Disorders of sex development in Indonesia:

The course of psychological development in late identified patients

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Stoornissen van seksontwikkeling in Indonesië:
Psychologische ontwikkeling in patiënten bij wie
op latere leeftijd een diagnose is gesteld

Proefschrift

ter verkrijgen van de graad van doctor aan de
Erasmus Universiteit Rotterdam
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Co-promotoren	Dr. A.B. Dessens Dr. E. Birnie

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For my family and Raja

Chapter 1

General introduction

General introduction

In individuals with a disorder of sex development (DSD), prenatal development into male or female has deviated. As a consequence, a child is born with anomalies of the genital tract and may have ambiguous sex characteristics. In addition to genetics, steroid hormones plays an important role in sex development. Steroids are particularly important in the development of psychological aspects of gender. Ambiguity in body or behavior is rare and confrontation with a person who raises doubt about his or her gender often leads to confusion. A DSD condition therefore makes patients vulnerable for stigmatization.

In Western patients with DSD, diagnostic work-up and treatment follows immediately after identification of DSD. Medical treatments are given to prevent life-threatening consequences of the disorder and progressive genital and body masculinization in children raised as girls or development of female characteristics in adolescents raised as boys. Psychological counseling is offered to help parents cope with their emotions and problems met in daily life. An important aspect of the offered medical and psychological help is to prevent stigmatization and to provide optimal social opportunities. This policy has been developed 50 years ago.

During the past 20 years, there has been a debate about the advantages and disadvantages of this policy of early interventions in children with DSD. These critics mainly focus on the fact that many decisions taken brought enormous impact on the future lives of these children whereas children are often too young to be involved in the decision making. In non-Western countries, doctors mostly see patients who seek medical care later in life. Many patients and parents will only consult a doctor after psychological or social problems with genital or body ambiguity have intensified. In Indonesia, DSD is not known widely; treatments are available in six type-A hospitals, medical professionals with expertise on DSD are very rare, and medical treatments are expensive. Delay of treatment allowed us to study the course of psychological development in patients with DSD who, for a long time, did not receive medical attention and the implications on gender development and psychosocial adaptation. To date, no such study had been done before in Indonesia, while such a study is almost impossible to achieve in Western countries.

This study is part of a clinical study on etiology and management of DSD in a large group of undiagnosed and untreated DSD patients in Semarang, Indonesia. It focuses on the psychosexual development and psychological wellbeing aspects in these patients: body image, sexual functioning, sexual orientation, gender development, emotional and behavioral problem, social stigmatization, and health-related quality of life. Findings from both studies will be used to develop a clinical guideline for providing an integrated treatment plan for our patients with DSD.

What is DSD?

Disorders of sex development (DSD) is an umbrella term covering congenital conditions in which the development of chromosome, gonads, internal and external genitalia did not follow the normal path of male or female (Hughes, Houk, Ahmed, & Lee, 2006). As DSD covers a broad range of sex anomalies, a new classification of DSD diagnoses had been proposed in the Chicago consensus which classified all DSD condition into three groups: a) 46,XX DSD; b) 46,XY DSD; and c) sex chromosome DSD (Hughes et al, 2006).

The three most common causes of DSD are: congenital adrenal hyperplasia (CAH), androgen insensitivity syndrome (AIS), and mixed gonadal dysgenesis (Hewitt & Warne, 2009). Table 1 summarizes the DSD diagnoses by cause as proposed in the Chicago consensus conference (Hughes et al., 2006).

Table 1 Classification of disorders of sex development (DSD)

Sex chromosome DSD	46,XY DSD	46,XX DSD
A: 47,XXY (Klinefelter syndrome and variants)	A: Disorders of gonadal (testicular) development 1. Complete or partial gonadal dysgenesis (e.g. SRY, SOX9, SF1, WT1, DHH etc) 2. Ovotesticular DSD 3. Testis regression	A: Disorders of gonadal (ovarian) development 1. Gonadal dysgenesis 2. Ovotesticular DSD 3. Testicular DSD (e.g. SRYþ, dup SOX9, RSP01)
B: 45,X (Turner syndrome and variants)	B: Disorders in androgen synthesis or action 1. Disorders of androgen synthesis LH receptor mutations Smithe-Lemlie-Opitz syndrome Steroidogenic acute regulatory protein mutations Cholesterol side-chain cleavage (CYP11A1) 3b-hydoxysteroid dehydrogenase 2 (HSD3B2) 17a-hydroxylase/17,20-lyase (CYP17) P450 oxidoreductase (POR) 17b-hydoxysteroid dehydrogenase (HSD17B3) 5a-reductase 2 (SRD5A2) 2. Disorders of androgen action Androgen Insensitivity Syndrome Drugs and environmental modulators	B: Androgen excess 1. Fetal 3b-hydoxysteroid dehydrogenase 2 HSD3B2 21-hydroxylase (CYP21A2) P450 oxidoreductase (POR) 11b-hydoxylase (CYP11B1) Glucocorticoid receptor mutations 2. Fetoplacental Aromatase (CYP19) deficiency Oxidoreductase (POR) deficiency 3. Maternal Maternal virilizing tumours (e.g. luteomas) Androgenic drugs
C: 45,X/46,XY (mixed gonadal dysgenesis)	C: Other 1. Syndromic associations of male genital development (e.g. cloacal anomalies, Robinow, Aarskog, Hand-Foot-Genital, popliteal pterygium) 2. Persistent Müllerian duct syndrome 3. Vanishing testis syndrome 4. Isolated hypospadias (CXorf6) 5. Congenital hypogonadotropic hypogonadism 6. Cryptorchidism (INSL3, GREAT) 7. Environmental influences Cloacal exstrophy	C: Other 1. Syndromic associations (e.g. cloacal anomalies) 2. Müllerian agenesis/ hypoplasia (e.g. MURCS) 3. Uterine abnormalities (e.g. MODY5) 4. Vaginal atresis (e.g. KcKusickeKaufman) 5. Labial adhesions Cloacal malformation Cloacal exstrophy
D: 46,XX/46,XY (chimerism)		

Source: Hughes, et al., 2006.

DSD and psychological consequences

The number of studies among individuals with DSD have been increased rapidly in the past decades, including the psychological field. Findings from previous psychological studies on patients with DSD, particularly diagnoses relevant to this study, will be summarized below.

46,XX Congenital adrenal hyperplasia (CAH)

CAH is an autosomal recessive disorder that mainly caused by the 21-hydroxylase enzyme deficiency (White & Speiser, 2000). This enzyme deficiency prohibits adrenals from producing cortisone and aldosterone from cortisol, consequently all cortisol will be metabolized into androgens. The excessive production of adrenal androgen will impact profoundly in female in which the body, and particularly external genitals, will be masculinized. In patients with a complete or nearly complete block of the 21-hydroxylase production, masculinization of the external genitals will be severe: a nearly normal male appearance at birth with a "penis" and an empty scrotum. In such newborn, a male gender may be assigned. In patients with an incomplete block of the 21-hydroxylase production, the masculinization of the external genitals will be less severe and will have an ambiguous appearance at birth (Hines, 2004). If left untreated, the adrenal glands will continue to produce large amounts of androgens and masculinization of the body will be progressive. In puberty, body masculinization will lead to a male appearance and failure in development of female characteristics or development of both male and female secondary sex characteristics (i.e. development of breasts as well as facial hair).

In Western countries, particularly countries that implement newborn screening for CAH, CAH can be identified soon after birth and therefore, medical treatment can be offered soon. These newborns will likely be raised as a girls, and will receive glucocorticoid treatment. It is chosen to raise these children as girls, as they have ovaries and a womb, and they are fertile as women but not as men. Parents will receive education about CAH, parenting of a child with CAH, and understanding the risks of CAH in the next pregnancy. However, different cultures might imposed different practices in gender assignment on newborn with an ambiguous genitalia. A newborn with 46,XX CAH might had been assigned male and raised as a boy (Lee, Houk, & Husmann, 2010), particularly when the affected individuals were referred late for identification (Sripathi et al., 1997; Julka, et al., 2006).

Gender identity, gender role behavior, gender dysphoria, sexual functioning, and sexual orientation had been the main focus of psychological research on patients with CAH (Stout, Litvak, Robbins, & Sandberg, 2010). Previous studies revealed that young girls with CAH behave more masculine than healthy girls (i.e. siblings, healthy control subjects), have fewer interests in feminine-type of activities and often prefer typically masculine-type of

activities (Beltz, Swanson, & Berenbaum, 2011; Berenbaum, Duck, & Bryk, 2000; Berenbaum & Hines, 1992; Berenbaum, Korman Bryk, Duck, & Resnick, 2004; Hines, Brook, & Conway, 2004). Girls born with more severe masculinization of the external genitalia displayed more masculine behaviors than girls who had milder genital masculinization at birth. It is assumed that severity of masculinization of the external genital at birth reflects the level of circulating prenatal androgens. Hence, there also seems to be a dose-effect of level of prenatal androgens on gender role behavior (Meyer-Bahlburg, Dolezal, Baker, Ehrhardt, & New, 2006). Another study revealed that parenting practice does not influence the development of masculine behavior in girls with 46,XX CAH (Pasterski, et al., 2005).

The prevalence of the social gender role change in adult women appears to be between 1.5 – 2%, which is higher than in the non-DSD population (Dessens, Slijper, & Drop, 2005), but not high enough to change the present practice of gender assignment, particularly not as there is no correlation found with neonatal genital masculinization.

Studies on sexual functioning in women with CAH reported some problems with sexual functioning and intimate relationships (Crouch, Liao, Woodhouse, Conway, & Creighton, 2008; Gastaud, et al., 2007; van der Zwan et al., 2012), whereas other studies reported satisfaction with sex life and no problem with sexual functioning after genital surgeries (Nordenström, et al., 2010).

Androgen insensitivity syndrome (AIS)

AIS is defined as a disorder resulting from complete or partial resistance to the actions of androgens in an XY individuals with normal testis determination and production of age-appropriate androgen concentrations (Hughes, et al., 2012). AIS is a genetic disorder, in which the affected XY individuals was inherited through the X-linked trait (Hines, 2004). Each cell contains the defective androgen receptor. As a consequence, the body is unable to response to testosterone and the body feminizes. The complete form of AIS (CAIS) is characterized by a female phenotype, while in the partial form of AIS (PAIS), the genitals appear ambiguous. Most individuals with CAIS are assigned female at birth. The disorder will become apparent in adolescence when menses stay out. A medical examination will reveal 46,XY karyotype, undescended testes, and no Müllerian structures (Hines, 2004).

The large majority of individuals with 46,XY CAIS develop a female gender identity and display feminine gender role behavior (Hines, Ahmed, & Hughes, 2003). The literature only comprises a few case reports of CAIS patients who developed a male gender identity (T'joen et al., 2011; Kulshreshtha et al., 2011). In contrasts, individuals with 46,XY PAIS will be raised as men or women. Studies on gender role behavior revealed that individuals with 46,XY PAIS raised as girls are more masculine in their behavior than healthy control girls, whereas individuals raised as boys prefer girls as their playmates compared to healthy boys who prefer male playmates only (Jürgensen, Hiort, Holterhus, & Thyen, 2007). Studies on gender identity revealed that gender dysphoria and social gender role change are seen in about 10% patients with PAIS (Mazur, 2005; Melo et al., 2003) either raised as females or males.

Review studies on the quality of life of women with 46,XY DSD revealed varying results: women with chromosomal male did not differ, or had better, or lower quality of life than the comparative groups assessed (Wisniewski & Mazur, 2005). Bouvattier and coworkers (2006) observed sexual functioning of adults with 46, XY PAIS raised as men. They reported sexual problems and impaired sexual functioning among this patient group.

