

European Society of Endocrinology audit and multi-country comparison of Adult Growth Hormone Deficiency (AGHD) treatment in clinical practice in Europe and Australia - how closely are protocols and best practice recommendations followed

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Introduction

- Current guidelines recommend that most pituitary patients, being susceptible of being GHD, should be tested and treated for AGHD.
- Still, it is not universally recognised as a distinct entity and reimbursement of GH replacement therapy is not available in some countries.

Aims of the study

- To record current practice of AGHD management throughout Europe and benchmark it against existing guidelines.
- To evaluate the educational status of health care professionals.

Patients & methods

- Practicing endocrinologists were encouraged by the ESE to complete an electronic questionnaire with aggregated data of AGHD patients diagnosed and/or treated in their centre between 2017 and 2018.

Results

- Twenty-nine centres from 17 European countries and 1 from Australia participated, including 2148 AGHD patients, of which 28% were of childhood onset (see Figure 1 and Table 1).
- The aetiology included, as most frequent causes of AGHD, non-functioning pituitary adenoma (26%), craniopharyngioma (14%) and genetic/congenital mid-line malformations (14%).
- In concordance with guidelines, the most common stimulation tests performed (n=1037) were GHRH plus arginine, insulin-tolerance test and glucagon test, although in 7% other less recommended tests were performed. However, in n=305/2148 patients (15%) the presence of 3 or more other pituitary deficiencies and a low baseline IGF-I, made a stimulation test unnecessary.
- Centres reported a maximum of 254 and a minimum of 9 patients with AGHD, of which 83% were treated with GH.
- While in some centres all AGHD patients diagnosed received substitution therapy with rhGH, in others none did, since it was not an approved indication or it was not reimbursed.
- Eighty-four percent of GH treatments were still ongoing at the end of the study period.
- The main reasons for interruption were adverse events (n=162, 27% of patients, including new cancer, tumour recurrence fluid retention, arthromyalgia or hyperglycaemia), administrative reasons (n=54, 14%), lack of compliance (n=61, 16%), lack of positive perceived effect by the patient (n=51, 13%) and death (n= 12, 3%).
- Adherence to guidelines varied in different countries regarding diagnostic tests, cut-off values for GH, treatment initiation and/or transitioning from childhood to adult care.
- In 64%, no quality-of-life (QoL) questionnaire was reported.
- Requirements for treatment initiation beyond a diagnostic biochemical test included, in some centres, patient compliance (72%), impaired QoL (45%), severe fatigability (35%), central obesity (10%), and age <65 years (10%).
- Full- public reimbursement was available in 23 out of 29 centres at the time of study and it was correlated with higher number of treatments prescribed (p=0.015).
- A frequently reported major cause of dissatisfaction among endocrinologists was low AGHD awareness among non-endocrine health care professionals, and to a lesser extent, quality of post-graduate AGHD curriculum training (see Figure 2).

