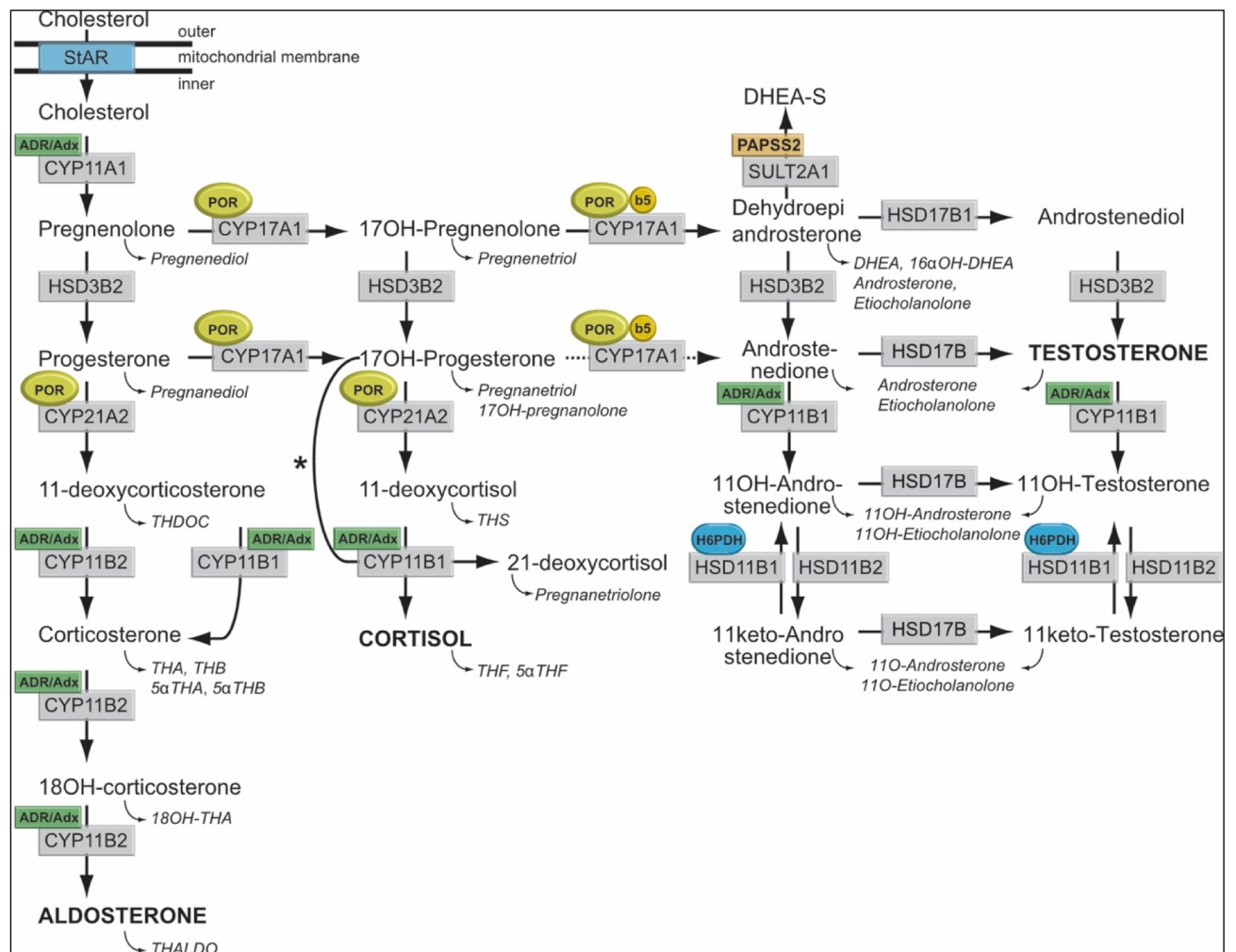


## Supplementary figures

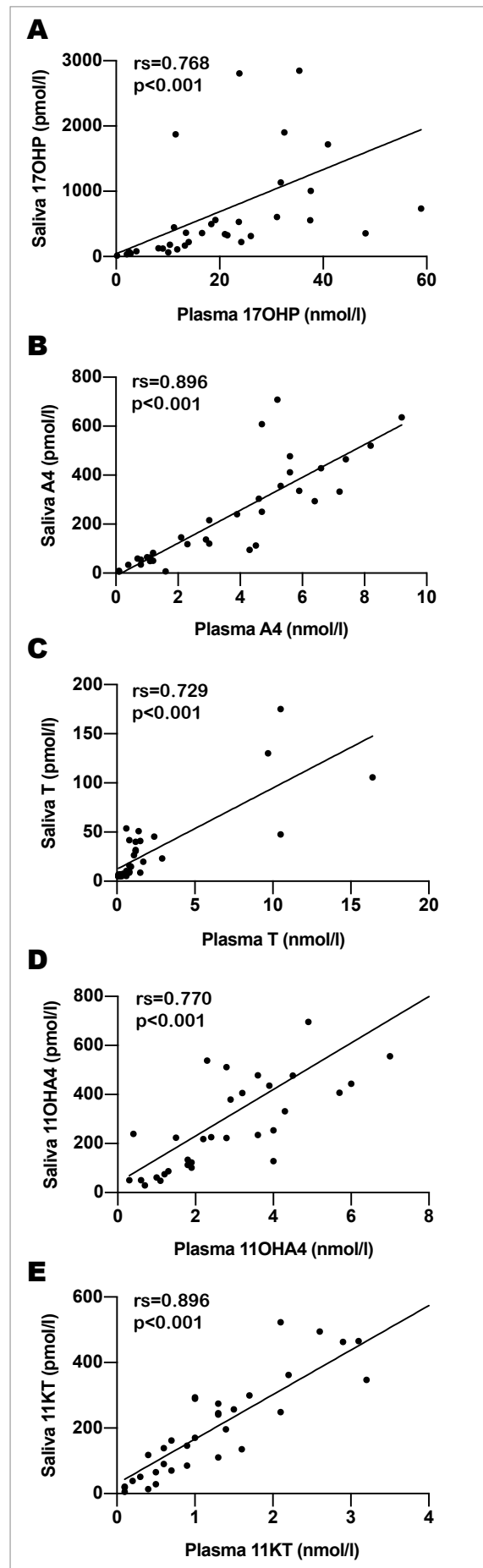
### Supplementary Figure 1



**Supplementary Figure 1. Pathways of adrenal steroid biosynthesis.** Enzymes are marked with boxes. Mitochondrial P450 cytochrome (CYP) type I enzymes requiring electron transfer via adrenodoxin reductase (ADR) and adrenodoxin (Adx) CYP11A1, CYP11B1, CYP11B2, are marked with a labelled box ADR/Adx. Microsomal CYP II enzymes receive electrons from P450 oxidoreductase, CYP17A1, CYP21A2, are marked by circled POR. The 17,20-lyase reaction catalyzed by CYP17A1 requires in addition to POR also cytochrome b5 indicated by a circled b5. Hexose-6-phosphate dehydrogenase (H6PDH) is the cofactor to HSD11B1 and given as ellipse. Recent evidence suggests that androstenedione and testosterone can be further metabolized by the adrenal. Urinary steroid hormone metabolites are given in italics below the plasma hormones. The asterisk (\*) indicates the pathognomonic 11-hydroxylation of 17OHP to 21-deoxycortisol in 21-hydroxylase deficiency. The conversion of androstenedione to testosterone is catalyzed by HSD17B3 in the gonad and aldoketoreductase (AKR) 1C3 (HSD17B5) in the adrenal. (StAR, steroidogenic Acute Regulatory protein; CYP11A1, P450 side-chain cleavage enzyme; HSD3B2, 3 $\beta$ -hydroxysteroid dehydrogenase