Gonadal dysgenesis

Gonadal dysgenesis includes various clinical conditions characterized by an abnormal and underdevelopment of the fetal gonads. Complete gonadal dysgenesis in 46,XY individuals is characterized by a female phenotype with full development of the female genitals, normally developed Müllerian structures, and streak gonads. The affected individuals may not be identified until adolescence when the onset of puberty does not occur (Öcal, 2011). Serum FSH and LH levels are high, due to primary gonadal failure. Since women with this condition have a uterus, hormone replacement therapy is able to induce secondary sex characteristics including menses. As they have non-functional gonads, these women are infertile (Warne, 2008), but childbirth may be achieved through ovum donation and in vitro fertilization. Gonadal removal is usually performed in early life to anticipate the increased risk of malignancy. Individuals with a 46,XY complete gonadal dysgenesis are usually assigned female and identify themselves as females. Gender identity confusion or gender reassignment has not been reported among patients with gonadal dysgenesis (McCarty et al., 2008). A follow-up study of 19 adults with mixed

or partial gonadal dysgenesis raised as men or women observed that women reported more sexual problems than men (Szarras-Czapnik, Lew-Starowicz, & Zucker, 2007).

Sex chromosomal DSD

Sex chromosomal DSD includes the 45,X Turner Syndrome (TS) and variants; 47,XXY Klinefelter Syndrome (KS) and variants; 45,X/46,XY with mixed gonadal dysgenesis; and 46,XX/46,XY chimerism. Women with TS are phenotypically female and raised as girls (Lippe, 1991). Women with TS have full development of the external female genitalia, normally developed Müllerian structures, and streak gonads. There is considerable heterogeneity in dysmorphic body characteristics, health status, and neuropsychological functioning in women with TS (Rovet, 2004). Studies on gender role behavior and gender identity show that females with TS are typically female (Theilgaard, 1972; Money & Mittenthal, 1970; Downey et al., 1987, Collaer et al., 2002).

Men with KS are phenotypically male and raised as men (Aksglaede & Juul ,2013). Most men with KS have small testes, hypergonadotropic hypogonadism, and azoospermia in the majority of cases. There is large heterogeneity in dysmorphic body characteristics, health status, and neuropsychological functioning among men with KS (Groth et al., 2013). The large majority of men with KS have masculine gender identities, but in the last 45 years some cases of gender dysphoria and the wish for a gender role change have been reported (Hoaken, et al., 1964, Miller & Caplan, 1965; Davidson, 1966; Müller, 1972; Cryan & O'Donoghue, 1992; Seifert & Windgassen, 1995).

45,X/46,XY and mixed gonadal dysgenesis is associated with marked phenotypic variability, including females with Turner syndrome features, children with ambiguous genitals, and normal males (Telvi, Lebbar, Del Pino, Barbet, & Chaussain, 1999). There is also large variability in neuropsychological functioning but it seems that those children raised as girls are more affected than those children raised as boys (Tosson, Rose, & Gartner, 2012). Not much is known on the gender identity development in individuals with mixed gonadal dysgenesis. Only a few larger studies and several case studies have been published (Richter-Appelt et al., 2005; Migeon et al., 2002; Reiner, 2005; Warne et al., 2005; Reiner, 1996; Birnbacker et al., 1999; Ammini et al., 2002, Öcal, et al.,2012). These data indicate that about 30% of patients who had been raised as females made a social gender role change in adolescence.

Patients with different DSD diagnoses reported impaired body image, problems in establishing romantic relationships, and difficulties with sexual functioning (Bouvattier, Mignot, Lefèvre, Morel, & Bougnères, 2006; Crouch, Liao, Woodhouse, Conway, & Creighton, 2008; Gastaud et al., 2007; Kojima et al., 2009; Migeon et al., 2002; Minto, Liao, Conway, & Creighton, 2003; Szarras-Czapnik, Lew-Starowicz, & Zucker, 2007; Wisniewski et al., 2000).

Schützmann, Brinkmann, Schacht, and Richter-Appelt (2009) found that 59% of the adults with DSD reported severe psychological distress. However, a study on adolescents with DSD concluded that DSD does not impact their mental health (Kleinemeier, Jürgensen, Lux, Widenka, and Thyen, 2010). Gender differences in emotional and behavioral problem among patients with DSD are inconclusive. Zhu and colleagues (2010) observed more emotional and behavioral problems in boys with DSD than the matched controls, but this was not found among girls. Trautman, Meyer-Bahlburg, Postelnek, and New (1995) and Hirvikoski et al. (2008) did not find behavioral problems in girls with CAH, but Öner and colleagues (2011) observed more externalizing behavior and general behavioral problems in patients than in the control girls. Tosson, Rose, and Gartner (2012) observed that children with 45,X/46,XY raised as girls were more likely than those raised as boys to have behavioral problems. In contrast, a study on adolescent German girls with DSD aged 13-16 reported that these young patients did not differ from the control girls in terms of quality of life (Kleinemeier, et al., 2010).

Gender and gender variance in Indonesian socio-cultural context

Indonesia is a country of over 237 million people with a large cultural and religious diversity: 300 native ethnicities, 724 local languages and dialects, and five religions (Islam, Roman Catholic, Protestan, Hindu, and Buddha). Javanese is the major ethnic group and Java island is the most populous island in Indonesia. *Bahasa Indonesia* is the national language used throughout the country and taught during formal education (schools).

In order to obtain citizenship, every newborn must be registered, as male or female, within 60 days after birth, also in case of genital ambiguity. A birth certificate is compulsory for school entry, and for obtaining a diploma, health insurance, and an ID card. Delayed birth registration or change of gender in the birth registry requires a legal procedure in an Indonesian state court. In case a gender change is requested, the court will request a medical review

before reaching a decision. Gender change for patients with DSD received support from the Indonesian Moslem clerics (Haryadi, 2010). DSD is not widely known among general population in Indonesia, and not even among many health practitioners. Moreover, knowledge about DSD was limited until the last decade when education about DSD and genetic counseling was initiated by the Faculty of Medicine, Diponegoro University (FMDU). However, in the general population of Indonesia, the term "hermaphrodite" is known and often perceived by mistake as persons with double genitals (in *Bahasa: "kelamin ganda"*).

Gender variances and transgenderism is known in Indonesia. Persons with transgender are called *waria* or *banci* (in *Bahasa*) or *bencong* or *wandu* (Javanese*)*. In daily live, girls who present themselves (with clothing, haircut, or behavior) in a masculine way are called *tomboi* (Blackwood, 2005). Transgender persons as well as gay men or lesbian women are not socially accepted, although their presence is known (Vaswani, 2010). In Indonesia, the term "homosexuality" is strongly associated with sin (Boellstorff, 2004). An anthropological study reported on *Bissu* in the Sulawesi, traditional priests believed to have both male and female characteristics (Graham, 2009). However, it seems that nowadays this Bissu cult is not practiced anymore. At least, this Sulawesian folklore is not well-known to the general population of Indonesia. Among the traditional Javanese puppets ('*wayang*') based on the Javanese Mahabarata, there is one figure that represents gender change, so-called *Srikandhi*. *Srikandhi* represents a female figure who has masculine traits and is represented as a female warrior or fighter (Sunindyo, 1998). The name or symbol *Srikandhi* has been used often by non-government initiatives, particularly in the field of women empowerment. This may suggests that masculinity in women is socially accepted in Javanese folklore.

In Indonesian society, marriage is a precondition for becoming a fully respected member of society and being unmarried, particular for women, is considered to bring shame to the family (Mulder, 1992). Shame (in Javanese: *'isin'*) is a fundamental element in Javanese culture and is taught from early childhood onwards (Keeler, 1983). When Indonesian adolescents enter adulthood, the social expectancies with respect to marriage and kinship and other social responsibilities will be intensified. Javanese people have been thought, since early life, to follow social norms and to ensure that social relations are in harmony.

Management of DSD in Indonesia

The government of Indonesian had appointed six state hospitals to provide medical treatment for patients with genital anomalies. The Sexual Adjustment Team/SAT *("Tim Penyesuaian Kelamin")* was established in 1989 in collaboration between the Dr Kariadi Hospital and the Faculty of Medicine of the Diponegoro University (FMDU) in Semarang, Central Java. Over the years, this team expanded. At present the multidisciplinary team includes many specialties, including pediatric, endocrinology, urology, andrology, obstetrics and gynecology, genetics, radiology, pathology, plastic surgery, psychology, psychiatry, social services, law and ethics.

Over the times, the SAT had been challenged mainly by the limited resources for diagnostic procedure and treatment. As a type A hospital in Central Java, the dr Kariadi Hospital receives referral particularly from poor people. The Indonesian government does provide universal health insurance called the Health Insurance Scheme for the Population, *('Jaminan Kesehatan Masyarakat'* or *'Jamkesmas')*, which aims to provide free health care services for common disease, including antenatal, delivery, or postnatal care services for mothers and infants (Ministry of Health Republic of Indonesia - The Directorate General of Community Health, 2008; Rokx, Schieber, Harimurti, Tandon, & Somanathan, 2009). However, this insurance policy was not widely known among poor people (Titaley, Hunter, Dibley, & Heywood, 2010), and does not cover hormonal and genetic tests. As a consequence, poor people often have to use their out of their own pocket money for obtaining medical treatment (Chee, Borowitz, & Barraclough, 2009), including our patients with DSD.

In 2004, an international collaboration was initiated by Prof. dr. Sultana M.H. Farads, MD, PhD (geneticist and coordinator of the SAT) and Prof. dr. S.L.S Drop, MD, PhD (pediatric endocrinologist and coordinator of the DSD team in the ErasmusMC-Sophia, Rotterdam) to improve our expertise through research and academic activities in the DSD field. Within this international collaboration, several seminars, workshops and teaching sessions were organized to increase awareness and expertise in management of DSD among Indonesian medical professionals. Between 1989 and 2010, 589 patients had been referred to SAT, in which 347 patients were evaluated clinically. Following the inclusion criteria applied for the study, 286 patients were included in the clinical study, and 118 were enrolled in the psychological study.

Aims of the study

This study was designed to give a comprehensive description on the psychological condition of patients with DSD in comparison with the matched control subjects. For the majority of these patients, diagnostic procedures were performed later in life and in some patients, treatment was initiated. Consequently, many patients had lived without treatment, in ambiguous bodies and gender, for most of their lives. In the Netherlands as well as most Western countries, diagnostic procedures and treatment start immediately following the identification of DSD.

This psychological study investigated gender identity, gender role behavior, body image, sexual functioning, sexual orientation, emotional and behavioral problems, social stigmatization, and health-related quality of life of children, adolescents, and adult patients with DSD in Semarang, Indonesia.

Outline of the thesis

Chapter 2 provides general information about the method of this cross-sectional study, which are not explained in detail in the following chapters, such as scale construction and validation and methodological challenges in conducting a case-control psychological study in Indonesia.

In **chapter 3**, findings from the study on body image and sexuality among 34 adult patients with DSD are reported. Sexuality, in this study, refers to male and female sexual functioning, female sexual distress, and sexual orientation.

Chapter 4 comprises a unique study on gender development among 60 children, 24 adolescents, and 34 adult patients with DSD. In this study, gender identity confusion and gender role behavior as well as satisfaction with the assigned gender are investigated. In addition to findings from the patient-matched control comparisons, we report findings on gender development among patients across DSD diagnoses. Furthermore we provide an evaluation on the gender development of patients who had changed their social gender role before entering medical service or patients who reported gender confusion at the time of study.

In **chapter 5**, we present our findings from a study on emotional and behavioral problems in patients with DSD. We identified different types of emotional and behavioral problems reported among patients and the percentage of patients with DSD who scored within the borderline range of emotional problems. More patients with DSD suffered from emotional and behavioral problems.

In **chapter 6**, we report on patients' experiences with social stigmatization. This study is relevant as for many years, early medical intervention in young patients with DSD had been under debate for its purpose of preventing stigmatization in later life but in fact, a systematic study on DSD patients' experiences with stigmatization is still lacking in the literature. In this study, quantitative and qualitative methods were applied in order to obtain insight in severity of stigmatization and the associated experienced distress. Qualitative data are used in addition to quantitative data obtained from measures developed specifically for the study of social stigmatization in patients and parents of youngsters with DSD.

In **chapter 7**, we describe our findings from a study on the health-related quality of life in patients with DSD. We compared the health-related quality of life in children, adolescents, and adult patients to their matched controls to find out to what extent the patients' quality of life was impaired.

