DSD-Life: Clinical European study on the outcome of surgical and hormonal therapy and psychological intervention in disorders of sex development (DSD)

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Objective 1: To improve clinical practice in the management of disorders of sex development (DSD)Objective 2: To develop accepted evidence-based clinical guidelines for a better clinical care of patients with DSD affected by distinct genetic...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON38614

Source
ToetsingOnline

Brief title
DSD-Life

Condition

- Other condition
- Endocrine disorders congenital
- Congenital reproductive tract and breast disorders

Synonym
intersex

Health condition

intersekse

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: disorders of sex development (DSD), hormonal and surgical interventions, psychosexual development, quality of life

Outcome measures

Primary outcome

Primary study parameter(s)

Health status, health related quality of life, psychological and social

well-being, gender dysphoria, experiences and satisfaction with sexuality.

Primary endpoints: Identification of factors influencing psychosocial

adaptation including, HRQoL and social - and psychological well-being, which

can be improved in future clinical care.

Secondary outcome

Secondary study parameter(s)

Sex assignment, genital surgery, hormone therapy, metabolism, fertility,

psychosocial care, satisfaction with health care, psychosexual development, and

hormone treatment.

Secondary endpoints: Identification of factors affecting metabolism, fertility,

surgical outcome and psychosexual development, which can be changed in future

clinical care.

Study description

Background summary

Disorders of sex development (DSD) are a conglomerate of rare diseases with an estimated total incidence of 1:4500. DSD are defined as a discrepancy of the chromosomal, gonadal and phenotypic sex. The causes of DSD include disorders of gonadal development in both sexes, gonadal disorders with decreased androgen synthesis or function in XY males and disorders with elevated androgen production in XX females.
Sex chromosome DSD consists mainly of disorders with gonadal dysgenesis due to sex chromosome imbalances as Turner syndrome (45,X0 and mosaicism) in females, Klinefelter syndrome (47,XXY) in males and individuals with mixed gonadal dysgenesis (45,X0/46,XY) or individuals with chimeric DSD (46,XX(46,XY). XY DSD comprises individuals with complete testicular dysgenesis or gonadal dysgenesis, which is the result of disturbed testes development.
Severe prenatal androgen imbalances result in ambiguous genitalia at birth in both sexes with DSD: in XY boys reduced prenatal androgen production or effect and in XX girls increased prenatal androgens cause ambiguous genital development. Furthermore, it is assumed that prenatal androgen priming of the brain has an effect on psychosexual development. In some cases with ambiguous genitalia taking the decision on sex of rearing is difficult. Genital constructive surgery is needed for heterosexual intercourse in many cases. Furthermore, corticoid or sex hormone substitution is needed in the majority of individuals with DSD. Individuals with CAH need lifelong cortisone (with/without aldosterone) substitution therapy to prevent life-threatening events.
Individuals with DSD due to gonadal dysgenesis or disorders of sex hormone synthesis need either estrogen or testosterone therapy starting at puberty. Decision on estrogen or testosterone therapy in these patients depends on the choice of sex of rearing. In addition to hormonal disturbances, many individuals with DSD are infertile. Decision on the sex of rearing, genital surgery and hormone therapies have a life-long impact on the affected individuals. Furthermore, in the recent years, taking into account the anticipated impact of DSD on psychosexual development, psychological counselling to cope with the disorder has been recommended by the multidisciplinary DSD treatment teams. So far, most research on DSD has been focused on studies investigating the genetic cause, pathogenesis and diagnostics of the disorders, but not the clinical outcome.
Treatment options in DSD are controversial and are questioned by many adults with DSD. Treatment options include off label therapies and have not been evaluated for long-term effectiveness and adverse effects. Furthermore,

