Project Periodic Report

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Project acronym: dsd-LIFE

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

Funding Scheme: Collaborative project

Date of latest version of Annex I against which the assessment will be made:

Periodic report: 1st ☒ 2nd ☐ 3rd ☐

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Section 1 - Publishable summary

dsd-LIFE

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

Website: www.dsd-life.eu

Contractors involved (dsd-LIFE consortium):

The project is coordinated by PD Dr. Birgit Köhler (Partner 01, Charité), Universitätsmedizin Berlin, Chariteplatz 1, 10117 Berlin, Germany.

Other partners and team leaders:

[Partner 02] – UZL – Universitaet zu Luebeck – Prof. Ute thyen
[Partner 05] – VUMC – Stichting VUMC – Dr. Annelou de Vries
[Partner 06] – RUNMC – Stichting Katholieke Universiteit – Prof. Hedi Claahsen-van-Grinten
[Partner 07] – BHAM – The University of Birmingham – Prof. Wiebke Art
[Partner 09] – CHUT – Centre Hospitaller Universitaire de Toulouse – Dr. Catherine Pienkowski
[Partner 10] – CHUM – Centre Hospitaller Universitaire de Montpellier – Prof. Charles Sultan
[Partner 12] – Ludwig-Maximilians-Universitaet Muenchen – Dr. Nicole Reisch
[Partner 13] – Karolinska Institutet – PD Anna Nordenström
[Partner 14] – Universytet Medyczny w Lodz – Prof. Jolanta Slowikoska-Hilczer
[Partner 15] – Universitaetsmedizin Goettingen – Prof. Claudia Wiesemann
[Partner 16] – GABO:mi mbH & Co. KG – Birgit Fuchs
[Partner 17] – Instytut Pomnik Centrum Zdrowia Dziecka – Dr. Szarras-Czapnik
[Partner 18] – APHP – Assistance Publique – Hopitaux de Paris – Prof. Claire Bouvattier

3 beneficiaries have been terminated and 1 beneficiary has been included at project start, please see Amendment 1.
1.1 Summary description of project context and objectives

dsd-LIFE is a clinical multidisciplinary European study investigating the long-term outcome of hormone therapies, surgery and psychological support in patients included in the medical umbrella term disorders/differences of sex development (dsd). The dsd-LIFE consortium consists of 14 multidisciplinary European centres of excellence with longstanding experience of clinical care in dsd and a centre for Medical Ethics.

Individuals with dsd often face problems such as impairment of health related quality of life (HRQoL), psychological well-being and psychosocial adaptation, which are influenced by sex assignment, hormone therapies, surgery in childhood or adulthood, psychological support, metabolism, psychosexual development, fertility, stigma, patients’ views, ethical issues and cultural influences. Subsequently, to improve clinical care health related quality of life (HRQoL), psychological well-being and psychosocial adaptation and co-founding factors will be analysed.

The first objective of dsd-LIFE is: To improve clinical practice in the management of disorders of sex development (DSD)

Involved in the study are individuals with the diagnoses included in the medical classification of dsd: 1. dsd with numeric sex chromosome aberrations, 2. XY dsd and 3. XX dsd. 1. Sex chromosome dsd comprises individuals with disorders with gonadal dysgenesis due to sex chromosome imbalances such as Turner syndrome (45,X0 and mosaicism), Klinefelter syndrome (47,XXY), mixed gonadal dysgenesis (45,X0/46,XY) and chimeric dsd (46,XX/46,XY). 2. XY dsd includes individuals with complete and partial forms of testicular dysgenesis, enzymatic defects resulting in disorders of androgen synthesis e.g. 5alpha-reductase II and 17beta-hydroxysteroid dehydrogenase (HSD) 3 deficiency, defects of androgen action such as complete and partial androgen insensitivity syndrome (CAIS, PAIS) and unclassified hypospadias. 3. XX dsd comprises individuals with ovarian dysgenesis or congenital adrenal hyperplasia (CAH).

The second objective of dsd-LIFE is: To develop accepted evidence-based clinical European guidelines for a better clinical care

Apart from an international consensus statement for treatment of dsd from 2005 no evidence based clinical guidelines do exist. Through dsd-Life, European guidelines for the management of dsd comprising sex assignment, surgery, hormone therapies and psychological intervention but also non-medical factors as ethical considerations, patients view, stigma and cultural differences will be developed. Finally, implementation of the guidelines will be promoted in Europe.

A further part of dsd-LIFE is dissemination of knowledge about dsd. Brochures informing about dsd will be developed for parents of children with dsd and for health care professionals. The general public will be informed through an article about dsd.
1.2 Work performed since the beginning of the project and main results achieved so far

During the first period of dsd-LIFE we could finalize the complex tasks of constitution of the study protocol, programming of the database in 6 languages and intake of ethical approvals. In February 2014, recruitment has started. Important activities such as dissemination, data analysis and guidelines development have been initiated.