In **chapter 8**, the findings from these five studies are discussed in broader context. Implications for future studies as well as for management of patients with DSD in Indonesia will be presented.

Chapter 9 contains a summary of findings from all studies reported above.

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Chapter 2

Methods of study

Methods of study

This chapter provides methodological details that are not described in the following chapters.

Study Design

This study is a unique investigation of the psychological development of Indonesian patients with DSD who had been referred to the Sexual Adjustment Team (SAT) of the Dr. Kariadi Hospital and the Faculty of Medicine, Diponegoro University (FMDU), Semarang, Indonesia for medical treatment. Before entrance, the majority of these patients had received little medical attention.

In the studies presented in Chapter 3, 4, 5, and 7, we compared patients with DSD to the healthy control subjects matched for gender, age, and residential setting (urban, suburban, rural) on the psychosexual development and psychological well-being.

As no Indonesian instruments were available to measure these constructs, instruments developed in Western countries were selected and translated for the Indonesian population. Application of internationally recognized measures in similar studies allow comparison between findings by other researchers and findings from Indonesian study. International comparison is valuable as it can give insight in cultural factors that play a role in the psychological aspects of DSD. We selected instruments based on two criteria: 1) the original version has good psychometric qualities, and 2) the measure has been used in previous studies in patients with DSD. Translated questionnaires may not have the same psychometric properties in the different language and culture they are introduced. Therefore, validity and reliability of the translated questionnaires need to be investigated. The procedures followed are described under Study preparation.

Study preparation: Scale adaptation/construction

Procedure

The scale adaptation procedures applied is illustrated in Figure 1. Translation of questionnaires was performed by certified translators from The Language Academy of the University of Amsterdam, the Netherlands (UVA Talen). For copy-righted questionnaires, translations rights were obtained. Prior to implementation, the Indonesian versions of the measurements were reviewed by the researcher (AE) and a Dutch anthropologist (Dr Saskia E. Wieringa) who is well-understood Indonesian culture, customs, and language, followed by an initial trial in healthy subjects. A few minor adaptations were made. Details can be found in the chapters 3-7.

Method

To assess the validity and reliability of adapted measures, we collected data through three different methods of survey: a) web-based survey, b) school-based survey, and c) face-to-face interview.

Web-based survey. Internet survey enables participation of a large sample of Indonesian adults, aged 18 years or older, across different provinces in Indonesia in a short period of time. Internet connection and familiarity with electronic surveys are required from potential respondents. We propagated our survey using mailing-lists and a Facebook page and reached well educated adults, aged 18-45 years. Details about this survey are provided in chapters 3 and 4.

School-based survey. The aim of this survey is to recruit a large sample of students from elementary schools, junior and senior high schools colleges and universities in Central Java and Yogyakarta provinces to fill out questionnaires as a paper-and-pencil test. Ten schools and four universities in Central Java and Yogyakarta provinces participated. Details about this survey can be found in chapters 5 and 7.

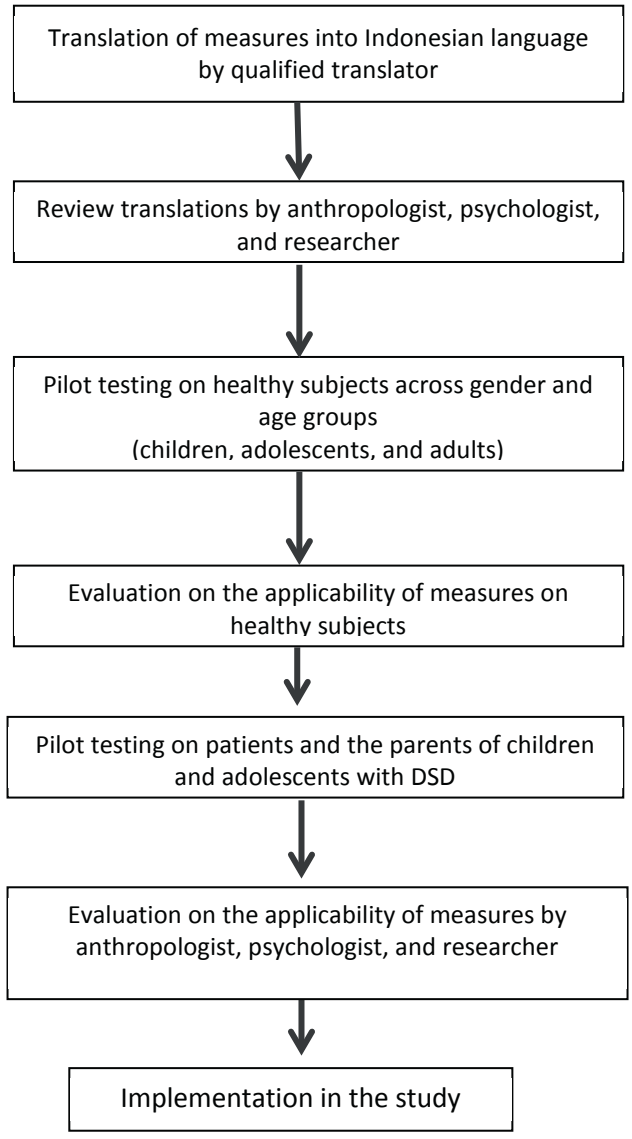

Figure 1. Procedures on adaptation of measures applied in the study

Face-to-face interview. Semi-structured interviews combines the opportunity of elaborative answers and quantitative measures. Elaborative answers were required in investigations in gender identity and social stigma. Detailed information can be found in chapters 4 and 6).

Measures

Table 1 summarizes the measures applied in the study, number of participants enrolled to assess validity and reliability of measures, and method applied to collect study participants. Detailed information on the validity and reliability of measures can be found in chapters 3-7.

Participants

To assess the psychometric properties of our measures, 5024 participants volunteered: 240 children and 245 parents, 1534 adolescents, and 3005 adults. See Table 1 for the number of participants based on the methods applied in the study and the relevant chapters discuss in details.

Statistical analysis for assessing validity and reliability of measures

In order to be able to compare data internationally, we followed methods in accordance with the method applied by the authors of the original scales. The principal component analysis was used to assess the factor structure of measure, whereas reliability was assessed using the internal consistency which was measured by the Cronbach's alpha. Detailed information on the applied procedures can be found in the chapter 3-7 as well as the psychometric properties of the applied measures.

Studies in patients with DSD

Participants

We eventually included 118 patients with a DSD condition, aged 6-41 years, and 118 healthy control subjects matched for age, gender, and residential setting (living in rural, suburban, or urban area).

Patients with DSD.

Inclusion criteria

Individuals with DSD aged 6 or older. Patients with the following diagnosis were included:

I. 46,XY DSD. Clinically the patients presented with underdeveloped or ambiguous external and/or internal genitalia

Table 1 Measures translated into Indonesian language, number of participants, and method used for scale validation

Instruments and reference	Outcome measure	Target population	Web-based survey (*n*)	School-based survey (*n*)	Individual interview (*n*)	Chapters
Body Image Scale (Lindgren & Pauly, 1975)	Body image and satisfaction	Adults aged 18 or older	243	n.a.	n.a.	3
Female Sexual Dissatisfaction Scale – Revised/FSDS-R (DeRogatis, Clayton, Lewis-D'Agostino, Wunderlich, & Fu, 2008)	Female sexual distress	Adults aged 18 or older	185	n.a.	n.a.	3
Female Sexual Functioning Index/FSFI (Rosen, 2002)	Female sexual functioning	Adults aged 18 or older	94	n.a.	n.a.	3
Kinsey Heterosexual-Homosexual Rating Scale (Kinsey, Pomeroy, & Martin, 1948; 1953)	Sexual orientation	Adults aged 18 or older	210	n.a.	n.a.	3
Male Sexual Health Questionnaire/MSHQ (Rosen, et al., 2004)	Male sexual functioning	Adults aged 18 or older	41	n.a.	n.a.	3
Activities Questionnaire (Hines, Ahmed, & Hughes, 2003)	Gender role behavior	Adolescents or adults aged 12 or older	254	n.a.	48 [a]	4
Gender Identity interview for children/GIIC (Zucker & Bradley, 1995)	Gender identity confusion	Children aged 6-11	n.a.	n.a.	120 [a]	4
Gender Identity Questionnaire for Children/GIQC (Cohen-Kettenis, et al., 2006)	Gender role behavior	Parents of children aged 6-11	n.a.	n.a.	120 [a]	4
Gender Questionnaire (Hines, et al., 2003)	Gender identity	Adolescents or adults aged 12 or older	316	n.a.	48 [a]	4
Adult Self Report/ ASR (aged 18-59) (Achenbach & Rescorla, 2001)	Emotional and behavioral problems	Adults aged 18 or older	n.a.	1091	n.a.	5
Child Behavior Checklist /CBCL 6-18 (Achenbach & Rescorla, 2001)	Emotional and behavioral problems	Parents of children aged 6-11	n.a.	n.a.	107	5
Youth Self Report/YSR (Achenbach & Rescorla, 2001)	Emotional and behavioral problems	Adolescents aged 12-15	n.a.	1154	n.a.	5

Instruments and reference	Outcome measure	Target population	Web-based survey (*n*)	School-based survey (*n*)	Individual interview (*n*)	Chapters
Social stigmatization scale on DSD – Parent report	Social Stigmatization [b]	Parents of patients aged 6-17 years	n.a.	n.a.	81 [c]	6
Social stigmatization scale on DSD – Adult report	Social Stigmatization [b]	Adults aged 18 or older	n.a.	n.a.	34 [c]	6
TACQOL PF 6-15 (Verrips, et al., 1999)	Health-related quality of life (generic)	Parents of children aged 6-15	n.a.	n.a.	57	7
TACQOL CF 8-15 (Verrips, et al., 1999)	Health-related quality of life (generic)	Children aged 8-15	n.a.	284	n.a.	7
TAAQOL (aged 16 year or older) (Verrips, et al., 1999)	Health-related quality of life (generic)	Adults aged 16 or older	n.a.	326	n.a.	7

[a] The participants comprised patients and matched control subjects; [b] The measure was developed specific for the study; [c] The participants comprised patients and parents of children and adolescents

a. Androgen Action Disorder. This group comprises patients with complete and partial androgen insensitivity syndromes (CAIS, PAIS). In these patients, testes are present but may be undescended uni-or bilaterally. Hormonal testicular function is normal but androgen action is presumed not to be fully effective. Ultimate proof is the demonstration of a mutation in the androgen receptor gene. In the absence of an AR gene mutation, the following criteria applied:
    - Pre pubertal age (0-12 years): No evidence of impaired action of androgens except in the infant 2-4 months with elevated serum levels of luteinizing hormone, follicle stimulating hormone, and testosterone (mini puberty condition).
    - Post Pubertal age (after 12 years): Serum levels of luteinizing hormone, testosterone, and anti-müllerian hormone are elevated.

b. Gonadal dysgenesis: This group comprises patients with underdeveloped testes and / or testes that cannot produce normal levels of steroids. Therefore

serum levels of luteinizing hormone, follicle stimulating hormone are high, of anti-müllerian hormone/Inhibin are low. The testosterone response in the human chorionic gonadotropin (HCG/Pregnyl) test is insufficient.

c. Under masculinization of unknown cause: This group comprises patients with underdeveloped external genitalia but with descended testes and normal internal male development in whom no cause for underdevelopment /under masculinization could be identified. Serum hormone values and response to HCG/Pregnyl are all normal for age.

.

II. 46,XX DSD:

Gonadal dysgenesis: In these patients, the development of the gonads and internal genitalia is abnormal. The external genitalia is often ambiguous and has been virilized depending on the function of the gonads.

- Pre-pubertal age (age 0-12): Hormonal evaluation: Low levels of inhibin and anti-müllerian hormone

- Pubertal and post-pubertal age (above 12 years old): Serum levels of luteinizing hormone and follicle stimulating hormone were elevated whereas testosterone, anti-müllerian hormone and Inhibin levels were low for age.

Androgen excess. This group comprises patients with congenital adrenal hyperplasia (CAH)[1]. In all included patients, a mutation of the gene of the CYP21 or 11B enzyme has been found. These patients presented with varying degree of virilization of the external genitalia whereas the internal genitalia were normally female. Serum levels of testosterone, 17-hydroxyprogesterone and or androstenedione are high.