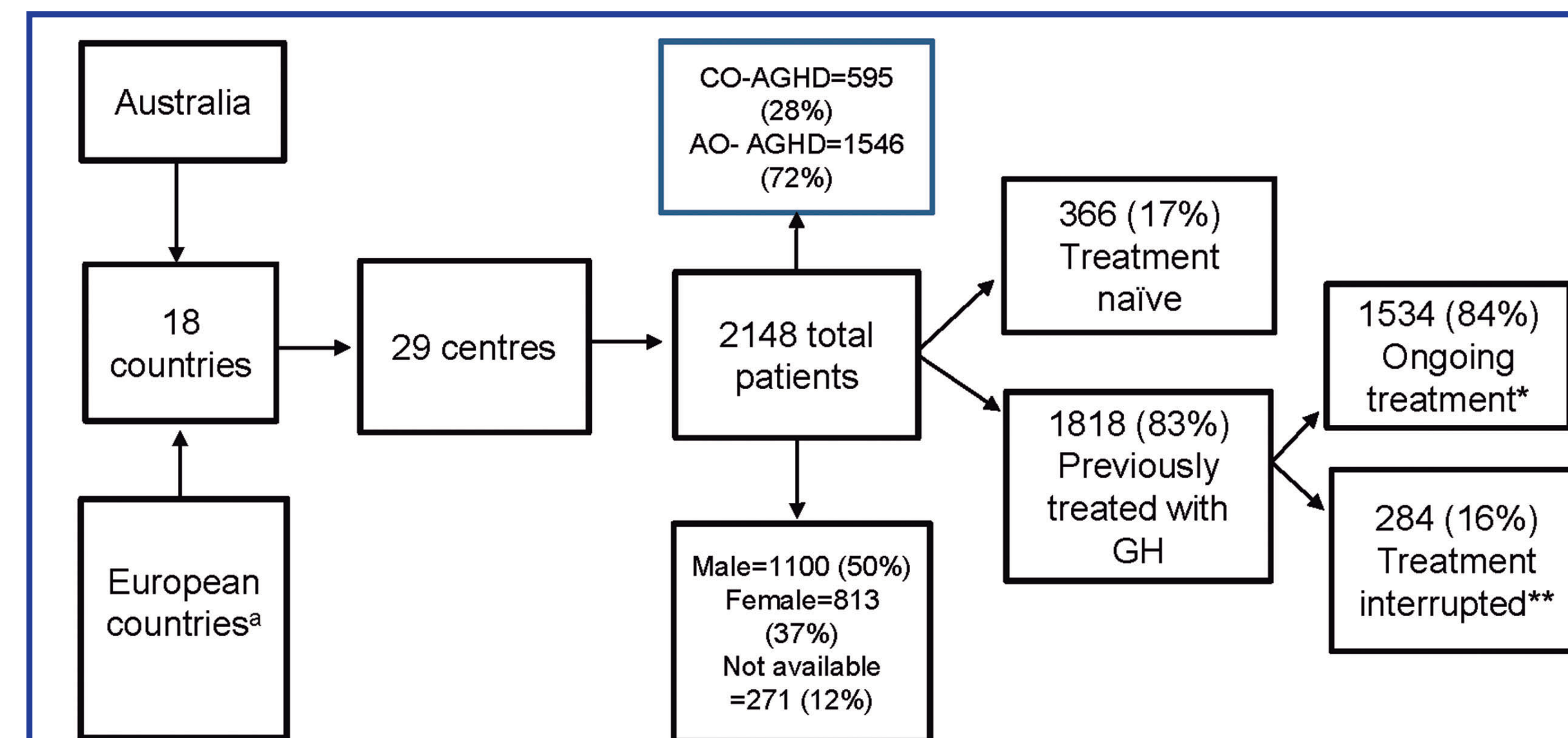


Figure 1. Number and general characteristics of countries, centres and patients involved in the study.

aCountries: Bulgaria, Croatia, Denmark, France, Greece, Hungary, Italy, Lithuania, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, UK.
*GH treatment ongoing at survey initiation (January 1st, 2017)
**Prior GH therapy received, but interrupted at survey initiation (January 1st, 2017)
Abbreviations: CO-AGHD, childhood onset adult growth hormone deficiency; AO-AGHD, adult onset adult growth hormone deficiency