Constitution of the study protocol (WP 1)
In the first period of the study we have developed the study protocol to analyse health related quality of life (HRQoL), psychological well-being and psychosocial adaptation and the co-founding factors. The study protocol was developed in different working groups (WGs) to bundle the expertise of the different European specialists: WG1: medical issues; WG2: psychology, HRQoL and psychosexuality; WG3: surgery including gynaecology/urology; WG4: ethical Issues. The study protocol was developed in close interaction with the different patient support groups for XY dsd, CAH, Turner and Klinefelter syndrome and with the scientific adviser from AISSG. The self-constructed part of the study questionnaire was pilot-tested for comprehensibility and accuracy of the questions by patients with XY dsd, Turner syndrome, Klinefelter syndrome and CAH at UCLH, London. The self-constructed English study questionnaire was translated according the international required guidelines (EORTC Translation Module) in German, French, Dutch, Swedish and Polish. Ethical approvals for dsd-LIFE were obtained from the consortium in D, F, NL, S and PL.

Programming of the dsd-LIFE database (WP 4)
The online study questionnaire was programmed in the 6 languages of the consortium. Medical issues were programmed in English. Programming of the database was performed at the Coordinating Centre of Clinical trials at Charité (D) using an Electronic Data Capture system (EDC). The system uses a secure data connection.

Recruitment and evaluation of affected persons (WP2)
Standard operating procedures (SOPs) were developed to perform the study in a standardised manner. Before recruitment training on SOP of physicians, psychologists and study nurses was conducted in the centres. Recruitment has started in February 2014.

Data analysis and publication (WP 3)
The outcomes and determinants of the study were defined. A statistical analysis plan was finalised. The publication strategy was developed and finalized. Publication proposals were collected and working groups for publications were constituted. An agreement related to authorship among the STC was accepted by all consortium partners.

Development of clinical guidelines (WP 5)
The major aim will be the development of guidelines for XY dsd conditions as no evidence based guidelines are available. Non-specified areas such as e.g. psychosocial care, ethical issues and patients’ views were identified for CAH, Turner and Klinefelter syndrome and will be the focus for clinical guidelines of these conditions. Working groups for development of guidelines for the different conditions were constituted.

Dissemination (WP 6)
The dsd-LIFE website with a participants section was developed in the first period of the project. Flyers for participants were developed in the 6 national languages. In addition, a project flyer for dissemination to the scientific audiences was finalised by the consortium with support of GABO-mi.s. So far, the study was advertised at several European and national meetings of dsd, gynaecology, endocrinology, psychology and urology. Moreover, the study was presented to the different national patient support groups for Turner and Klinefelter syndrome, XY dsd, and congenital adrenal hyperplasia (CAH). A press release of the study was initiated at month 12 at Charité (D). A website of dsd-LIFE was created for Horizonhealth.eu: http://www.horizonhealth.eu/project/clinical-european-study-outcome-surgical-and-hormonal-therapy-and-psychological-intervention.
1.3 The expected final results and their potential impact and use (including the socio-economic impact and the wider societal implications of the project so far)

So far dsd-LIFE is the largest clinical outcome study of dsd worldwide. Six European countries are involved: D, F, NL, UK, S and PL. It is the first study evaluating the results of different medical and psychological off-label treatment regimens on HRQoL, psychological well-being and psychosocial adaptation in a representative cohort of patients with different genetic entities of dsd. Data on health outcome, well-being, patients perception of treatment and care and ethical issues of dsd will be gathered. Evaluation of the data of the rare conditions included in dsd of the 6 European countries will give a broad overview of the health status, patient reported outcome and enables representative analysis of the different treatment regimen. Moreover, analysis of country specific and cultural differences is possible.

The final aim of dsd-LIFE is to improve care of dsd through development of clinical guidelines in Europe. Health, psychosocial and ethical aspects of the different conditions will be considered in the development of clinical guidelines. But also the specific needs of the different genetic entities included in the umbrella term dsd will be respected. Patients’ views will be also included in the development of clinical European guidelines in addition to the medical, psychosocial and ethical issues. Moreover, new insights will be gained through the patients’ view on their condition and the medical catagorisation of dsd.

A core part of dsd-LIFE is to involve affected persons, particularly patient support groups (XY dsd, CAH, Turner and Klinefelter syndrome) in all phases of the study. The consortium is in continuous contact and cross-talk with national patient support groups to reach the study aim cooperatively.

Dissemination of knowledge about dsd is a further important activity of the project. The dsd-LIFE website for scientific information about the project, a participant web-site and a patient flyer in the 6 national languages have been developed. A special part of the ongoing discussion and criticism of the term dsd within the different national patient support groups has been included on the website. But also information of specialised care in national dsd centers is provided on the website so that the affected individuals can find appropriate care according the actual medical state of the art for their rare condition.

Moreover, dsd-LIFE will develop information material about dsd for health care providers to improve treatment and care. An ongoing activity of dsd-LIFE is to inform the general public about dsd to enhance acceptance in the society and social participation of the affected individuals.