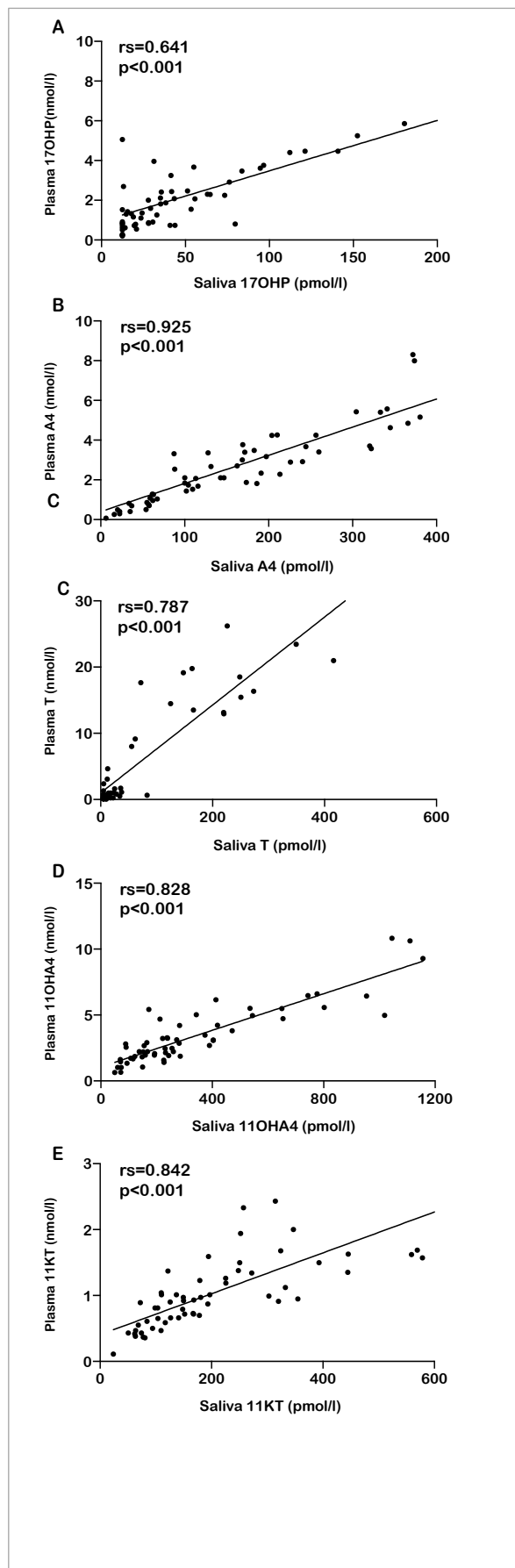
type 2; CYP17A1, 17 $\alpha$ -hydroxylase; CYP21A2, 21-hydroxylase; CYP11B1, 11 $\beta$ -hydroxylase; CYP11B2 aldosterone synthase; HSD17B, 17 $\beta$ -hydroxysteroid dehydrogenase facilitated by AKR1C3 and/or HSD17B3; SULT2A1, sulfotransferase 2A1; PAPPS2, 3'-phosphoadenosine 5'-phosphosulfate synthase 2; PAPPS2, 3'-phosphoadenosine 5'-phosphosulfate Synthase 2)

