

Thyroid function in children with Prader-Willi syndrome (PWS) treated with Growth Hormone (GH)

Musthaffa, Yassmin¹; Hughes, Ian²; Harris, Mark¹; Leong, Gary¹; Crock, Patricia³

1. Lady Cilento Children's Hospital, Queensland, Australia
2. Mater Research Institute, The University of Queensland, Australia
3. John Hunter Hospital, New South Wales, Australia

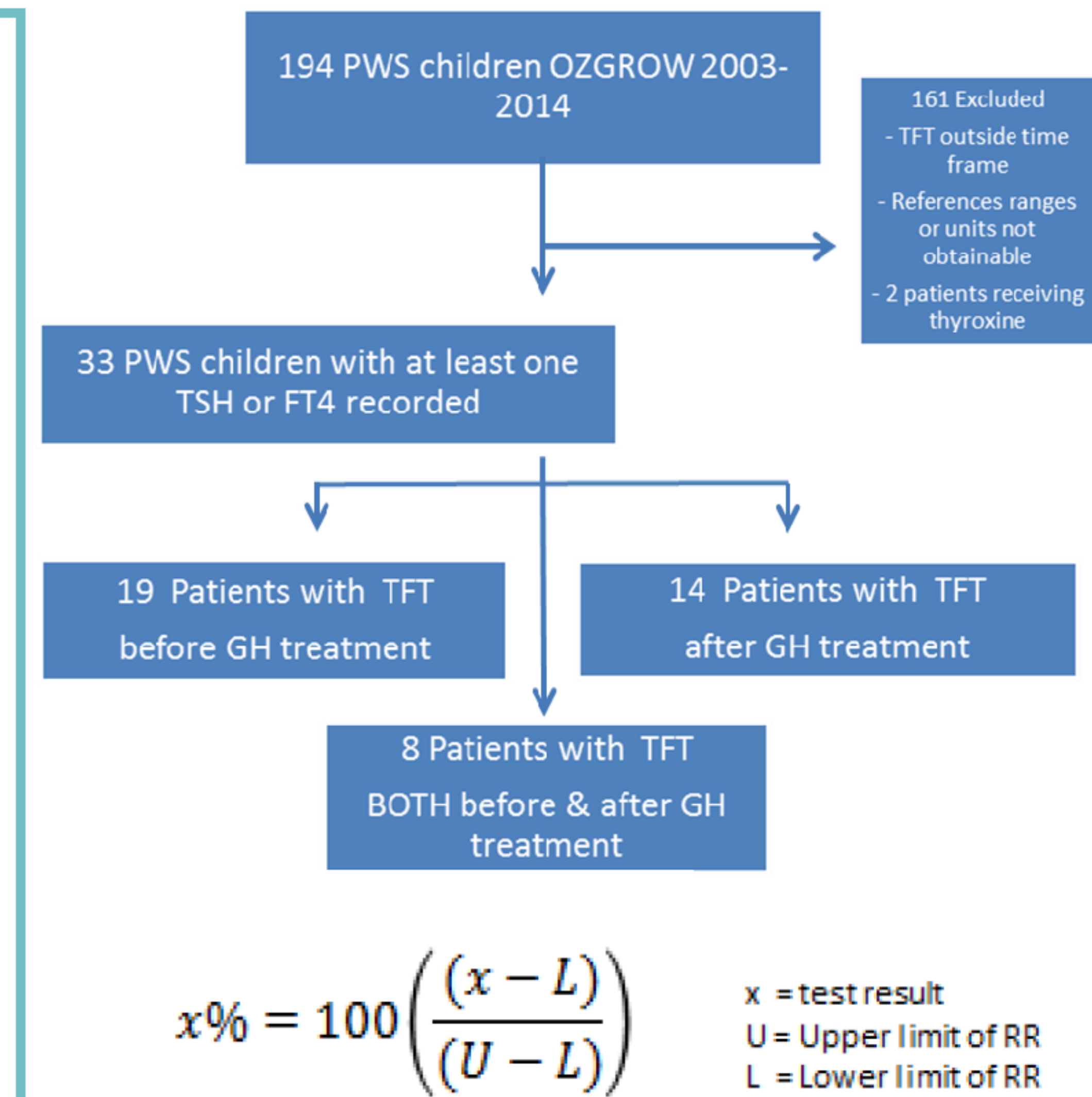
OBJECTIVE

Growth is optimal in the euthyroid state. Growth Hormone (GH) treatment may perturb the Hypothalamic-Pituitary-Thyroid Axis through both central inhibition of TSH (Thyroid Stimulating Hormone) release and increased peripheral conversion of T4 to T3. Hypothalamic dysfunction is common in Prader Willi Syndrome (PWS), and these children may be at risk of central hypothyroidism following GH treatment.

Objective: To assess thyroid function in children with PWS (1 year) before and (1 year) after GH treatment.

