

# Management of gonads in adults with androgen insensitivity: an international survey

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## Background

Individuals with androgen insensitivity syndrome (AIS) have an increased risk for developing a germ cell cancer (GCC). The risk is high from childhood; therefore, gonads are commonly preserved until after puberty in women with CAIS and men with PAIS to allow for spontaneous development. Preservation of gonads thereafter is controversial given that little is known about GCC development in adulthood and given the lack of tools for conservative follow-up of gonads *in situ*. This question is particularly relevant as many adult AIS women decline gonadectomy.

## Aims and objectives

We wanted to gain insight in attitudes towards gonadectomy in various DSD centers around the world and estimate the proportion of AIS adults who have retained gonads, reasons for declining gonadectomy and frequency of GCC occurrence. We hypothesize that many adult women with CAIS, especially in lower-income countries have retained gonads without ever developing a GCC.

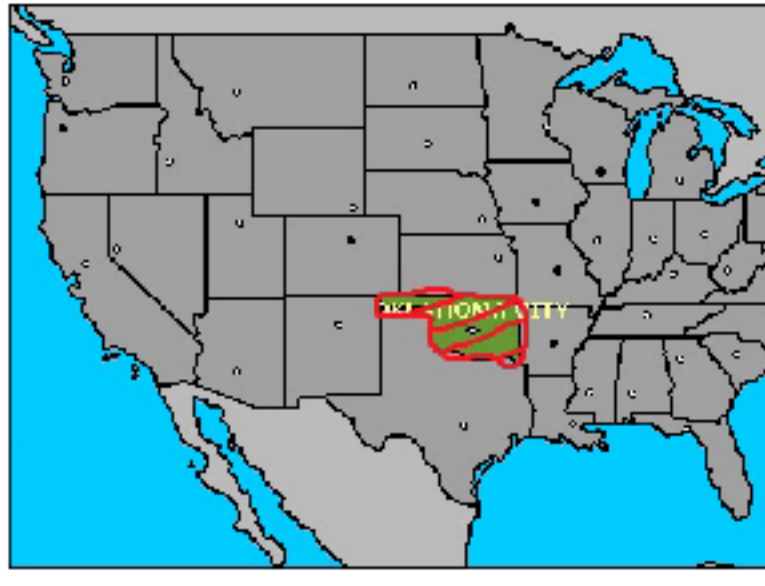
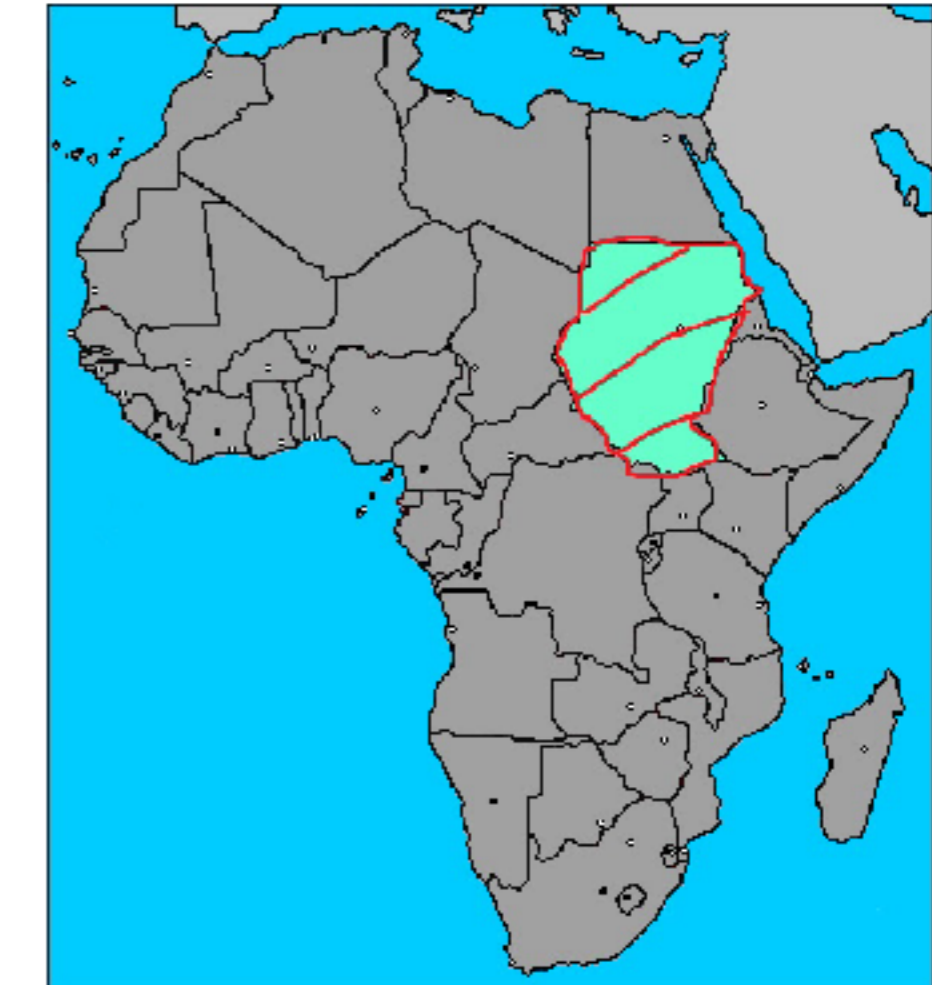
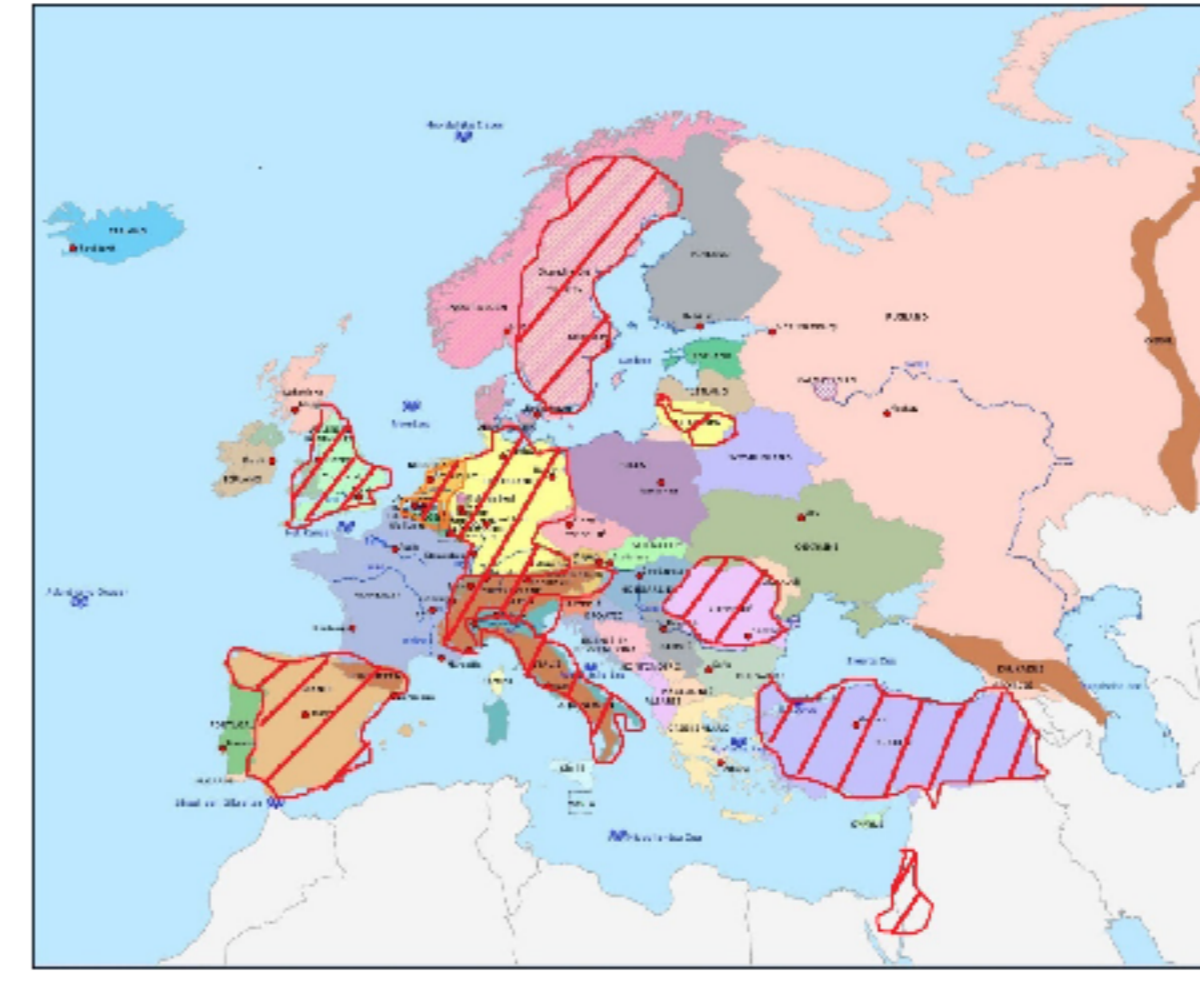
## Methods