Cloacal malformation: due to an anomalous development of the abdomen, the genital region remained severely underdeveloped. Gonads are normally developed and function well.

III. Sex Chromosome DSD: All patients with a sex chromosome abnormalities including Turner and Klinefelter mosaics.

1 This group also comprised three patients with virilization and normal female internal genitalia without high testosterone, 17-hydroxyprogesterone and or androstenedione but excluded in this study due to age below six years.

Exclusion criteria

Patients with all other types of DSD were excluded because these patients present different types of additional problems outside the focus or our study objectives:

- 46,XY DSD and syndromic associations of male genital development
- 46, XX DSD and syndromic associations
- Sex Chromosome DSD: Klinefelter and Turner syndromes without mosaicism

In addition, patients with limited intellectual capacities were excluded. The instruments applied in this study were designed for participants with intellectual abilities in the normal ranges. Judgments on intellectual functioning were based on interaction with the patients and (parental) reports on academic achievements. Due to the large variety of the development of gender identity and gender role behavior, the psychological assessment applied in gender development cannot assess well in children younger than 6 years old. Among other types of DSD, disorders in biosynthesis testosterone would follow the inclusion criteria but no patients entered the hospital.

Participation rate. Figure 2 displayed the patient selection for psychological study. From 286 patients diagnosed with DSD (Juniarto et al., 2013), 161 patients matched the inclusion criteria. Twenty-one patients were lost for follow-up, 29 patients declined participation due to unspecified reasons. Seven patients were diagnosed during the period of the study and were added to the research group. In total, 118 patients eventually joined the study.

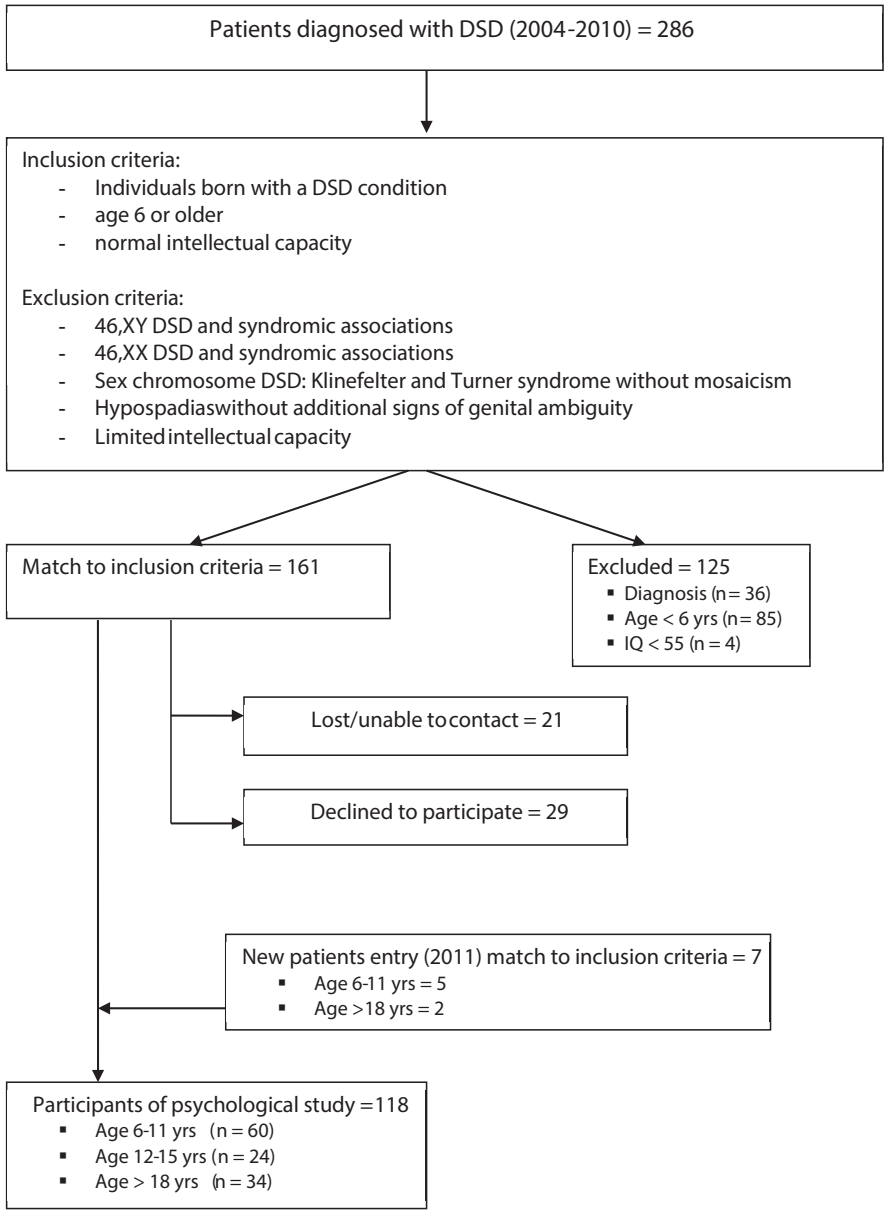

Figure 2. Patient selection for psychological study

Matched Control subjects

Initially, we planned to include non-affected siblings being raised in the same gender as the most appropriate control subjects because they share many social as well as biological characteristics, i.e. socioeconomic status, family characteristics to be raised in genetic similarities. Whenever it was impossible to choose a sibling (e.g. the patient has no same gender sibling), another family member or best friend was selected as control as long as the individual matched the inclusion criteria. While carrying out the study, difficulties in fulfilling the matching criteria became evident: Patients were the only child, the siblings were in the opposite gender, or no consent was given to involve sibling in the study because DSD was undisclosed in the family. Only three siblings joined the study. Therefore, the inclusion criteria for matched controls were expanded to include non-family-related individuals as control subjects. In order to serve as control the following criteria had to apply:

- Sibling or relative or best friend
- Healthy (having no DSD condition)
- In about similar age as patients (± 3 years)
- raised in the same gender
- Living in the same residential setting
- Voluntary participation in this study

Procedures

Data were collected between March 2007 until February 2011. The following procedures were applied in recruiting the participants and conducting the psychological assessment.

Patient recruitment. All patients in this study were under the care of the Sexual Adjustment Team (SAT) of Dr Kariadi Hospital and FMDU, Semarang, Indonesia. They were referred to SAT from in-patient or out-patient clinics (general practitioners, pediatricians, endocrinologists, gynecologists, urologists), and primary level of health providers. Other patients came by self-referral.

During the initial visit, the patients had a meeting with members of the SAT such as the clinical geneticist, pediatric endocrinologist, andrologist, and psychologist who are entitled to perform clinical, physical, and psychological examinations. These examinations were performed in the Dr. Kariadi Hospital. The medical diagnostic work up was performed by the geneticist in collaboration with the andrologist, endocrinologist, gynecologist, and other specialist member of the SAT. Information about the psychological study was given by the medical doctor, Achmad Zulfa Juniarto, to patients and/or parents. Subsequently, patients were invited to enroll into the medical and psychological study. After the parents and adult patients gave written consent to participate in the psychological study, the psychological assessment was conducted by a trained psychologist (AE), in the hospital or, if not feasible, at the patient's home.

Matched controls recruitment. Siblings were approached by parents or adult patients approval. Non-family matched controls were approached through local leaders (*Pak RT* or *Pak Lurah*) or midwives. In rural area, the *Pak Lurah* and midwife usually know very well the people who live in their neighborhood, so does the *Pak RT* in the urban areas. *Pak Lurah* and *Pak RT* are the leaders of the lowest level of government hierarchy. Study information was given by the researcher (AE). They were informed about this study comprised an evaluation on psychological well-being across children through adulthood initiated by the Psychology Faculty of the Diponegoro University in order to protect the patients from being identified by the matched controls subjects. Detailed information was described in chapter 4.

Psychological assessment. Subjects aged 6-17 years were interviewed separately from their parents. The original English versions of the questionnaires applied in this study were developed as paper-and-pencil measures. We came across about 15% of the patients and 20% of the parents who had received limited education or even were illiterate and many patients and parents had difficulties to fill out questionnaires due to unfamiliarity with self-reports (details on social demographic characteristics are described in chapter 3-7). In these patients and parents, we read the questions and response alternatives. The entire psychological interview took approximately 90 minutes for each patient. In case specialized help was needed for patients experiencing serious psychological problem, professional help was offered after assessment.

Instruments

See Table 1. The instruments are mainly quantitative measures, except the Social Stigmatization Scale for DSD (see Chapter 6) in which qualitative data were obtained to supplement the quantitative data. The Social Stigmatization scale for DSD is the instrument we developed for this study as no such scale was available.

Statistical Analysis

Various statistical methods have been applied in order to test for differences between patient and control groups. Detailed descriptions of applied statistical tests can be found in the chapters 3-7. Mainly quantitative methods were applied; however in the study on stigmatization (chapter 6), qualitative data were obtained as supplement to the quantitative data.

Methodological shortcomings

This study has several limitations. ***First***, concerning patient's participation. Twenty-one patients were lost to follow-up and 29 patients declined study participation. The reasons why patients moved out without notice or refused further contact with the DSD team remains unknown. One reason might be related to the geographical condition of the country. Indonesia is an archipelago, in which travelling between the island Java and other islands can be very costly. It is difficult to maintain contact and adhere to medical treatment when the patients move outside Java island. Besides the transportation and medical costs, patients often have to take day off from work which could reduce their income; these make the total costs of treatment very expensive for poor people. In view of the increasing number of newborns and toddlers suspected of DSD who were referred to our center, it is crucial to develop a structured program or treatment plan that provides the patient with life-long care.

Second, regarding sample representativeness. The majority of patients in this study came from poor families, living in the rural areas of the Central Java region, had received little to moderate education and earned a modest income. The same for the parents of children and adolescents. In order to be able to compare patient and control subjects on our psychological measures, we selected control subjects with a similar social background. We do not know to what extent findings of this study can be generalized to other patient groups in and outside Java, or to patients from other ethnicities. We have no

information regarding patients with DSD from higher socio-economic class or other ethnicities. We assume that more affluent Indonesian patients seek treatment in private clinics or visit hospitals abroad (i.e. in Singapore).

Third, we applied measures developed in Western society on non-Western participants. Several concepts we studied, i.e. concepts of femininity and masculinity are rooted in the culture. They may not have been culture-free. This raised the discussion if it was useful to translate questionnaires and semi-structured interviews and copy western methods of administration to a non-western country. From the study on psychometric properties we learned that most of the questionnaires had a scale structure in accordance with the original versions and that reliability was fair. However, methods to analyze psychometric properties of questionnaires demands participation of large groups of subjects. Methodologically it is best when this sample is representative for the entire population the measure is aimed for. Our sample contained students from different types of schools, colleges and universities in two provinces in the Central Java region. The students lived in sub-urban and urban areas. These areas have better infrastructures and living in these areas provides a larger access to all kind of social facilities such as schools, health care, better paid jobs etc. So our sample for the psychometric analysis was not fully representative for the entire Javanese population. As most of our patient and matched control groups lived in remote areas, here is a methodological shortcoming we could not overcome. Another methodologically shortcoming we could not solve is that we could apply paper and pencil or electronic versions of questionnaires to the reference groups, but had to administer questionnaires orally to our patient and matched control groups.

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Chapter 3

Body image and sexuality in Indonesian adults with disorders of sex development

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Abstract

In Indonesia, disorders of sex development (DSD) are not well-recognized and medical care for affected individuals is scarce. Consequently, many patients live with ambiguous genitalia and appearance. We compared reported outcomes on body image, sexual functioning, and sexual orientation of 39 adults with DSD (aged 18-41) and 39 healthy controls matched for gender, age, and residential status (urban, suburban, rural). Differences in gender and treatment status (treated or untreated) were also explored. On body image, adults with DSD reported dissatisfaction with sex-related body parts. Compared to the matched controls, women with DSD reported greater sexual distress; men with DSD reported lower erectile and ejaculation frequencies, more dissatisfaction with sexual life but not in sexual desire and activities. Men with DSD who had undergone genital surgery reported higher erectile and ejaculation frequencies than untreated men. More women than men in the DSD group reported a non-exclusive heterosexual orientation. DSD and infertility had a great impact on sexuality. Fear of ostracism complicated DSD acceptance. Findings were compared to those of Western studies. Based on these results, education about DSD and its psychosexual consequences may help to reduce the sexual distress and problems in adults with DSD and improve their quality of life.