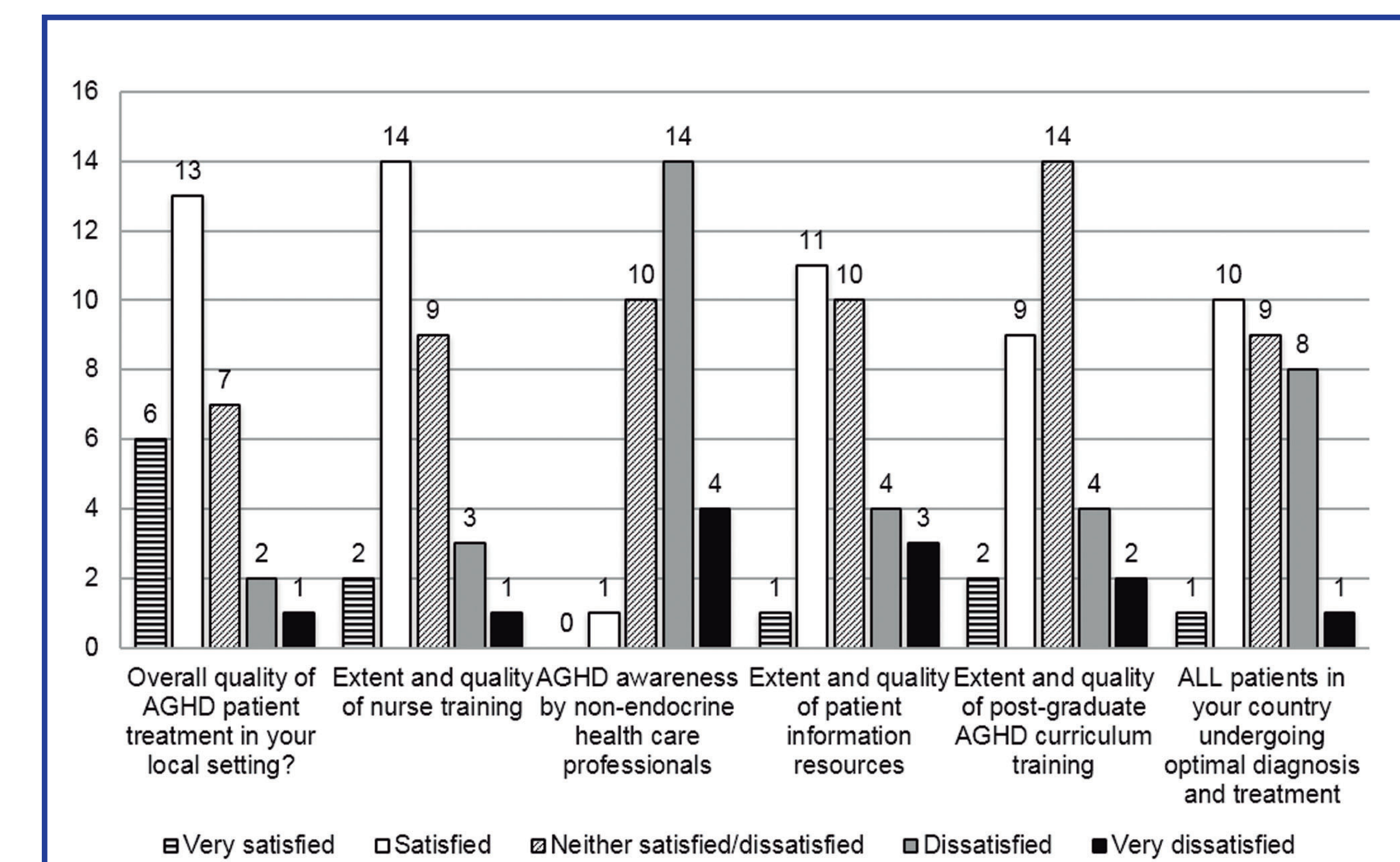


Figure 2. Level of satisfaction across centres (n= individual centres)

Table 1. Estimated and captured prevalence of patients with adult growth hormone deficiency per country (1)

| Countries | Population (million inhabitants) | Estimated AGHD patients | AGHD patients captured | Estimated % of total AGHD patients per country |
|-------------|----------------------------------|-------------------------|------------------------|--|
| Australia | 24 | 4200 | 9 | 0.2% |
| Bulgaria | 7 | 1225 | 87 | 7% |
| Croatia | 4 | 700 | 25 | 4% |
| Denmark | 5 | 875 | 281 | 32% |
| France | 66 | 11550 | 206 | 1% |
| Greece | 10 | 1750 | 28 | 2% |
| Hungary | 10 | 1750 | 45 | 3% |
| Italy | 60 | 10500 | 622 | 6% |
| Lithuania | 3 | 525 | 10 | 2% |
| Portugal | 10 | 1750 | 65 | 4% |
| Romania | 19 | 3325 | 83 | 2% |
| Serbia | 7 | 1225 | 30 | 2% |
| Slovenia | 2 | 350 | 70 | 20% |
| Spain | 46 | 8050 | 192 | 3% |
| Serbia | 7 | 1225 | 30 | 2% |
| Sweden | 10 | 1750 | 254 | 14% |
| Switzerland | 9 | 1575 | 18 | 1% |
| UK | 66 | 11550 | 91 | 1% |

1. Regal M, Páramo C, Sierra JM, Garcí-Mayor R V. Prevalence and incidence of hypopituitarism in an adult Caucasian population in Northwestern Spain. Clin Endocrinol (Oxf). 2001;55(6):735-740.

Conclusion

- Despite available guidelines on AGHD since 2007 recommending GH replacement in adult hypopituitary patients, there are still countries in Europe where AGHD substitution therapy is not reimbursed.
- Knowledge among non-endocrine professionals and health administrators of AGHD deserves improving, in order to optimize care of adults with hypopituitarism and GHD.