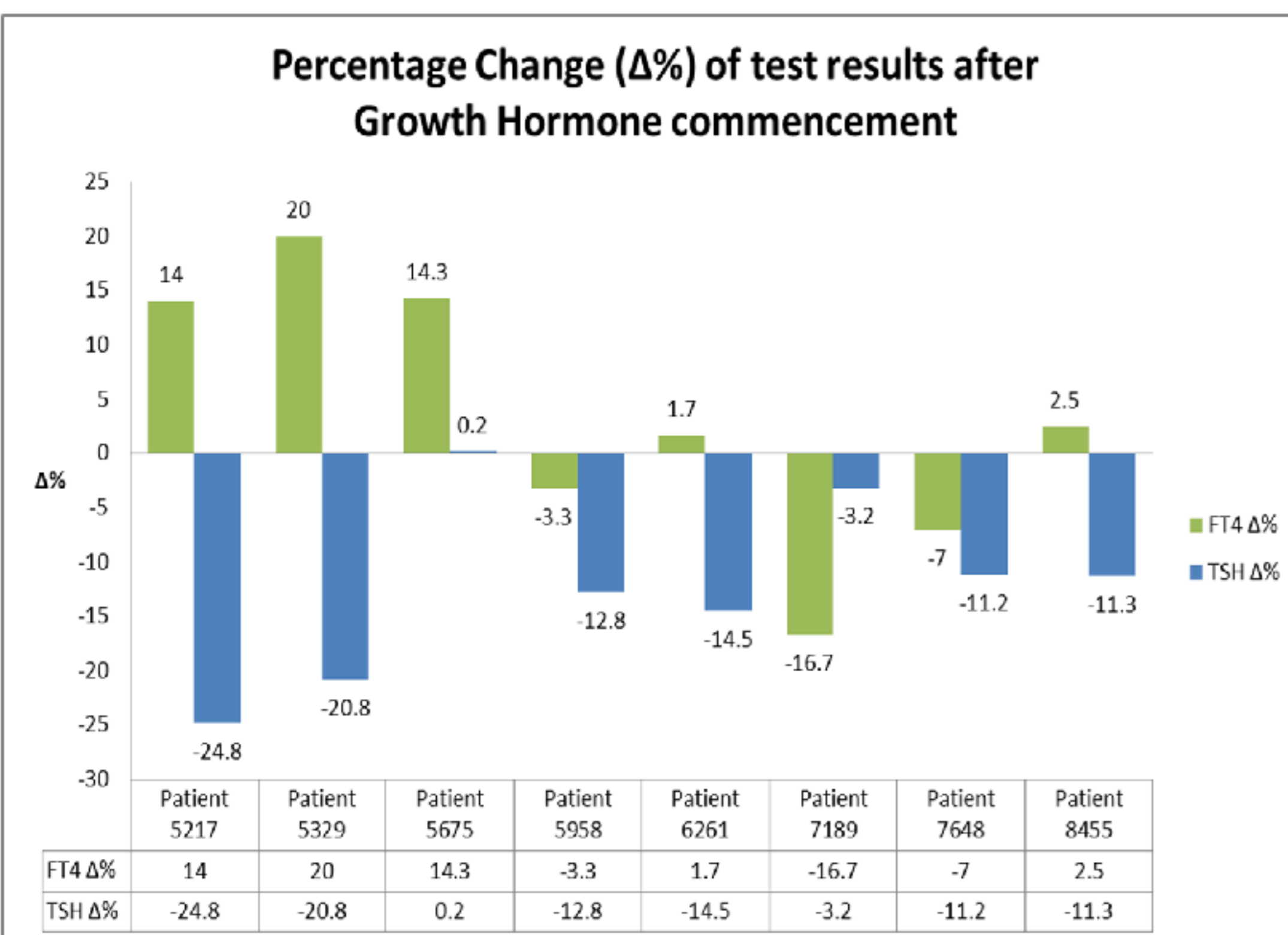
METHODS AND STATISTICAL ANALYSIS

This was a retrospective analysis of children with PWS from the Australian GH database, OZGROW, between 2003 and 2014. OZGROW records de-identified data for all children treated with GH based on the current national guidelines as well as FT4 (Free Thyroxine) and TSH when supplied. As FT4 and TSH were tested using different assays, we standardized the results by expressing them as a % of the reference range (RR) using the equation described. For results from either the year before and in the first year following GH treatment, one sample t-tests were used to compare standardized mean FT4 or TSH values against the expected mean of 50%. For patients who had tests available from both before and after GH treatment, the mean change in TSH and FT4 test % ($\Delta\%$) was calculated. A paired t test was used to compare the $\Delta\%$ against a hypothesis of no change (ie. 0%).



