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# Management of endocrine aspects of Noonan syndrome across Europe: A sub-analysis of a European clinical practice survey

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## Background

- Noonan syndrome (NS) is characterised by the presence of distinctive facial features, congenital heart disease, short stature, skeletal abnormalities, mild developmental delay, and predisposition to myeloproliferative disorders.[1]
- The **European Medical Education Initiative on NS** developed a clinical practice survey to assess the diagnosis and management of diseases within the NS phenotypic spectrum across Europe.
- Here, we present a sub-analysis of the overall survey results focussing on the endocrine aspects of NS.

## Methods

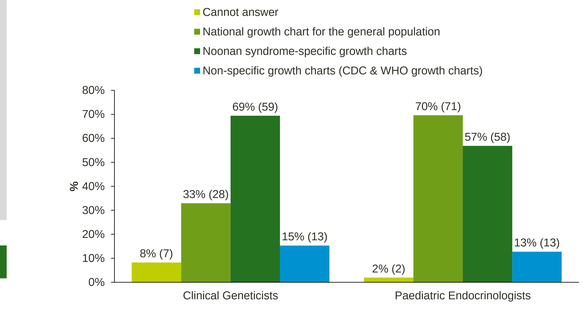
- A 60-question survey was distributed to clinical geneticists, paediatric endocrinologists, and paediatric cardiologists by several European and national specialist societies.
- In this sub-analysis, the responses of paediatric endocrinologists were mainly reported, analysed according to their country of origin, and compared with those of clinical geneticists and paediatric cardiologists where appropriate.
- Differences between specialities and countries were assessed using contingency tables and the Chi-Squared test for independence. The Friedman´s test was used for related samples.

## Results

- Answers from 364 respondents were included in the final analysis set:
  - 146 (40%) Paediatric Endocrinologists
  - 110 (30%) Paediatric Cardiologists
  - 108 (30%) Clinical Geneticists

### Screening and investigation of short stature

- Paediatric endocrinologists mostly refer to national growth charts for the general population when monitoring growth ($p < 0.0001$), whereas geneticists mostly refer to NS-specific growth charts ($p = 0.005$) (**Figure 1**).

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|---|---|---|
| **Total respondents** | **85 (79%)** | **102 (70%)** |
| **Total responses** | **107** | **144** |

**Figure 1 – Responses to survey question "Which growth charts do you use for the follow-up of patients with Noonan syndrome?"**

### Initiation of growth hormone (GH) treatment

- 2/3 of paediatric endocrinologists said the optimal age period to start GH treatment for patients with NS and short stature is early childhood (4–6.9 years) (**Figure 2**).

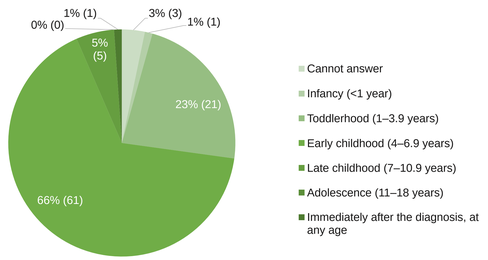
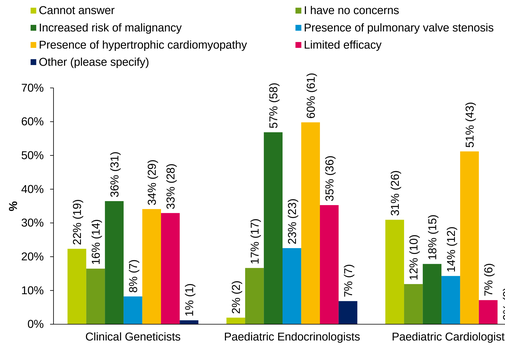



**Figure 2 – Responses to survey question "In your experience, which is the optimal age at which to begin growth hormone treatment for patients with Noonan syndrome and short stature?"**

### Concerns about GH treatment

- There are three main concerns regarding GH treatment for patients with NS (**Figure 3**):
  - **Hypertrophic cardiomyopathy** (HCM): Geneticists were less concerned about HCM compared with paediatric endocrinologists and cardiologists ($p = 0.041$).
  - **Increased risk of malignancy**: Paediatric cardiologists were less concerned about the increased risk of malignancy compared with paediatric endocrinologists ($p < 0.0001$).
  - **Limited efficacy**: 33% of geneticists and 35% endocrinologists were concerned about limited efficacy.

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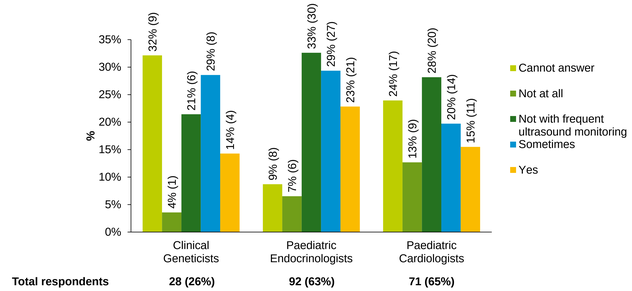
| **Total responses** | **129** | **204** | **112** |
| **Total respondents** | **85 (79%)** | **102 (70%)** | **84 (76%)** |

**Figure 3 – Responses to survey question "Are you concerned about any of the following regarding growth hormone treatment in children with Noonan syndrome?**

### HCM as a contraindication to GH treatment

- When respondents were asked if they consider HCM as a contraindication for GH treatment, 1/3 skipped the question, and of those who replied, 2/3 selected 'cannot answer', suggesting a high level of uncertainty (**Figure 4**).

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| **Total respondents** | **28 (26%)** | **92 (63%)** | **71 (65%)** |

**Figure 4 – Responses to survey question "Do you consider hypertrophic cardiomyopathy a contraindication to the use of growth hormone therapy?"**

## Conclusions

- International guidelines regarding the screening and management of the endocrine aspects of NS are needed.
- A knowledge gap regarding GH therapy in the presence HCM has been identified.
- Possible genotype-phenotype correlations in terms of efficacy and safety of GH need to be studied.

**References**

1. 1. Roberts, A. E., et al. (2013). Lancet 381(9863): 333-342.

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