Keywords: body image, sexual functioning, sexual orientation, disorders of sex development, Indonesia

Background

The management of disorders of sex development (DSD) in Indonesia faces significant barriers. In addition to the lack of diagnostic facilities, DSD conditions are also not well-recognized among the Indonesian population, including the majority of health care providers. Anomalies of the genital tract are often considered abnormal and shameful, leading to secrecy, social isolation, and stigmatization (Warne & Raza, 2008).

The most recently held consensus statements for clinical practices in DSD favor to prevent an ambiguous body appearance by giving hormonal treatment, removing gonads of individuals with 46,XY karyotype raised as females who were at risk for developing gonadal malignancies, and performing genital surgery (Joint LWPES/ESPE CAH working group, 2002; Hughes, Houk, Ahmed, Lee, & LWPES1/ESPE2 Consensus Group, 2006). Although still subject to debate (Köhler et al., 2012; Minto, Liao, Woodhouse, Ransley, & Creighton, 2003), these consensus statements also recommend early surgical correction of moderate to severely deviant genitalia. It is assumed that prevention of an ambiguous body and surgical correction will prevent social stigmatization and facilitate psychological adaptation to the assigned gender and sexual intercourse in adulthood (Carmichael & Alderson, 2004). Studies on psychosexual functioning have been initiated among patients with DSD who are living as either men or women. Impaired body image, problems in establishing romantic relationships, and difficulties with sexual functioning have been reported among patients with different diagnoses of DSD (Bouvattier, Mignot, Lefèvre, Morel, & Bougnères, 2006; Crouch, Liao, Woodhouse, Conway, & Creighton, 2008; Gastaud et al., 2007; Kojima et al., 2009; Migeon et al., 2002; Minto, Liao, Conway, & Creighton, 2003; Szarras-Czapnik, Lew-Starowicz, & Zucker, 2007; Wisniewski et al., 2000).

Before entrance, many Indonesian patients with DSD have never received medical assistance and consequently, they have been raised with ambiguous genitals and bodies for many years. In 1989, a multidisciplinary team was set up in collaboration between Dr. Kariadi Hospital and the Faculty of Medicine at Diponegoro University (FMDU), Semarang, Indonesia to provide diagnostic and medical care for these patients. The team was often confronted with psychosocial and psychosexual problems related to DSD. In collaboration with the Erasmus University Medical Center Rotterdam, a multidisciplinary study on the clinical diagnosis and treatment options for Indonesian patients with

DSD was initiated (Juniarto et al., 2012). As part of that study, we investigated body image and psychosexual functioning among Indonesian adults with DSD who became under medical attention late in life. Although genital ambiguity was often recognized at birth or body ambiguity developed in childhood or in adolescence, medical help-seeking was delayed for many years as patients, parents, and local health workers were ignorant about possibilities for medical help. So the majority of our patients never had received medical treatment for their DSD conditions before they entered our hospital in adolescence or adulthood. We therefore were able to study the course of development and its impact on the psychosexual and psychosocial aspects in whom medical treatment for the DSD were absent for most of their life.

Methods

Study design

The study was granted ethical approval by the board of the ethical commission at Faculty of Medicine, Diponegoro University (FMDU), Semarang Indonesia. This is a cross-sectional study comparing body image and psychosexual functioning between patients with DSD and their matched controls. All patients were managed clinically by the Sexual Adjustment Team of the Dr. Kariadi Hospital-FMDU.

Participants

The study sample was comprised of 39 patients, ages 18-41, diagnosed with DSD, who were living as man or woman (Table 1). Under Indonesian national law, legal gender assignment is obligatory and a third gender designation is impossible. All patients had normal intellectual functioning. Of 54 patients aged 18 or older who were diagnosed with DSD (Juniarto et al., 2012), five patients could not be contacted (due to invalid contact information) and ten patients refused to participate without giving explanation.

The matched control group consisted of 18 healthy women and 21 healthy men matched for age (with maximum age disparity of 3 years), gender, and residential settings (urban, suburban, or rural).

For the purpose of assessing psychometric properties of the measures that were utilized, a web-based survey has been set up to involve large group

of Indonesian adults. This web-based group comprised of 377 healthy adults who volunteered to respond this survey.

Instruments and Procedures

Translation and adaptation of the measures. In addition to qualitative data obtained from interviews, we evaluated the issues and concerns of participants in the areas of body image and psychosexual functioning with established measures. Since no validated Indonesian measures for psychosexual functioning were available, we therefore utilized Western measures that had been used in comparable studies on sexuality: Female Sexual Functioning Index (FSFI), Female Sexual Distress-Revised (FSDS-R), Body image scale (BIS), Male Sexual Health Questionnaire (MSHQ) (DeRogatis, Clayton, Lewis-D'Agostino, Wunderlich, & Fu, 2008; Lindgren & Pauly, 1975; Gastaud et al., 2007; Rosen et al., 2000; Rosen et al., 2004). Backward translation of these instruments into Indonesian language (Bahasa Indonesia) was conducted by a certified translator (UvA Talen). Prior to implementation, the researcher (AE) and a Dutch anthropologist specialized in research on sexuality in Indonesia and a good understanding of *Bahasa Indonesia* and English reviewed the Indonesian translations. The instruments' original scoring procedures were applied. All measures were piloted prior to the study. This pilot indicated that the questionnaires were best administered orally to clarify subjects' understanding of the questions prior to giving their response, particularly if subjects were unfamiliar with self-report questionnaires or had limited education

Table 1. Clinical characteristics and treatment history of patients with DSD

Subject	Karyotype	Diagnosis	Age (in year)		Type of treatments received
			at first visit*	at study visit	
Living as women (n=18)					
P01	46,XX	Congenital adrenal hyperplasia (CAH) [a]	11	19	Clitorodectomy at age 16 and HRT at age 16
P02	46,XX	Congenital adrenal hyperplasia (CAH) [a]	33	36	Clitoral reduction at age 34; HRT at age 36
P03	46,XX	Congenital adrenal hyperplasia (CAH) [a]	16	18	Clitoral reduction at age 7; HRT at age 8
P04	46,XY	Androgen Action Disorder (AAD) [b]	16	18	Gonadectomy at age 16; HRT at age 17
P05	46,XY	Androgen Action Disorder (AAD) [b]	12	18	None
P06	46,XY	Androgen Action Disorder (AAD) [b]	20	24	None
P07	46,XY	Androgen Action Disorder (AAD) [b]	19	19	None
P08	46,XY	Gonadal Dysgenesis (GD) [c]	13	18	Gonadectomy at age 10; HRT at age 14
P09	46,XY	Gonadal Dysgenesis (GD) [c]	39	39	None
P10	46,XY	Gonadal Dysgenesis (GD) [c]	27	27	None
P11	46,XY	Gonadal Dysgenesis (GD) [c]	23	23	None
P12	46,XY	Gonadal Dysgenesis (GD) [c]	19	19	None
P13	45,X (99%) / 46 XX,iXq	Gonadal Dysgenesis (GD) [c]	25	29	HRT at age 23; HRT (different types) at age 30
P14	46,XidicY	Gonadal Dysgenesis (GD) [c]	20	20	None
P15	46,Xi (X)(q10) (85%) / 45,X (15%)	Gonadal Dysgenesis (GD) [c]	20	20	None
P16	46,XY-(73%)/45,X(27%)	Gonadal Dysgenesis (GD) [c]	19	19	None
P17	46,X i(X)(q10) (24%) / 45,X (76%)	Gonadal Dysgenesis (GD) [c]	18	18	None
P18	46,XX	Other [d]	15	19	None

(continued)

Table 1. Clinical characteristics and treatment history of patients with DSD

(continued)

Subject	Karyotype	Diagnosis	Age (in year)		Type of treatments received
			at first visit*	at study visit	
Living as men (n=21)					
P19	46,XX	Congenital adrenal hyperplasia (CAH) [a]	17	22	None
P20	46,XX	Congenital adrenal hyperplasia (CAH) [a]	24	24	None
P21	46,XX	Gonadal Dysgenesis (GD) [c]	10	18	(received treatment at aged 7months and 7yr in other clinics; detailed information about the treatment was not available)
P22	46,XY	Androgen Action Disorder (AAD) [b] / PAIS	26	31	Gyneacomasty correction and chorda correction at age 24; hypospadia correction at age 26
P23	46,XY	Androgen Action Disorder (AAD) [b] / PAIS	16	20	Gyneacomasty reduction, chordectomy and hypospadia corrections at ages 14 and 15
P24	46,XY	Androgen Action Disorder (AAD) [b] / PAIS	12	18	Hypospadia correction at age 15
P25	46,XY	Androgen Action Disorder (AAD) [b]	23	26	Gynecomasty correction, chordectomy, hypospadia correction at age 23
P26	46,XY	Androgen Action Disorder (AAD) [b]	11	18	None
P27	46,XY	Androgen Action Disorder (AAD) [b]	27	27	None
P28	46,XY	Androgen Action Disorder (AAD) [b]	23	23	None
P29	46,XY	Gonadal Dysgenesis (GD) [c]	14	19	Gonadectomy at age 14
P30	46,XY	Gonadal Dysgenesis (GD) [c]	21	21	Chordectomy at age 11
P31	46,XY	Gonadal Dysgenesis (GD) [c]	14	21	None
P32	46,XY	Gonadal Dysgenesis (GD) [c]	41	41	None

(continued)

Table 1. *Clinical characteristics and treatment history of patients with DSD*

(continued)

Subject	Karyotype	Diagnosis	Age (in year)		Type of treatments received
			at first visit*	at study visit	
P33	46,XY	Gonadal Dysgenesis (GD) [c]	26	26	None
P34	46,XY	Unknown Under Masculinization [e]	14	19	Chordectomy at age 15; urethroplasty at age 19
P35	46,XY	Unknown Under Masculinization [e]	15	20	Hypospadia correction at age 5
P36	46,XY	Unknown Under Masculinization [e]	15	20	Penis bend (twice) and hypospadia corrections at ages 13, 15, and 16
P37	46,XY	Unknown Under Masculinization [e]	15	18	Chordectomy at age 15; urethroplasty at age 16
P38	46,XY	Unknown Under Masculinization [e]	29	29	Chordectomy at age 22 (in other clinic)
P39	46,XY	Unknown Under Masculinization [e]	17	20	None

Note. Men and women with DSD were assessed according to the gender they were living in at the time of study. HRT = hormone replacement therapy

* First time visit for medical treatment in our center (the Sexual Adjustment Team, FMDU/Dr. Kariadi Hospital).

[a] 46,XX CAH confirmed CYP 21 mutation in all patients.

[b] 46,XY DSD and under virilization. AR gene mutations had been confirmed in four men diagnosed with partial androgen insensitivity syndrome (PAIS) but not in the remaining patients. All subjects in this group had a normal hormonal testicular function with uni/bilaterally undescended testes. Androgen action is presumed not to be fully effective. Their clinical and biochemical presentation were close to those of subjects with a mutation in the androgen receptor with elevated serum levels of luteinizing hormone, testosterone, and anti-müllerian hormone, but the androgen receptor mutation could not be demonstrated.

[c] This group comprised of 10 patients with 46,XY karyotype (five men, five women), one men with 46,XX karyotype, and five women with sex chromosome abnormalities. All subjects had a normal hormonal testicular function with uni/bilaterally undescended testes. Androgen action is presumed to be fully effective. Their clinical and biochemical presentation is close to those of subjects with a mutation in the androgen receptor. Serum levels of luteinizing hormone and follicle stimulating hormone were elevated but levels of testosterone, anti-müllerian hormone, and Inhibin are low for age, and there was no diminished serum testosterone response to HCG.

