

**Objective :** Assess management of patients referred to endocrine with low FT4 and normal TSH including; investigation, diagnosis and pharmacological intervention and compare to current guidelines and recommendations.

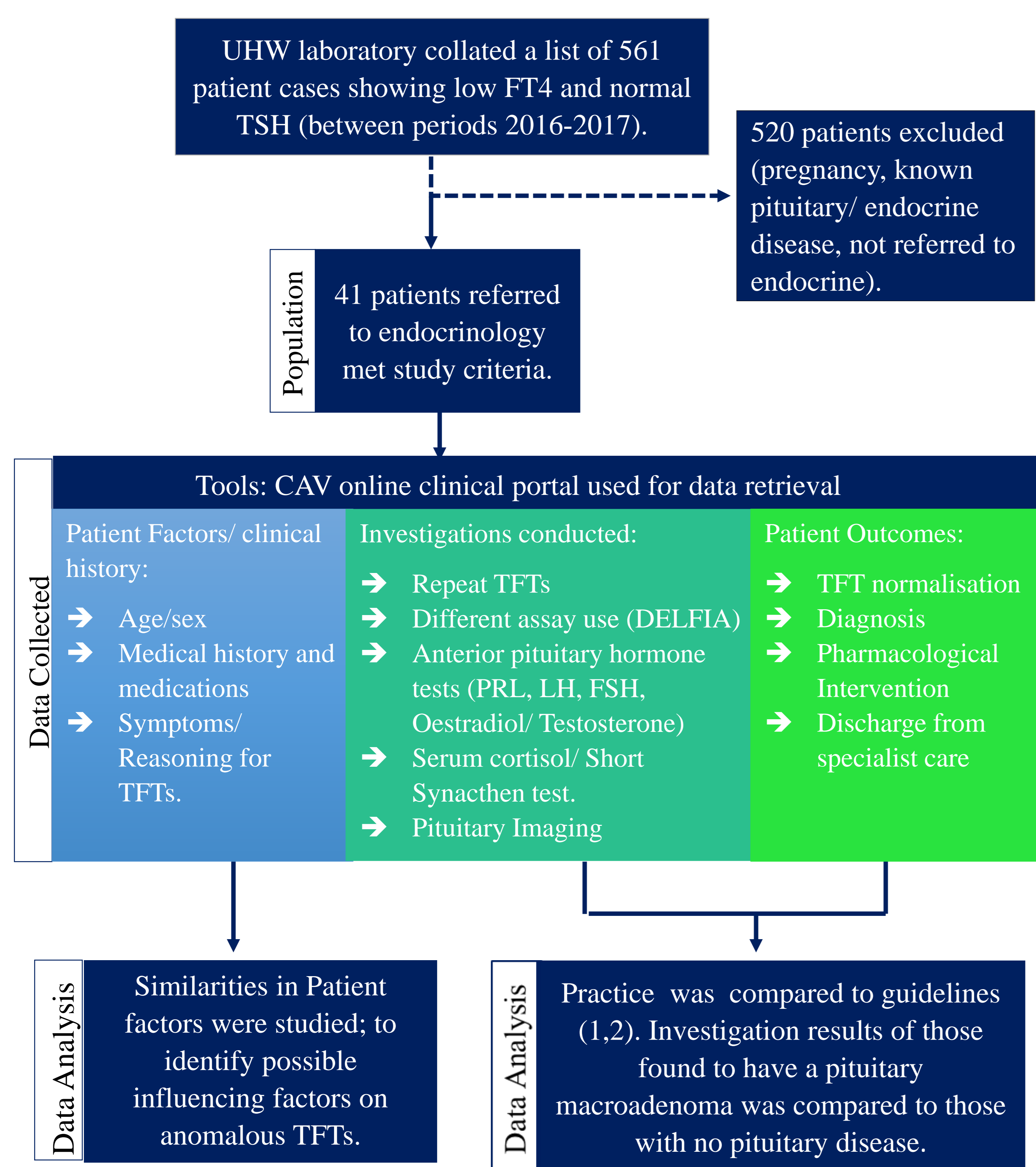
## Background

- Low free thyroxine (FT4) (<9pmol/L) and inappropriately normal thyrotropin (TSH) (0.3-4.4 mU/L) is a relatively common referral to endocrinology; however there is no clear consensus between endocrinologists on how these patients should be managed.
- Current guidelines on use of Thyroid function tests (TFTs) (1), recommend use of anterior pituitary hormone testing, free triiodothyronine (FT3) measurements, along with clinical history to distinguish secondary hypothyroidism from non-thyroidal illness. Assay interference, confounding drugs or intercurrent illness, should be excluded as cause of anomalous results before considering imaging (2).
- Some literature suggests abnormalities in anterior pituitary hormones may be a late manifestation of pituitary tumours (3); hence some endocrinologists may favour imaging at initial referral.