RESULTS

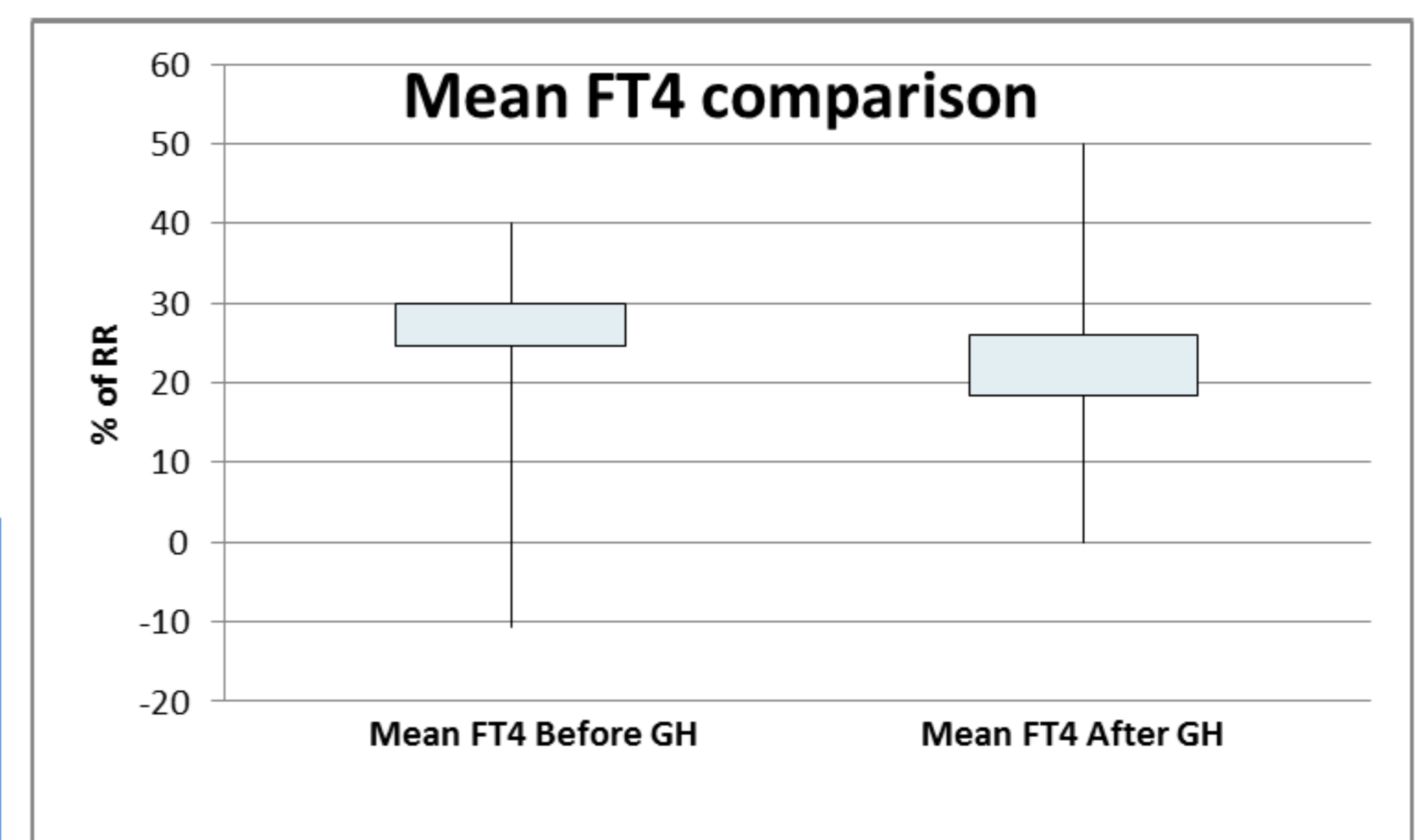
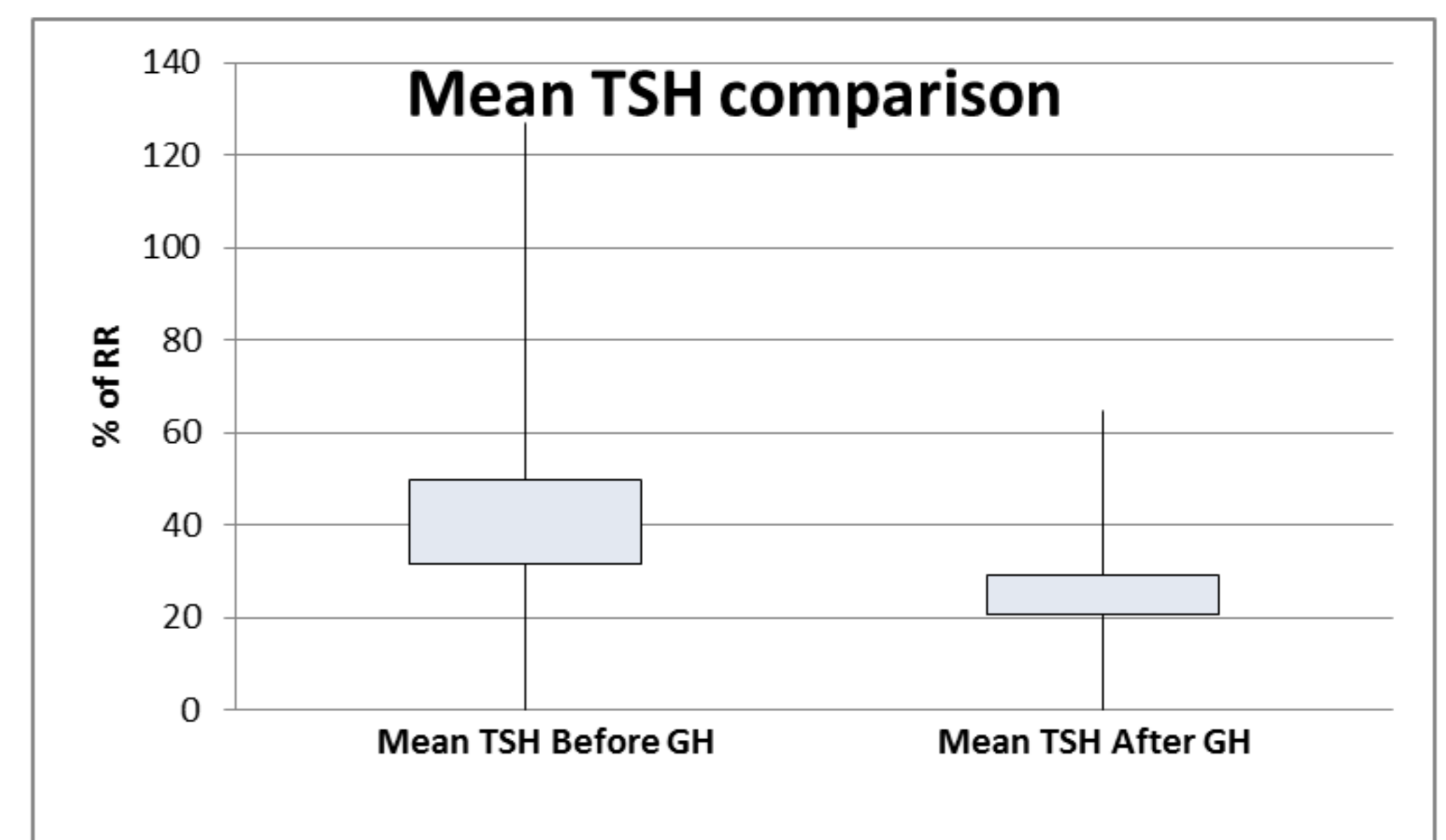
| BASELINE DEMOGRAPHICS AT GH COMMENCEMENT | Study group | Entire OZGROW PWS group | |
|--|-------------|-------------------------|--------------------------|
| N | 33 | 194 | |
| Sex (M/F) | 2:1 | 1:1 | $\chi^2 = 0.13$ |
| Mean Age (years) (sd) | 12.6 (3.8) | 7.7 (4.8) | $P = 4.0 \times 10^{-5}$ |
| Mean Height SDS (sd) | -0.82 (1.2) | -0.5 (2.2) | $P = 0.47$ |
| Mean BMI SDS (sd) | 1.28 (1.1) | 1.26 (1.2) | $P = 1.0$ |