[d] 46,XX DSD and cloacal malformation with genital ambiguity.

[e] 46,XY and under virilization. No cause for under masculinization could be identified. Serum hormone values and response to HCG were all normal for age.

Socio-demographic characteristics. Participants were asked about their age, gender, residential status, region of residence, religion, ethnicity, highest completed education level, marital status, and employment.

Body image. The Body Image Scale (BIS) measures the degree of (dis) satisfaction with body parts (Lindgren & Pauly, 1975). This scale consists of 30 items measuring the degree of (dis)satisfaction with different body parts, with a 5-point scale response options ranging from very satisfied (1) to very dissatisfied (5). The BIS originally consisted of three domains: primary sex characteristics, secondary sex characteristics, and so-called neutral body parts that are hormonally unresponsive e.g. eyes, hair (Lindgren & Pauly, 1975).

Female sexual distress. The Female Sexual Distress Scale-Revised (FSDS-R) measures frequency of sexual distress in women (DeRogatis et al., 2008). It consists of 13 items with a 5-point rating scale for response mode that varied from never (0), seldom (1), sometimes (2), often (3), and always (4). The Cronbach's alpha of the original FSDS-R is .86

Female sexual functioning. The Female Sexual Functioning Index (FSFI) measures sexual functioning in women who have been sexually active in the past four weeks (Rosen et al., 2000). It consists of 19 items with a 5-or-6 point response mode measuring different aspects of sexual functioning in sexually active women. Rosen et al (2000) reported that the FSFI consists of six domains of female sexual functioning: sexual desire, sexual arousal, lubrication, orgasm, satisfaction, and sexual pain. These domains demonstrated good internal reliability (Cronbach's alphas > .90 for all subscales) and good test-retest reliability (test-retest reliability scores ranged from .79 to .88). A section of the FSFI can be applied to women who have not been sexually active in the past four weeks; the number of items that can be applied is limited to sexual desire (item 1 and 2) and satisfaction of the overall sexual life (item 16) (Meyer-Bahlburg & Dolezal, 2007). The combined results of the FSFI and FSDS-R allow for the diagnosis of one or more sexual dysfunction(s) according to the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association. & American Psychiatric Association Task Force on DSM-IV, 2000). A FSFI score < 26.55 combined with a FSDS-R score > 11 implies the existence of at least one sexual dysfunction according to the DSM-IV-TR (Rosen et al., 2000).

Male sexual functioning. The Male Sexual Health Questionnaire (MSHQ) assesses male sexual functioning. It consists of 25 items with a 5 point response mode. The original English version of MSHQ has three domains of

sexual function: ejaculation, erection, and sexual satisfaction. A high degree of internal consistency and test-retest reliability of those domains were reported: Cronbach's alpha = .81, Pearson's *r* = .86 for erection; Cronbach's alpha = .90, Pearson's *r* = .87 for ejaculation; Cronbach's alpha = .90, Pearson's *r* = .88 for sexual satisfaction (Rosen et al., 2004).

Sexual orientation. The Kinsey Rating Scale on adult sexual orientation measures sexual orientation using a 7-point rating scale ranging from exclusively homosexual to exclusively heterosexual (Kinsey, Pomeroy, & Martin, 1948, 1953) in sexual attraction, sexual relationships, romantic fantasy, erotic fantasy, and self-identification. To enable a proper statistical analysis, one option of response ('no experience') was added. Subsequently, the subjects' responses were recoded into four categories: exclusively homosexual (1), exclusively heterosexual (2), nonexclusive orientation (3), and no experience (4) (Zucker et al., 1996). We presented subjects' response on each item. The concepts of heterosexuality and homosexuality were used in this study in accordance with the presented gender, not the chromosomal sex. In Indonesia, the term "homosexuality" is unfamiliar and often misunderstood or perceived negatively by the general population. Therefore, we applied the terms of 'man-to-man' or 'woman-to-woman' or 'same sex' to refer to homosexuality or homosexual. The interviewer began assessing subjects' experiences on their first love, dating, and sexual activities with the opposite gender, then probing to possibility of having similar experiences (imagery or behavior) with person of the same sex.

Procedures. Data were collected between March 2007 and May 2011. Following diagnostic procedures confirming the diagnosis of DSD (Juniarto et al., 2012), patients were invited to participate. Verbal and written study information was provided by a physician (AZJ). After the patient agreed to participate and had given written consent, an appointment for a psychological assessment was made. This assessment was performed at the hospital in all cases, except one in which the patient asked to have the assessment at home. The psychological assessment was conducted by a clinical psychologist (AE) who had been trained to deliver the applied measures and to conduct interviews with patients with DSD. A small gift or reimbursement of transportation and a meal were provided for their participation. Men and women with DSD were interviewed according to the gender they lived in at the time of study.

Initially, the study design aimed to include siblings as matched controls

but this was unfeasible in terms of the demographic matching and secrecy of the DSD condition within the family. The researcher (AE) subsequently recruited healthy participants who matched those with DSD in terms of residential status, gender, age (matching factors). The researcher informed the matched control subjects about the study but only said that they were asked to participate in a study on psychosexual development in adults carried out by the Psychology Faculty of the Diponegoro University in Semarang, in order to protect the patients from being identified as patients with DSD by their matched controls. After they received study information, the healthy control subjects were invited to join the study. After giving written consent, matched control subjects followed procedures similar to the patient group. A small gift was provided for their participation. All matched control subjects requested that the assessments to be conducted at home.

Regarding the web-based survey that was setup to assess psychometric properties of the instruments that were utilized, we sent an email invitation to several mailing lists for Indonesian adults. The recipient was encouraged to forward the email invitation to other adults in their contacts. The study aim, principal investigator and affiliation, time estimated for completion of the measures and confidentiality assurance were provided on the welcome page prior to participation. The survey was conducted within a period of four weeks. Socio-demographic data, such as occupation and educational level, showed that the web-based control group differed substantially from the patient and matched control groups with respect to socioeconomic status and education; the web-based control subjects came from well to do families (university graduates and have well-paid jobs) whereas most patient and matched control subjects came from poor families. This socio-demographic differences affected results. Data from the web-based controls were not presented for the targeted comparisons but were used to validate the measures only.

Statistical analysis

Construct validity was explored using principal component analysis (PCA) with varimax rotation and Kaizer normalization. Instrument reliability was evaluated as internal consistency with Cronbach's Alpha as the outcome measure. We report the optimal model for the Indonesian data, even when that model deviates from the original Western model. Only responses without missing data were used in the statistical analyses. Differences in continuous data

between groups were compared using the Mann-Whitney *U* test. Differences in categorical data were compared using the Fisher's Exact test. Differences were considered significant at $p < .05$ (two-sided). Because of the small number of patients (Table 1), comparison among diagnostic subgroups was impossible.

Results

Participants

Table 2 shows participant's socio-demographic characteristics. The matched control and patient groups were not significantly different, except in marital status. There were no significant differences between treated and untreated patients. However, untreated patients tended to be older than treated patients when they first visited our hospital.

Table 2. *Sociodemographic characteristics of study participants*

Sociodemographic characteristics	Adults with DSD (*n*=39)	Matched Controls (*n*=39)	*p*[a]	Treated patients (*n*=18)	Untreated patients (*n*=21)	*p*[b]
Age of visit (in year)	*M* ± SD	*M* ± SD		*M* ± SD	*M* ± SD	
at first admission	19.9 ± 7.3	-	.09	18.0 ± 6.6	21.5 ± 7.6	.09
at study visit	22.6 ± 5.9	23.3 ± 4.7		22.0 ± 5.5	23.1 ± 6.3	.31
	n (%)	*n* (%)		*n* (%)	*n* (%)	
Gender						
Male	21 (53.8)	21 (53.8)	.99	12 (66.7)	9 (42.9)	.20
Female	18 (46.2)	18 (46.2)		6 (33.3)	12 (57.1)	
Residential settings						
Rural	18 (46.2)	18 (46.2)	.99	7 (38.9)	11 (52.4)	.54
Suburban	13 (33.3)	13 (33.3)		6 (33.3)	7 (33.3)	
Urban	8 (20.5)	8 (20.5)		5 (27.8)	3 (14.3)	
Residence/province						
Central Java	32 (82.1)	37 (94.9)	.23	14 (77.8)	18 (85.7)	.47
Other provinces in Java	4 (10.3)	1 (2.6)		3 (16.7)	1 (4.8)	
Outside Java island	3 (7.7)	1 (2.6)		1 (5.6)	2 (9.5)	
Ethnicity						
Javanese	35 (89.7)	38 (97.4)	.36	15 (83.3)	20 (95.2)	.32
Non Javanese	4 (10.3)	1 (2.6)		3 (16.7)	1 (4.8)	
Religion						
Islam	38 (97.4)	32 (82.1)	.05	18 (100.0)	20 (95.2)	.99
Other	1 (2.6)	7 (17.9)		0	1 (4.8)	
Marital status						
Men						
Married	3 (14.3)	21 (100)	<.001	2 (16.7)	1 (11.1)	.99
Never married	18 (85.7)	0		10 (83.3)	8 (88.9)	
Women						
Married	1 (5.6)	18 (100)	<.001	1 (16.7)	0	.33
Never married	17 (94.4)	0		5 (83.3)	12 (100)	
Highest Educational level*						
Men						
Illiterate	2 (9.5)	1 (4.8)	.55	0	2 (22.2)	.08
Elementary school	2 (9.5)	2 (9.5)		2 (16.7)	0	
High school	16 (76.2)	14 (66.7)		10 (83.3)	6 (66.7)	
Higher education	1 (4.8)	4 (19.0)		0	1 (11.1)	
Women						
Illiterate	2 (11.1)	0	.52	1 (16.7)	1 (8.3)	.71
Elementary school	1 (5.6)	0		0	1 (8.3)	
High school	12 (66.7)	14 (77.8)		5 (83.3)	7 (58.3)	
Higher education	3 (16.7)	4 (22.2)		0	3 (25.0)	
Occupation						
Men						
Unemployed	8 (38.1)	1 (4.8)	.06	5 (41.7)	3 (33.3)	.92
Labor	7 (33.3)	9 (42.9)		3 (25.0)	4 (44.4)	
Self-employed	3 (14.3)	4 (19.0)		2 (16.7)	1 (11.1)	
Staff	3 (14.3)	7 (33.3)		2 (16.7)	1 (11.1)	
Women						
Unemployed	5 (27.8)	10 (55.6)	.14	3 (50.0)	7 (58.3)	.54
Labor	1 (5.6)	1 (5.6)		1 (16.7)	0	
Self-employed	4 (22.2)	0		0	0	
Staff	8 (44.4)	7 (38.9)		2 (33.3)	5 (41.7)	

[a] Patients and the matched controls comparison. [b] Treated and untreated patients's comparison.

Reliability and validity of the measures

As mentioned in the method section, the validity and reliability of measures applied in this study were obtained using data of the web controls. The results of reliability and validity analyses are presented in Table 3.

The Indonesian versions of the instruments had good psychometric properties and the components generated from these analyses were relevant to the constructs assessed in the original measures. The BIS comprises one component similar to the original version; the FSDS-R comprises one component similar to the original model but also facilitates a 2-component model to assess cognitive and affective components of sexual distress. In the FSFI, items measuring frequency and difficulties in lubrication and orgasm are loaded separately. Similarly, in the MSHQ, items measuring frequency and difficulties in erection and ejaculation functioning are loaded separately. A few minor differences with the original versions are addressed in Table 3.

Body image

In general view on the body (Table 4a), men with DSD did not differ significantly from the matched control men whereas in women, there was a tendency towards significance that women with DSD reported greater dissatisfaction with their body than the matched control women.