## Methods

### Design

Retrospective audit in management of outpatients with low FT4 and normal TSH, at referral, in University hospital wales (UHW). Abbott diagnostics assay was used to measure the concentration of FT4 and TSH providing reference ranges 9.0- 19.1 pmol/L and 0.3- 4.4 mU/L respectively.



**Figure 1:** shows the process by which subjects were identified, data collected and analysed. For nominal variables results have been recorded simply as numbers of patients or percentages. The Students T-test had been used to compare the baseline FT4 of patients found to have pituitary macroadenomas to those with no pituitary pathology on imaging.

## Results

### Patient characteristics

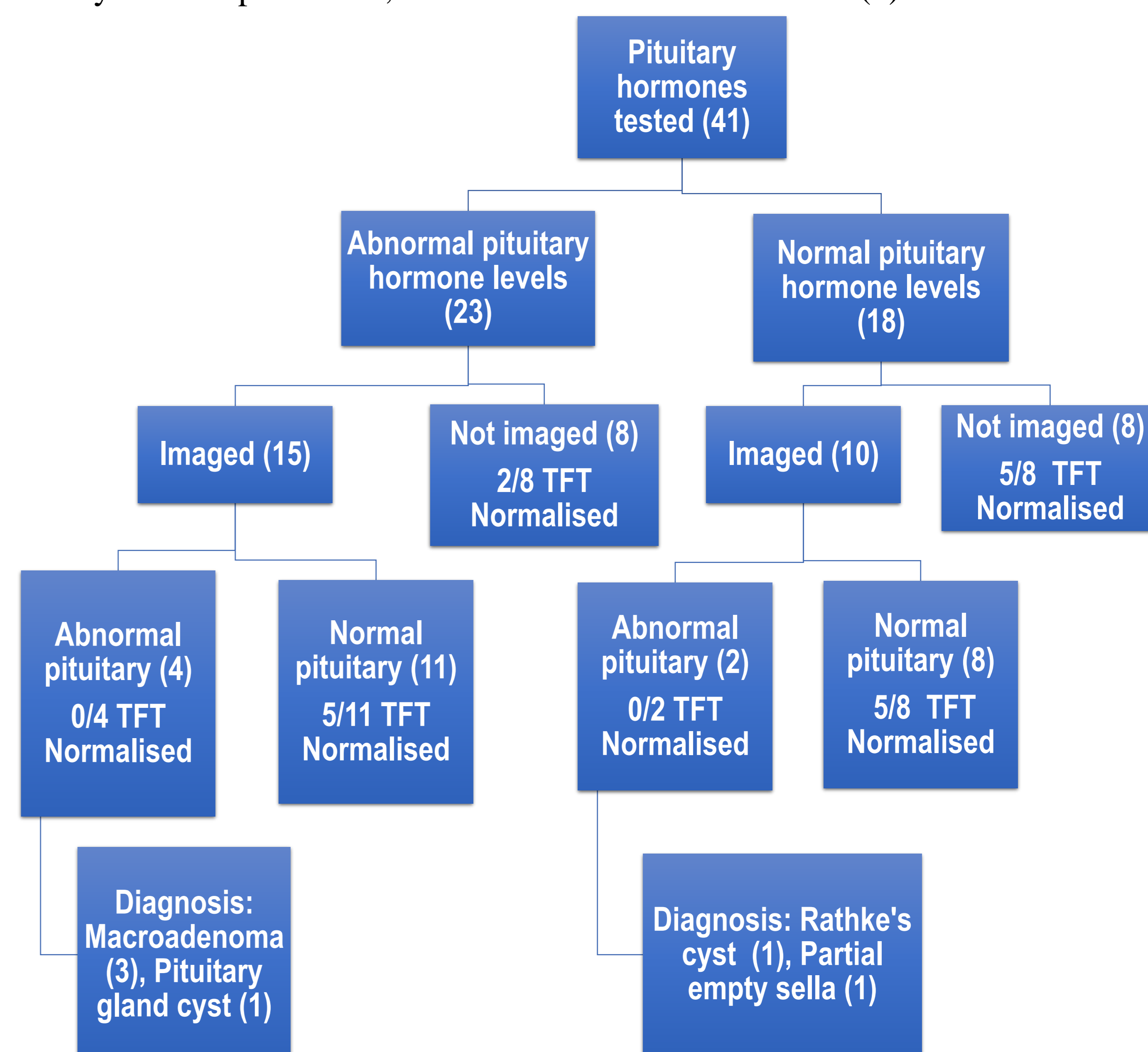
- Concurrent illness and medication – 22/41 (53.7%) of patients were found to have neuro-psychological conditions.
- Common medications- 19/41 patients were on antidepressants and 11/41 on anticonvulsants.