FT4 was below the RR in 3/19 patients before GH treatment but no patients had FT4 levels below the RR during the first year of GH treatment. All TSH values were within the RR before and during the first year of GH treatment. In 8 patients with results both before and after the first year of GH treatment with a significant decrease seen in TSH $\Delta\%$ mean(sd) = -12.3 (8.2), $P=0.004$ whilst FT4 remained at a similar low level.

| | Patients with results EITHER before or after GH Treatment | |
|---------------|---|--|
| | Baseline | 1st Year of GH |
| N | 19 | 14 |
| Mean FT4 (sd) | 18.8% (16.9%) $p = 2 \times 10^{-7}$ | 20.5% (13.5%) $p = 1.7 \times 10^{-6}$ |
| Mean TSH (sd) | 37.7% (27.1%) $p = 0.06$ | 23.1% (15.7%) $p = 2.2 \times 10^{-5}$ |

| | Patients with results BOTH before and after GH Treatment | |
|-------------------------|--|----------------|
| | Baseline | 1st Year of GH |
| N | 8 | |
| FT4 $\Delta\%$ mean(sd) | +1.4(11.6) | $p = 0.7$ |
| TSH $\Delta\%$ mean(sd) | -12.3(8.2) | $p = 0.004$ |



CONCLUSIONS

Our study shows that most children with PWS have FT4 and TSH levels lower than the expected mean of 50% of RR. A small proportion of children have evidence of hypothyroidism at baseline, consistent with the central dysfunction that has been reported in PWS. After GH treatment, a decrease in TSH without any change in FT4 could result from alterations in Thyroxine metabolism. Our study does not support the routine use of Thyroxine in children with PWS who are commenced on GH. It does highlight the importance however, of screening for central hypothyroidism at baseline and during treatment. One question of interest is if our finding of central hypothyroidism in 16% of children with PWS is reproduced on a larger scale, whether Thyroxine alone will improve their growth and metabolic picture. Larger, prospectively conducted studies should examine all aspects of thyroid metabolism with measurement of T4, TSH, T3, rT3 and correlate these with the clinical impact on growth velocity.

References

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