## Supplementary Figure 2



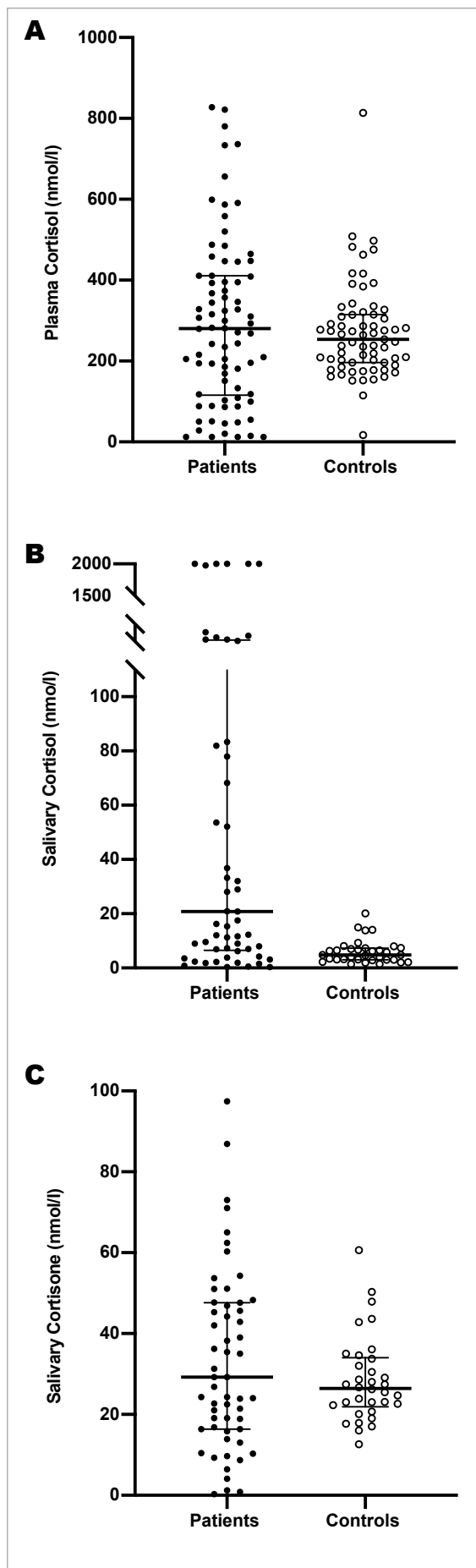
**Supplementary Figure 2.** The scatter graphs show the relation between plasma (horizontal axis) and salivary (vertical axis) steroid concentrations in patients with CAH for 17-hydroxyprogesterone (A), androstenedione (B), testosterone (C), 11-hydroxyandrostenedione (D) and 11-ketotestosterone (E). The analysis was restricted to patients with plasma concentrations of 17-hydroxyprogesterone between 0 and 60 nmol/l. The upper left corner of each scatter graph depicts the results of the Spearman correlations ( $r_s$  and  $p$  value). (17OHP: 17-hydroxyprogesterone, A4: androstenedione, T: testosterone, 11OHA4: 11-hydroxyandrostenedione, 11KT: 11-ketotestosterone)