### Investigations

- Good clinical history, repeat TFTs and anterior pituitary tests were obtained for all patients as per guidelines (1,2).
- 3 patients were found to have pituitary macroadenomas; all 3 of these had abnormal anterior pituitary hormone tests (specifically raised prolactin) but normal FT3.
- Using a 2 tailed students T- tests no significant difference was found in baseline FT4 of patients with pituitary macroadenomas to those with no pituitary pathology on imaging.
- No assay interference was found in 7/7 samples retested.
- Imaging was not carried out in 8/23 patients with abnormalities in anterior pituitary hormone tests (see figure 2); potentially missing diagnosis of secondary hypothyroidism.
- 17/41 patients TFTs normalised spontaneously during repeat testing (average time 4.25 months from baseline); TFT normalisation was more common in patients with normal anterior pituitary hormones tests.

### Outcomes and Management

- Majority of patients discharged with no diagnosis or intervention.
- Only 5 people had a clinically relevant diagnosis; 3 patients were diagnosed with Pituitary macroadenoma and 2 with central hypothyroidism.
- Hormone replacement with levothyroxine +/- prednisolone was required in 4 of these patients.
- Cortisol was checked and appropriately replaced in all patients prior to levothyroxine replacement, so as to avoid Addisonian crisis (1).



**Figure 2:** Illustration of Pituitary imaging results in patients with normal and abnormal pituitary tests. The number of patients is illustrated in brackets. The number of patients whose TFTs normalised in relation to investigation findings is also shown.

## Conclusion

- Findings highlight that neuro-psychiatric conditions and/or their drugs may contribute to abnormal TFTs and should be considered when taking history.
- Patients found to have clinically important diagnosis were more likely to have abnormalities in anterior hormone tests; imaging may not necessarily be required in all patients presenting with low FT4 and normal TSH.
- A pathway for managing patients with anomalous TFTs for General Practitioners may aid in appropriate referrals to specialist care.

## Acknowledgements

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## References

1. Beastall G, Beckett G, Franklyn J, Frasier W, Kichey J, John R, et al. UK Guidelines for the use of thyroid function tests. The association for Clinical Biochemistry/British Thyroid Association/British Thyroid Foundation. 2006. Available from: [http://www.btf-thyroid.org/images/documents/tft\\_guideline\\_final\\_version\\_july\\_2006.pdf](http://www.btf-thyroid.org/images/documents/tft_guideline_final_version_july_2006.pdf) [Access 20th April 2018].
2. Gurnell M, Halsall DJ, Chatterjee VK. What should be done when thyroid function tests do not make sense? Clinical Endocrinology. 2011;74(6):673-8. Available from: doi: 10.1111/j.1365-2265.2011.04023.x
3. Ontjes D, Ney R. Pituitary tumours. Cancer Journal for Clinicians. 1976;26:330-50. Available from: doi: 10.3322/canjclin.26.6.330