r_s = 0.096$ $p = 0.494$

Supplementary Table 9. Results of Spearman correlations between salivary androgens and cortisol, salivary cortisol and cortisone in the control group.

	Plasma Cortisol	Salivary Cortisol	Salivary Cortisone
Salivary 17-Hydroxyprogesterone	$r_s = 0.297$ $p = 0.045$	$r_s = 0.452$ $p = 0.003$	$r_s = 0.479$ $p = 0.002$
Salivary Androstenedione	$r_s = 0.300$ $p = 0.023$	$r_s = 0.251$ $p = 0.079$	$r_s = 0.313$ $p = 0.027$
Salivary Testosterone	$r_s = 0.316$ $p = 0.044$	$r_s = 0.373$ $p = 0.023$	$r_s = 0.416$ $p = 0.011$
Salivary 11-OHAndrostenedione	$r_s = 0.494$ $p < 0.001$	$r_s = 0.531$ $p < 0.001$	$r_s = 0.543$ $p < 0.001$
Salivary 11-Ketotestosterone	$r_s = 0.313$ $p = 0.017$	$r_s = 0.363$ $p = 0.009$	$r_s = 0.427$ $p = 0.002$

Supplementary Table 10. Plasma and salivary hormone concentrations in treatment control groups expressed in median with interquartile range. The statistical difference was explored by the Mann Whitney U test. (17OHP: 17-hydroxyprogesterone, A4: androstenedione, T: testosterone, 11OHA4: 11-hydroxyandrostenedione, 11KT: 11-ketotestosterone)

	Good control	Undertreatment	Overtreatment	Under-treatment vs. good control	Over-treatment vs good control
Plasma concentrations (nmol/l)					
A4	4.7 (2.4-6.9)	13.8 (5.6-27.1)	2.3 (0.8-3.9)	$p=0.001$	$p=0.030$
T	1.2 (0.6-1.9)	3.2 (1.1-9.4)	0.7 (0.2-1.5)	$p=0.007$	$p=0.422$
11OHA4	3.9 (2.2-7.1)	11.9 (6-20.2)	1.6 (0.7-3.6)	$p=0.001$	$p=0.009$
11KT	1.3 (0.9-2.3)	4.2 (2.5-8.4)	0.7 (0.4-1.4)	$p<0.001$	$p=0.020$
Saliva concentrations (pmol/l)					
17OHP	360 (320-545)	2767(1452-5261)	123 (64-223)	$p<0.001$	$p=0.004$
A4	251 (87-438)	707 (340-1474)	91 (45-256)	$p=0.006$	$p=0.115$
T	26 (8-45)	94 (33-198)	14 (7-36)	$p=0.010$	$p=0.427$
11OHA4	406 (235-487)	1608(477-3058)	175(58-235)	$p=0.005$	$p=0.166$
11KT	161 (137-355)	661(312-1799)	94 (26-279)	$p=0.001$	$p=0.008$