We performed an international survey among health care professionals working in DSD centers around the world, retrieved through the I-DSD Registry.

Respondents were invited to participate in this survey by email or by an announcement and flyer distributed at the ESPE 2014 meeting. The questionnaire was sent by e-mail.

## Limitations of our study

A major restriction of our study is the limited information per patient. We chose not to focus on detailed individual patient record data to increase the response rate. This led to a response rate of 50% (15/30 centers) providing data on 226 patients (188 CAIS, 38 PAIS). At the University of Sudan, Israel and the USA, we received mainly information from European centers (19/22 – 86,3%). A second restriction is the lack of secondary pathology review of gonadectomy material was performed.

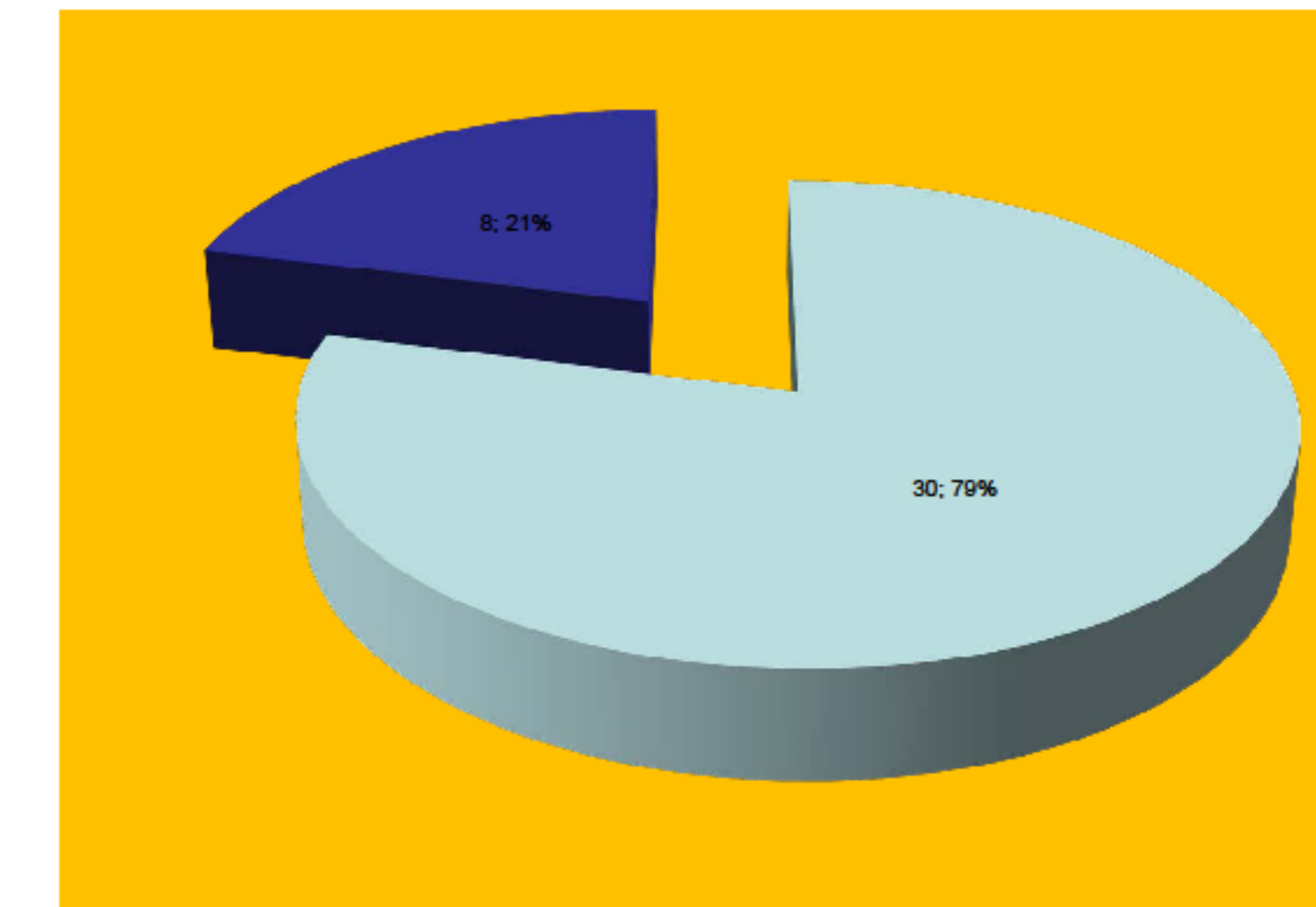
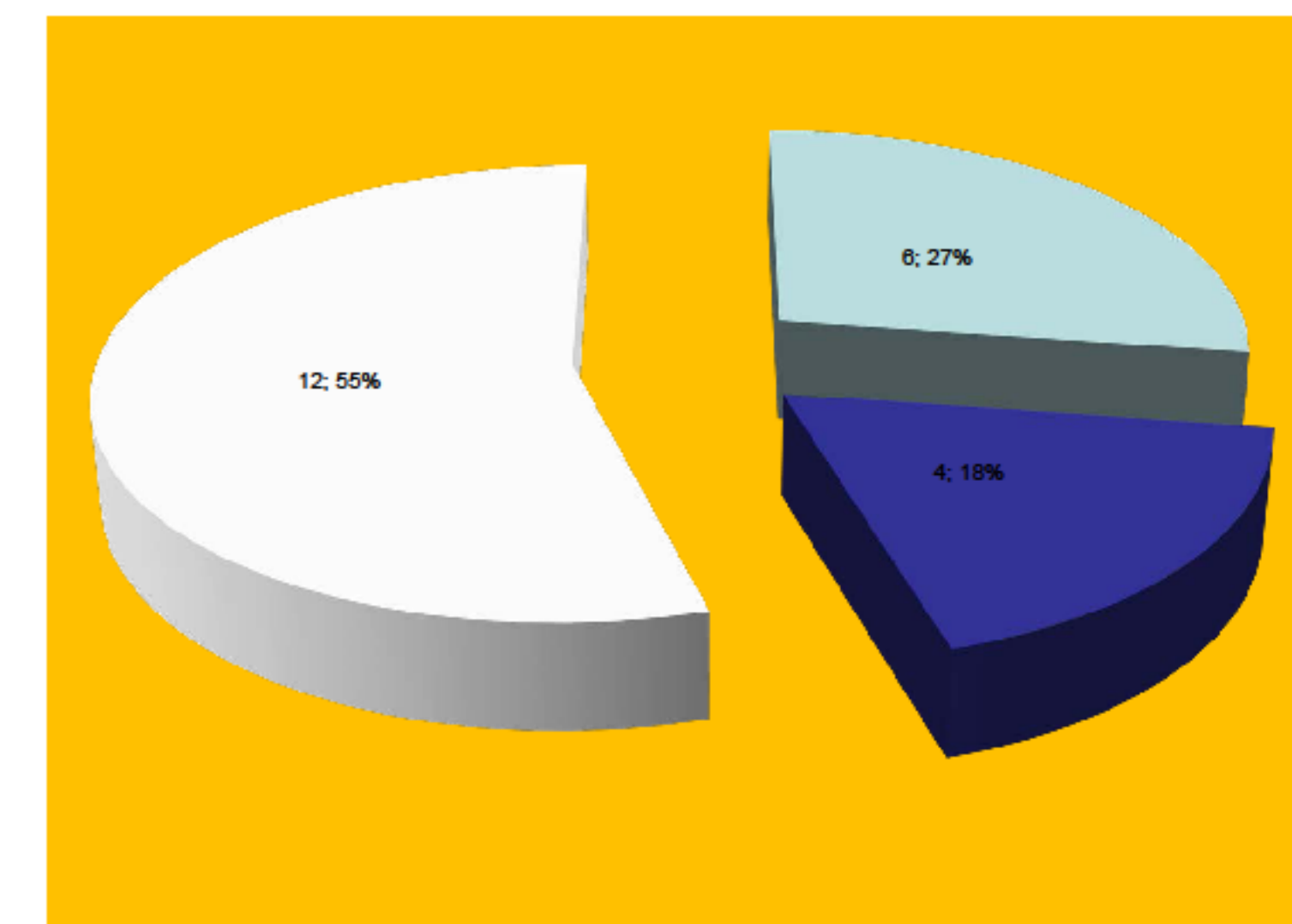