Table 4a. Body Image Scale: Global score of body image across groups

Subjects	Adults with DSD	Matched controls	p^a	Treated patients	Untreated patients	p^b
Women	$n = 18$ 3 (2-3)	$n = 18$ 2 (1-3)	.06	$n = 6$ 2.5 (2-3)	$n = 12$ 3 (2-3)	.99
Men	$n = 21$ 2 (1-3)	$n = 21$ 3 (1-3)	.59	$n = 12$ 3 (1-3)	$n = 9$ 2 (1-3)	.29

Note. Data were presented in median and range. A higher value indicates greater dissatisfaction with the body parts. The Mann-Whitney U-test was applied. Men and women with DSD were assessed according to the gender they were living in at the time of study. Adopted from the Body Image Scale (BIS) from Lindgren, T. W., & Pauly, I. B. (1975). A body image scale for evaluating transsexuals. *Archives of Sexual Behavior, 4*(6), 639-656. doi:10.1007/bf01544272. A five-point response mode was applied: very satisfied (1), satisfied (2), neutral (3), dissatisfied (4), and very dissatisfied (5).

[a] Comparison between the patients and the matched control groups

[b] Comparison between treated and untreated group of patients.

Table 3. Results of principal component analysis (PCA) and reliability analysis

Measures	N	N of components (% of total variance explained)	Components and item distributions	Cronbach's alpha (α)
Body Image Scale (BIS) Woman version [a]	161	1 PC (53.4)	General body image (all items) Sex-related body parts: items 6,9,14,22,24	.97 .86
Man version [a]	82	1 PC (66.7)	General body image (all items) Sex-related body parts: items 6,9,14,18,22,27	.98 .93
Female Sexual Distress Scale-Revised / FSDS-R [b]	185	2 PC (55.1)	Affective sexual distress (items 1,2,3,4,5,11,12) Cognitive sexual distress (items 6,7,8,9,10,13) Overall sexual distress (all items)	.91 .85 .93
Female Sexual Functioning Index / FSFI [c]	94	6 PC (66.7)	Sexual desire (items 1,2) Arousal/lubrication frequency (items 3,4,5,6,7,9) Difficulty in lubrication & orgasm (items 8,10,12) Orgasm frequency & pleasure (items 11,13) Satisfaction with sexual life (items 14,15,16) Pain (items 17,18,19)	.79 .81 .90 .69 .91 .89
Male Sexual Health Questionnaire / MSHQ [d]	41	4 PC (53.8)	Erection & ejaculation frequency (items 1,2,3,5,6,7,11,21) Erection & ejaculation dysfunction (items 4, 8,9,10,12,20,24) Satisfaction with sexual life (items 13-18) Sexual desire & activity (19,22,23,25)	.77 .58 .89 .61
Kinsey Rating Scale of Adult Sexual Orientation [e]	210 (142 women; 68 men)	1 PC (96.6)	All items	.99

Note. [a] BIS was originally developed for assessing body image in transgender persons. Three domains of sexual characteristics were measured in the original scale: primary, secondary, and neutral (hormonally unresponsive). The test-retest reliability of the original BIS showed good consistency (Lindgren & Pauly, 1975). Our findings correspond to one component of general body image. As DSD conditions might impact in body image, in this study we included primary sexual characteristics for further comparison analysis after evaluated the internal consistency.

[b] Originally FSDS-R consists of one component measuring overall sexual distress using total score. The Cronbach's alpha of the original scale is .86 (DeRogatis et al., 2008). Our findings demonstrated two components of sexual distress: cognitive and affective components of sexual distress. In this study, we included overall sexual distress for further comparison analysis after evaluating the internal consistency.

[c] The Cronbach's alphas of the original FSFI scales are: Desire scale: α = .92; Arousal scale: .95; Lubrication

scale: α = .96; Orgasm scale: α = .96; sexual satisfaction scale: α = .89; Pain scale: α = .94 (Rosen et al., 2000). In our study, items measuring frequency and difficulties in lubrication and orgasm were loading into two different components. Due to lack of sexual activity and absence of a partner during the past four weeks, we applied items of sexual desire (items 1 and 2) and of satisfaction with overall sexual life (items 16) for further analysis.
[d] The Cronbach's alphas of the original MSHQ scales are: erection scale: α = .81; ejaculation scale: α = .90; sexual satisfaction scale: α = .90 (Rosen et al., 2004). In our study, items measuring frequency and difficulties in erection and ejaculation functioning were loading into two different components.
[e] Statistical analysis using sum score was inapplicable because the majority of patients reported lack of sexual experiences. Subsequently, comparison analysis was performed on each item.

However, as demonstrated in Table 4b, patients with DSD generally experienced greater dissatisfaction with their genitalia and other sex- related body parts than controls. Significant differences were reported, particularly on ovaries/uterus, breasts, vagina (in women); penis, scrotum, testes (in men). There were no differences between treated and untreated men and women (Tables 4a and 4b). Almost all patients had ambiguous genitalia, and ambiguous sex-related body parts such as underdeveloped breasts, low-pitched voice in women, and sparse facial hair in men.

Table 4b. Body Image Scale: dissatisfaction and satisfaction with sex-related body parts

Sex-related body parts	Dissatisfaction		Satisfaction		*p*
	Adults with DSD	Match controls	Adults with DSD	Match controls	
Women	*n* = 18	*n* = 18	*n* = 18	*n* = 18	
Ovaries/uterus	7 (38.9)	0	4 (22.2)	16 (88.9)	<.001
Breasts	6 (33.4)	0	6 (33.3)	14 (77.8)	.02
Voice	4 (22.3)	0	9 (50.0)	13 (72.2)	.37
Vagina	4 (22.2)	0	7 (38.9)	15 (83.4)	.05
Clitoris	2 (11.1)	0	7 (38.9)	13 (72.2)	.11
Men	*n* = 21	*n* = 21	*n* = 21	*n* = 21	
Penis	17 (81.0)	0	1 (4.8)	14 (66.7)	<.001
Scrotum	12 (57.2)	0	6 (28.6)	10 (47.6)	<.001
Testes	10 (47.6)	0	5 (23.8)	10 (47.6)	.004
Facial hair	4 (19.0)	2 (9.5)	8 (38.1)	6 (28.6)	.62
Body hair	3 (14.3)	1 (4.8)	10 (47.6)	8 (28.1)	.40
Breasts	4 (19.1)	0	10 (47.6)	10 (47.6)	.30

Notes. Data were presented as *n* (%). Dissatisfaction responses comprised "dissatisfied" and "very dissatisfied" responses on the Body Image Scale (BIS) whereas satisfaction responses comprised "satisfied" and "very satisfied" responses on BIS. The Fisher's Exact test was applied.

Sexual functioning

Table 5 summarizes the findings on sexual functioning across groups.

Female sexual functioning (FSFI). In line with marital status (Table 2), only one woman with a DSD reported she had been sexually active in the

last four weeks whereas all matched control women reported they had been sexually active during that period. Women with DSD reported no differences from the matched control women in terms of sexual desire. They reported less satisfaction with their overall sexual life than control women. In response to the item measuring satisfaction with the overall sexual life, only two (11.1%) women with DSD reported satisfaction with their sexual life compared to 88.9% of matched-control women. Treated and untreated women with DSD did not differ in sexual desire or satisfaction with sexual life.

Female sexual distress (FSDS-R). Women with DSD reported greater affective and cognitive sexual distress than the matched control women; 72% of women with DSD reported a sexual distress (score above the cut-off point of 11), whereas among matched control women this percentages was 11% ($p < .001$). No differences in sexual distress were found between treated and untreated women with DSD although the median values of FSDS-R are above the cut-off score (Table 5).

Male sexual functioning (MSHQ). Men with DSD reported lower frequencies of erections and ejaculations or less satisfaction with sexual life than control men, but they did not report better functioning in erections and ejaculations or lower sexual desire or less sexual activities (Table 5). Men with DSD who had received treatment reported higher frequencies of erections and ejaculations than untreated men with DSD; however, they did not report better functioning in erections and ejaculations, or greater satisfaction with sexual life, or higher sexual desire or more sexual activities than untreated men with DSD. Two out of four married men with DSD reported an inability to penetrate. This made them feel less capable of satisfying their wives.

Table 5. Sexual functioning across groups (data on FSFI, FSDS-R, and MSHQ)

Measures	Adults with DSD	Matched controls	p^e	Treated patients	Untreated patients	p^f
	Mdn (min-max)	*Mdn* (min-max)		*Mdn* (min-max)	*Mdn* (min-max)	
FSFI [a]	*n* = 18	*n* = 18		*n* = 6	*n* = 12	
Sexual Desire (sum of items 1 & 2)	4 (2-8)	5.5 (3-8)	.13	4 (2-8)	4 (2-8)	.79
Satisfaction with sexual life (item 16)	0 (0-5)	5 (2-5)	**<.001**	0 (0-5)	0 (0-0)	.09
FSDS-R [b]						
Overall sexual distress	19.5 (0-49)	2 (0-21)	**<.001**	15.5 (0-30)	20 (0-49)	.42
Affective sexual distress [c]	12.9 (0-30.4)	0 (0-15.2)	**<.001**	10.5 (0-15.2)	12.9 (0-30.4)	.39
Cognitive sexual distress	8 (0-24)	1 (0-8)	**<.001**	9 (0-17)	8 (0-24)	.73
MSHQ [d]	*n* = 21	*n* = 21		*n* = 12	*n* = 9	
Erection and ejaculation frequency [a]	32 (13-40)	37 (26-40)	**.03**	36.5 (18-40)	31 (13-38)	.05
Erection and ejaculation dysfunction [d]	27 (15-31)	29 (24-31)	.33	27 (15-31)	27 (15-31)	.51
Satisfaction with sexual life [a]	18 (13-27)	24 (17-30)	**<.001**	18 (13-27)	18 (14-24)	.85
Sexual desire and activity [a]	11 (9-20)	13 (8-17)	.54	11 (9-15)	12 (9-20)	.92

Note. Men and women with DSD were assessed according to the gender they were living in at the time of study. FSFI = Female Sexual Functioning Index; FSDS-R = Female Sexual Distress Scale-Revised; MSHQ = Male Sexual Health Questionnaire.

[a] It consists of 19 items with five or six point response mode. Score range: 0-5 or 1-5. A higher value indicates better sexual functioning.

[b] It consists of 13 items with a five point response mode: never (0), seldom (1), sometimes (2), often (3), and always (4). A higher value indicates greater sexual distress.

[c] Sum scores multiplied by 1.17 for equal comparison to cognitive-related distress.

[d] It consists of 25 items with a five and six point response mode. Score range: 0-5 or 1-5. A higher value indicates better sexual functioning, except in the Erection and ejaculation dysfunction that a higher value indicates a higher degree of (sexual) dysfunction.

[e] Comparison between the study group and the matched control group.

[f] Comparison between the treated and the untreated groups of patients with DSD.

Sexual relationships. Sixteen women and 20 men with DSD reported they had been "in love". For this subgroup, 14 women (77.7%) and seven men (35%) had never had romantic relationships (Table 6). During the interviews with patients, it appeared that fear of rejection by a partner due to infertility was the major reason they did not pursue romantic relationships. Women with DSD also appeared to be emotionally sensitive and preferred to delay or refuse to engage in a romantic relationship to avoid partner's rejection. One woman and three men with DSD had preferred to end their dating relationships without disclosing their infertility. Three married men with DSD noted the importance of family support in helping them live with DSD and disclose infertility to their spouses. Interestingly, their spouses verbalized acceptance of their DSD condition. Another man with DSD changed his stated intention to marry a single woman and instead, married a widow with children from her previous marriage. This helped him to reduce his anxiety that he would not be able to satisfy his spouse because of his inability to penetrate and to make her pregnant. A married woman with DSD, who received emotional support from parents and siblings, finally disclosed her infertility to her husband. The result was divorce, after she declined his request for polygamy.

Sexual orientation

Table 6 shows that more patients than controls had no sexual experiences. Nine patients (23.1%) reported they had never had romantic/erotic fantasies and 21 patients (53.8%) never engaged in sexual relations because they considered it sinful or taboo. Generally, more women with DSD reported non-exclusive or exclusive homosexual orientation than matched control women with respect to falling in love and sexual relationships. In contrast, men with DSD were similar to the matched control men with respect to their sexual orientation, favoring an exclusively heterosexual focus.