### Supplementary Figure 3



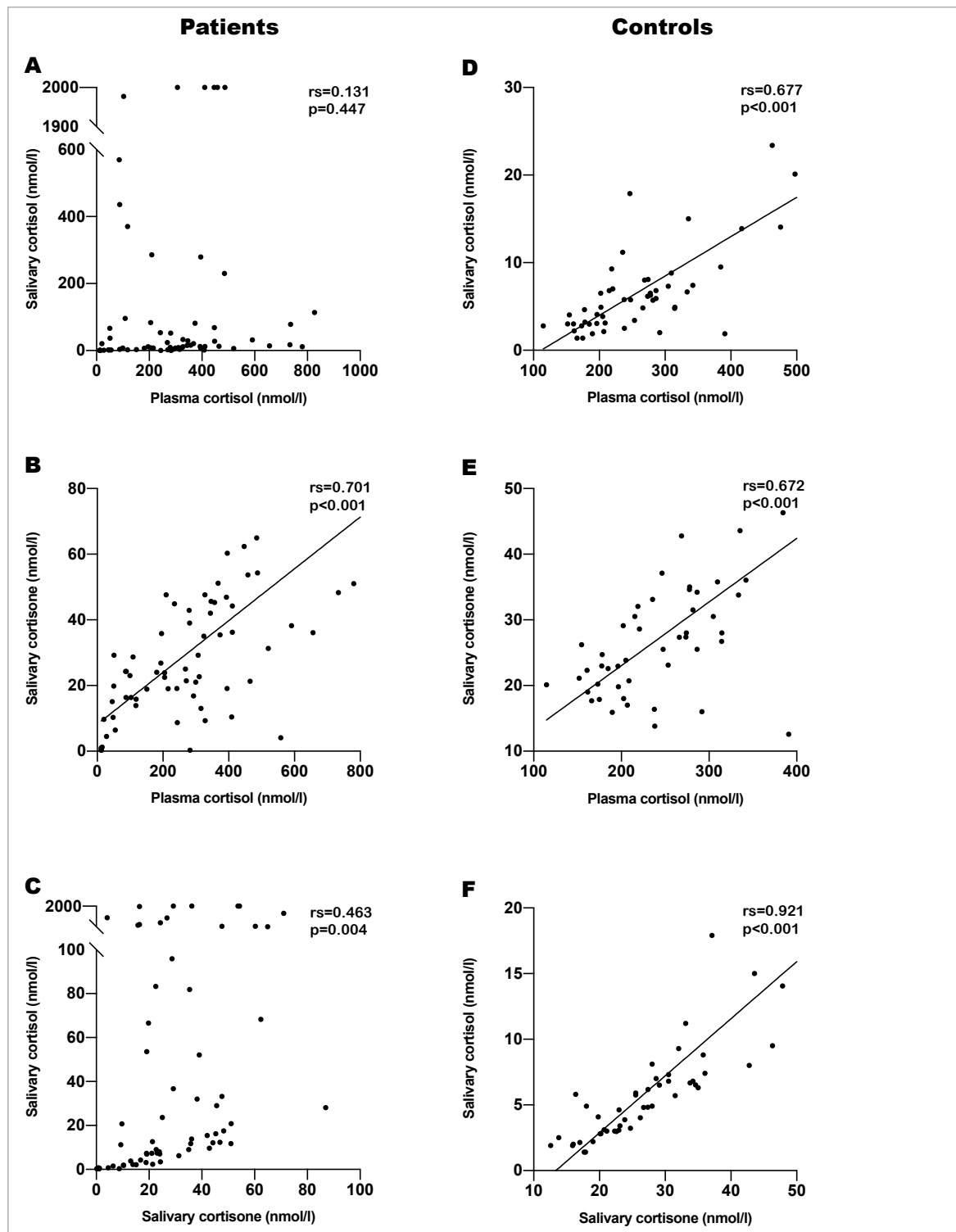
**Supplementary Figure 3.** The scatter graphs show the relation between plasma (vertical axis) and salivary (horizontal axis) steroid concentrations in controls for 17-hydroxyprogesterone (A), androstenedione (B), testosterone (C), 11-hydroxyandrostenedione (D) and 11-ketotestosterone (E). The results of the Spearman correlations ( $r_s$  and  $p$  value) are shown in the upper left corner of each scatter plot. (17OHP: 17-hydroxyprogesterone, A4: androstenedione, T: testosterone, 11OHA4: 11-hydroxyandrostenedione, 11KT:11-ketotestosterone)