## Results and Discussion

In **CAIS**, 16/22 centers routinely propose gonadectomy before (4/22) or at the end (12/22; 145/188 patients (77%)) of puberty. 23/188 (12.2%) of CAIS individuals have retained gonads, either because gonadectomy was not proposed, or because patients refused this procedure (13/23). Reasons for declining are being anxious about surgery and its complications and worries about long-term effects of hormone replacement therapy, timing of surgery and not having processed the diagnosis. One invasive and one *in situ* neoplasia were reported in two patients who had both received routine gonadectomy at the end of puberty, suggesting a tumor risk of 1,2 %.

Decision and timing of gonadectomy in **PAIS** is highly variable; overall, only 8/38 (21.0%) of PAIS males in this survey still have one or both gonads (62,5% scrotal testes, 12,5% inguinal testes, 25% no information about testes position). No (invasive) GCC were mentioned, not in the patients with retained gonads, nor in the gonadectomized group.

The fact that only two tumors occurred in 2/226 individuals (0.8%), mainly adults, is reassuring. Since premalignant changes and CIS have previously been shown to occur in 15 - 44%, this questions at least in AIS the hypothesis that all CIS progresses towards invasiveness over time, or alternatively, that there is an important tendency to overdiagnose CIS in AIS.



## Conclusion

Differences in attitudes towards gonadectomy exist in centers caring for AIS individuals. Affected persons are concerned about surgery and generally accept gonadectomy at the end of puberty. The occurrence of (an invasive) GCC seems rare in AIS adults, questioning the need for routine gonadectomy in this population. Expert histological review is necessary to optimize diagnostic accuracy and to avoid overdiagnosis. Gaining further knowledge about the eventual progression of (pre)neoplastic changes towards invasiveness in AIS and in different ethnic populations specifically will help to improve counseling and patient-oriented management.

\* Evaluation of retained testes in adolescent girls and women with complete androgen insensitivity syndrome. Nakhal et al. Radiology 2013 Jul;268(1):153-160.

\* Timing of gonadectomy in adult women with complete androgen insensitivity syndrome (CAIS): patient preferences and clinical evidence. Deans et al. Clinical Endocrinology 2012;76:894-898.

\* Managing the risk of germ cell tumourigenesis in disorders of sex development patients. Cools et al. Endocrin Dev 2014;27:185-96.

\* Complete androgen insensitivity syndrome: factors influencing gonadal histology including germ cell pathology. Kaprova-Pleskacova et al. Mod Pathol 2014; 27 (5): 721-30.