there is great variation in the therapeutic approaches to DSD across Europe. Clinical outcome studies in DSD are often limited by small numbers, a mixture of diagnoses and different outcome measures. The so far largest clinical outcome study has been performed from 2003-2008 in Germany (German Clinical Evaluation Study, BMBF). Despite being the so far worldwide largest clinical outcome study of DSD, conclusions of the study were also limited by small patient numbers of known genetic entities. Different genetic entities were summarized in subgroups reflecting the sex of rearing, the karyotype and the androgenization level to obtain sufficient patient groups for statistical analysis.
Moreover, in the last decade the issue of treatment of DSD, in particular surgery, has reached a political level in several countries. In 2010, the Committee on the Elimination of Discrimination against Women (CEDAW) of the United Nations Human Rights has advised governments to take charge of the regulatory control of treatment in DSD. In 2011 e.g., the German Ethics Committee (Deutscher Ethikrat) has been mandated to develop ethical recommendations for the treatment of DSD. However, development of ethic recommendations is also hampered by the lack of clinical evidence of treatment. For these reasons the different treatment and intervention regimens in known genetic entities should be investigated in a large cohort in the EU.

Study objective

Objective 1: To improve clinical practice in the management of disorders of sex development (DSD)

Objective 2: To develop accepted evidence-based clinical guidelines for a better clinical care of patients with DSD affected by distinct genetic entities for which no dedicated treatment is currently approved

Study design

DSD-Life is a descriptive observational study.
DSD-Life investigates and compares the long-term outcome of not evidence based treatments such as 1. Sex assignment, 2. Surgery, 3. Hormone therapies, 4. Psychological interventions in adolescents and adults (>= 16 years) that are used in patients with various causes of DSD. An estimated total number of 1500 individuals with sex chromosome, XY DSD and XX DSD >= 16 years will be included in the study from 14 clinical sites in Europe.
To investigate the main hypotheses the probands will answer questionnaires on HRQOL and social - and psychological well-being.
To investigate the secondary hypotheses the patients will get a medical exam including investigation of their hormonal and metabolic status, ultrasound of the uterus, ovaries or testes, investigations of bone mineral density and body composition. To investigate surgical outcome the probands will be offered a standardized gynaecological/urological exam (optional) and/or a questionnaire

about satisfaction with the outcome of genital surgery.
Furthermore, the probands will answer questionnaires on sociodemographics, psychosexual development, stigma, shame, previous and actual health care situation including satisfaction, previous treatments including satisfaction and a questionnaire investigating the patients* view of treatment with current knowledge about their condition including also ethical considerations and patients* rights.
The physician will fill in questionnaires regarding precise diagnosis, presentation and phenotype at diagnosis, history of hormonal, surgical and psychological therapies, previous and actual medical/psychiatric problems and family history.

Study burden and risks

The individual benefit for the proband is that she/he obtains a thorough medical check up and medical counselling including evaluation of metabolic problems and complications after genital surgery. If the proband has no access to a specialist for regular metabolic and/or gynaecologic/urologic follow-up contacts to specialized endocrinologists or gynaecologist/urologist will be promoted. If needed, assistance to find a psychologist for psychological counselling or psychotherapy will be given. Moreover, the proband will be instructed in self management of her/his condition by the study team.
There might be a psychological crisis of the probands when confronted again with memories of earlier negative experiences with medical care which are related to the disorder through the study. A psychologist is available for psychological counselling and support if needed. The need and benefit of psychotherapy for the individual proband will be evaluated and supported if indicated.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Individuals with sex chromosome, XY DSD and XX DSD >= 16 years. Patients with psychiatric disorder will not be excluded. Their medical records are required
Probands >= 16 -<18 years will be included as pubertal development is largely completed in this period. Complete pubertal development is mandatory to evaluate psychosexual development.

Exclusion criteria

Individuals without the mental capability to answer the questionnaires themselves
Simultaneous participation in other studies investigating drugs or hormones.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-11-2013
Enrollment:	205
Type:	Anticipated

Ethics review

Approved WMO

Date:	11-11-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL46220.029.13