**Supplementary Figure 4**



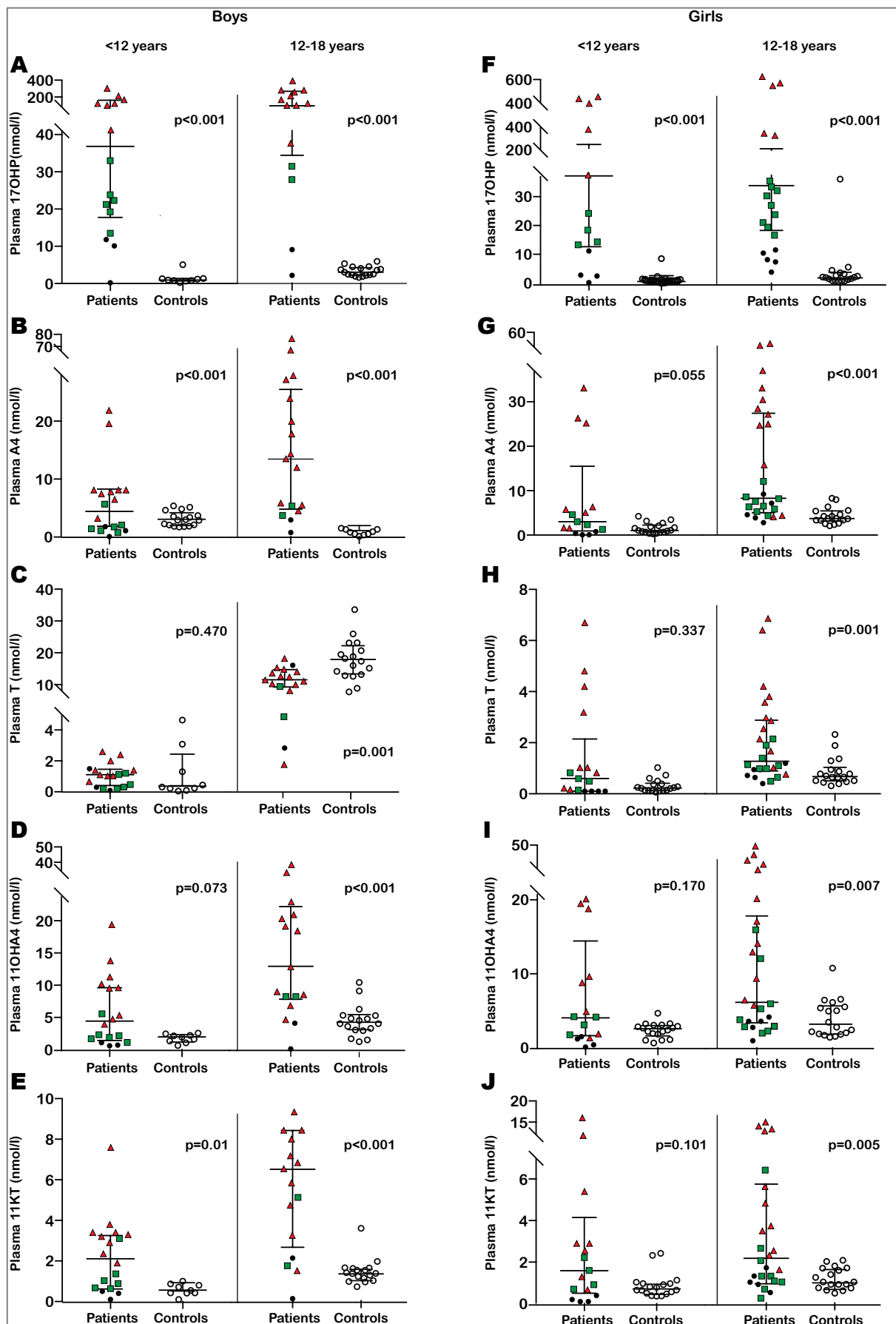
**Supplementary Figure 4.** Comparison between patients (dark dots) and controls (clear dots) for plasma cortisol (A), salivary cortisol (B) and salivary cortisone (C) concentrations. The horizontal bars within the scatter columns correspond to the median and interquartile range.

## Supplementary Figure 5



**Supplementary Figure 5.** The scatter graphs show the correlations for patients (left column) and controls (right column) between plasma and salivary cortisol (A and D), plasma cortisol and salivary cortisone (B and E) and salivary cortisol and cortisone (C and F). The upper right corner of each scatter graph depicts the results of the Spearman correlations ( $r_s$  and  $p$  value).

Supplementary Figure 6



**Supplementary Figure 6.** Comparison of plasma steroid concentrations between patients and controls. Patient values are represented by colored shapes, classified according to 17-hydroxyprogesterone concentrations as low (black circles), normal (green squares) and high (red triangles); control values are represented by clear circles. The left column represents the results obtained for boys younger than 12 years of age (left pair of scatter columns) and 12 to 18 years of age (right pair of scatter columns) for 17-hydroxyprogesterone (A), androstenedione (B), testosterone (C), 11-hydroxyandrostenedione (D) and 11-ketotestosterone (E). The right column represents the results obtained for girls younger than 12 years of age (left pair of scatter columns) and 12 to 18 years of age (right pair of scatter columns) for 17-hydroxyprogesterone (F), androstenedione (G), testosterone (H), 11-hydroxyandrostenedione (I) and 11-ketotestosterone (J). The horizontal bars within the scatter columns correspond to the median and interquartile range. Statistical analysis was performed by Mann Whitney U test. (17OHP: 17-hydroxyprogesterone, A4: androstenedione, T: testosterone, 11OHA4: 11-hydroxyandrostenedione, 11KT: 11-ketotestosterone).