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)
	p<0.001		*p<0.001*		*p=0.681*		*p<0.001*		*p<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)
	p<0.001		*p=0.015*		*p=0.138*		*p=0.029*		*p=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)
	p<0.001		*p<0.001*		*p=0.006*		*p=0.002*		*p=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)
	p<0.001		*p=0.005*		*p=0.512*		*p=0.011*		*p=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)
	p<0.001		*p<0.001*		*p=0.573*		*p<0.001*		*p=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/m^2.

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-hydroxyprogesteone, 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-hydroxyprogesteone, 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 expressed in median with interquartile range in patient subgroups based on 17-hydroxyprogesterone concentration. The statistical difference was explored by the Mann Whitney U test. (17OHP: 17-hydroxyprogesteone, A4: androstenedione, T: testosterone, 11OHA4: 11-hydroxyandrostenedione, 11KT: 11-ketotestosterone)

	17OHP within target range	**High 17OHP (Undertreatment)**	**Low 17 OHP (Overtreatment)**	**Undertreatment vs. normal**	**Overtreatment vs. normal**
Plasma concentrations (nmol/l)					
A4	4.6 (2.4-6.9)	15.0 (5.7-27.3)	2.2 (0.7-4.4)	*p<0.001*	*p=0.069*
T	1.1 (0.4-1.6)	3.2 (1.0-9.2)	0.9 (0.3-1.5)	*p=0.002*	*p=0.892*
11OHA4	3.5 (2.2-6.4)	12.7 (6.1-20.4)	1.2 (0.6-3.6)	*p<0.001*	*p=0.006*
11KT	1.3 (0.9-2.3)	4.2 (2.5-8.4)	0.5 (0.2-1.2)	*p<0.001*	*p=0.005*
Saliva concentrations (pmol/l)					
17OHP	362 (291-572)	2846(1762-5421)	94 (52-168)	*p<0.001*	*p=0.001*
A4	233 (100-415)	762 (333-1482)	59 (33-304)	*p<0.001*	*p=0.101*
T	26 (8-45)	94 (36-199)	23 (10-41)	*p=0.003*	*p=0.821*
11OHA4	358 (195-455)	2035(516-3144)	222 (50-239)	*p<0.001*	*p=0.021*
11KT	218 (137-387)	737(317-1863)	65 (21-274)	*p=0.001*	*p=0.043*