Table 6. Response distribution on the Kinsey Rating Scale of sexual orientation

Items and response categories	Adults with DSD	Matched controls	p^a	Treated patients	Untreated patients	p^b
Living as women	*n = 18*	*n = 18*		*n = 6*	*n = 12*	
1. Falling in love	*n* (%)	*n* (%)		*n* (%)	*n* (%)	
Exclusively homosexual	2 (11.1)	0	.04	0	2 (16.7)	.85
Exclusively heterosexual	13 (72.2)	18 (100.0)		5 (83.3)	8 (66.7)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	2 (11.1)	0		1 (16.7)	1 (8.3)	
2. Sexual relationships						
Exclusively homosexual	1 (5.6)	0	<.001	0	1 (8.3)	.99
Exclusively heterosexual	3 (16.7)	15 (83.3)		1 (16.7)	2 (16.7)	
Non-exclusive orientation	0	0		0	0	
No experience	14 (77.8)	3 (16.7)		5 (83.3)	9 (75.0)	
3. Romantic fantasy						
Exclusively homosexual	2 (11.1)	0	.17	0	2 (16.7)	.64
Exclusively heterosexual	11 (61.1)	16 (88.9)		5 (83.3)	6 (50.0)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	4 (22.2)	2 (11.1)		1 (16.7)	3 (25.0)	
4. Erotic fantasy						
Exclusively homosexual	2 (11.1)	0	.11	0	2 (16.70	.87
Exclusively heterosexual	10 (55.6)	16 (88.9)		4 (66.7)	6 (50.0)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	5 (27.8)	2 (11.1)		2 (33.3)	3 (25.0)	
5. Self-identification						
Exclusively homosexual	0	0	.49	0	0	.99
Exclusively heterosexual	16 (88.9)	18 (100.0)		6 (100)	10 (83.3)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	1 (5.6)	0		0	1 (8.3)	
Living as men	*n = 21*	*n = 21*		*n=12*	*n=9*	
1. Falling in love						
Exclusively homosexual	0	0	.11	0	0	.99
Exclusively heterosexual	20 (95.2)	17 (81.0)		11 (91.7)	9 (100.0)	
Non-exclusive orientation	0	4 (19.0)		0	0	
No experience	1 (4.8)	0		1 (8.3)	0	
2. Sexual relationships						
Exclusively homosexual	0	0	.28	0	0	.99
Exclusively heterosexual	14 (66.7)	17 (81.0)		8 (66.7)	6 (66.7)	
Non-exclusive orientation	0	1 (4.8)		0	0	
No experience	7 (33.3)	3 (14.3)		4 (33.3)	3 (33.3)	
3. Romantic fantasy						
Exclusively homosexual	0	0	.23	0	0	.99
Exclusively heterosexual	21 (100.0)	18 (85.7)		12 (100.0)	9 (100.0)	
Non-exclusive orientation	0	1 (4.8)		0	0	
No experience	0	2 (9.5)		0	0	

(continued)

Table 6. Response distribution on the Kinsey Rating Scale of sexual orientation
(continued)

Items and response categories	Adults with DSD	Matched controls	p^a	Treated patients	Untreated patients	p^b
Living as men	*n = 21*	*n = 21*		*n=12*	*n=9*	
4. Erotic fantasy						
Exclusively homosexual	0	0	.99	0	0	.99
Exclusively heterosexual	20 (95.2)	20 (95.2)		11 (91.7)	9 (100.0)	
Non-exclusive orientation	0	0		0	0	
No experience	1 (4.8)	1 (4.8)		1 (8.3)	0	
5. Self-identification						
Exclusively homosexual	0	0	.99	0	0	.17
Exclusively heterosexual	19 (90.5)	20 (95.2)		12 (100.0)	7 (77.8)	
Non-exclusive orientation	2 (9.5)	1 (4.8)		0	2 (22.2)	
No experience	0	0		0	0	

Note. Men and women with DSD were assessed according to the gender they were living in at the time of study. Initially, a seven-point scale of response mode was applied, range from exclusively homosexual to exclusively heterosexual. However, sum scores could not be obtained due to participant's lack of sexual experiences. To enable a proper statistical analysis, the participant responses were categorized into four groups: exclusively homosexual, exclusively heterosexual, non-exclusive orientation, and no experience.

[a] Comparison between the patient and the matched control groups.

[b] Comparison between the treated and the untreated groups of patients with DSD. The Fisher's Exact test was applied.

All four patients with 46,XX karyotype and CAH reported exclusively heterosexual orientations: two patients with 46,XX karyotype and CAH, living as men reported they only felt sexually attracted to women whereas two patients with 46,XX karyotype and CAH living as women reported they only felt sexually attracted to men. Non-exclusive heterosexual orientation was reported by six out of 14 untreated patients with the 46,XY karyotype, living as men or women. Among these patients, one man with an androgen action disorder and one man with gonadal dysgenesis identified themselves as non-exclusive heterosexual focus, but did not report any non-exclusive heterosexual fantasies or behaviors. Both men concluded that their sexual identification could not be exclusively heterosexual because of their DSD condition. Four out of nine women with 46,XY karyotype (two women with androgen action disorder, two women with gonadal dysgenesis) reported varying degrees of non-exclusively heterosexual fantasies or behaviors, but identified themselves as exclusively heterosexual.

Discussion

We studied psychosexual functioning among Indonesian adults with DSD who had been identified and treated late in life. These patients had been raised with and continued to live with ambiguous bodies and encountered barriers to seek a spouse and marry; in Indonesia a major step forward into being respected as an adult and acquire full independency, particularly for women. Concerns about these psychosocial issues of gender and sexuality presented to the health care professionals on the Sexual Adjustment Team at the Dr Kariadi Hospital/Faculty of Medicine, Diponegoro University gave rise to the study. Our major aim was to quantify these psychosexual problems in patients with DSD and compare them to healthy subjects. To our knowledge, this is the first such study performed in Indonesia.

Body image, sexual distress, and sexual functioning

Results on body image revealed that patients with DSD, untreated or treated late in life, were dissatisfied with their sex-related body parts, but not with their bodies in general. These results suggest that body ambiguity causes considerable distress in adults affected with DSD. Early diagnosis and treatment may decrease body ambiguity during puberty and hence, prevent these psychosocial consequences and may improve quality of life. As stated in the Consensus statement (Hughes et al., 2006), treatment of DSD comprises the entire diagnostic process, education on parents about diagnosis and treatment possibilities, surgically and hormonally, and facilitating parents and/or adult patients to make decisions with respect to treatment/no treatment they consider will be best for their child. Educating health care practitioners and raising public awareness of DSD as a medical condition are essential for improving the social functioning and quality of life of patients with DSD.

Most women with DSD had never been involved in romantic relationships. They also reported greater sexual distress, less sexual experiences, and felt less satisfied with their sexual life than control women. Low libido and lack of initiatives to seek a partner despite social expectancy to do so, and fear of social consequences due to infertility probably lowered their satisfaction with sexual life. The qualitative interviews indicated that body ambiguity induced negative thoughts and feelings about themselves in women with DSD. Studies in Western women with DSD also observed problems in sexual

desire, sexual arousal, and entering partner relationships (Gastaud et al., 2008; Köhler et al., 2012).

Treated and untreated women with DSD reported sexual distress. The interview data suggested that their DSD conditions and related infertility were related to this sexual distress. Fear of disclosure and possible negative consequences of disclosure on their social position (divorce or polygamy) prevented these women from entering romantic relationships. One significant consequence of this was a failure to meet the social expectation of marriage, which caused substantial distress. Western studies on psychosexual functioning in women with DSD have also reported low desire and lack of sexual experiences among other problems in sexual functioning (Gastaud et al., 2007; Minto et al., 2003; Szarras-Czapnik et al., 2007). These women also felt reluctant to enter sexual relationships because of the need for disclosure of their DSD condition and uncertainty about the partner response—which could include outright rejection. In contrast, Western societies are less collectively driven than the Indonesian society is, and thus, there is less pressure to marry and have children.

Previous studies reported increased erectile functioning and ejaculations among men with DSD who had received treatment i.e. hypospadia corrections (Bouvattier et al., 2006; Kojima et al., 2009; Migeon et al., 2002). In our study, men with DSD who had received hypospadia corrections reported better erectile functioning and more ejaculations than untreated men. As we had no data on genital and sexual functioning before surgery, we had to rely on patients' self-reports. In comparison to their matched controls, men with DSD reported lower frequencies of erection and ejaculation but this did not influence their sexual desire and activities.

Sexual relationships

In Indonesia, intimate relationships are only legalized within marriage; premarital sex is socially unacceptable and regarded as sinful from a religious perspective. Although, premarital sex does occur as suggested from our web-based study, very limited or no sexual experience was reported by patients with DSD. These findings differ from prior studies reporting marital and premarital sexual experiences in men and women with DSD (Gastaud et al., 2007; Kojima et al., 2009), indicating that culture plays a significant role in sexual behavior in individuals with DSD.

Our study group included more men than women in established, romantic relationships. There are two explanations for this. First, men and women may use different strategies to cope with DSD. Women with DSD appear to be more emotionally sensitive and tended to avoid the risks of social rejection by delaying or not engaging in romantic relationships. Men with DSD also experienced distress but were more willing to enter into these types of relationships. Second, women are more subject to blame in terms of infertility rather than men. Pregnancy undoubtedly indicates female fertility; however, the absence of pregnancy was more often regarded as the impact of female infertility rather than male infertility. As procreation is a major reason for marriage among Indonesians, in the case of infertility, particularly among Moslem, men has more options than women: to divorce and marry another woman, or go for polygamy. No one will blame the infertile man because he obeys the social demand to procreate and he is allowed to do so by his religious values. He might receive sympathy for being unfortunate not to have children after several marriages. His infertility remains undisclosed unless he intends to reveal it through fertility tests. Infertility due to DSD makes life much harder for adults. The fear of rejection led to unwillingness to disclose DSD and related infertility, even within the family. As a consequence, patients dealt with their sadness alone and their lack of initiatives to seek a partner was often not understood, even by their own relatives who pressured them to get married and have children. Facilitating disclosure, family support, and more realistic expectations may reduce this sense of isolation, psychological distress, and level of acceptance for both patient and family. Four men in this study reported this type of family support, however, few women in the study experienced this and one woman was faced with divorce when she disclosed her DSD. This may explain why men with DSD in this study were more willing to take initiatives to seek romantic partners than did the women with DSD.

Sexual orientation

Two out of 20 men with DSD identified themselves as non-exclusively heterosexual. They thought having a DSD was abnormal, and therefore, their sexual orientation should not be similar to people without a DSD. Non-exclusive heterosexual orientation was higher among women with DSD than among the matched controls. Similar findings have been reported in Western studies of women with 46,XX karyotype and CAH and patients with 46, XY karyotype and partial action of and sensitivity for androgens, stressing the importance of prenatal action of androgens (Köhler et al., 2012; Meyer-Bahlburg, Dolezal, Baker, & New, 2008; Nordenstrom et al., 2010). Women with DSD who reported various degrees of non-exclusively heterosexual orientation in fantasy or behavior did not identify themselves as non-exclusive heterosexually-oriented possibly to conform to socially acceptable norms and attitudes. This indicates that social influences are important in reporting sexual orientation among patients with DSD living in a collectively-driven society. Unfortunately, lack of published data disallows any comparison of our findings on sexual orientation to similar studies in Asian patients with DSD or data on homosexuality or bisexuality among the Indonesian population.

Treated and untreated groups comparison

Comparison between treated and untreated groups of patients did not reveal any differences in reported (dis)satisfaction with their body parts, sexual distress, and main aspects of sexual functioning.

Despite early detection of the ambiguous genital, for all patients (except five patients) medical help was delayed for many years as patients, parents and medical helpers were not aware that medical treatment was available, Both treated and untreated groups of patients entered our medical service in adolescence or adulthood. Prior to entering our medical service, six patients had received some medical help but proper diagnostic procedures and sufficient education on DSD had stayed out. From studies on hypospadias repair, we know there is an optimal time window for treatment; corrections performed in early childhood gives better urinary and sexual functioning than surgery performed after transition into adolescence (Woodhouse & Christie, 2005). The absence of differences between treated and untreated patients found in this study may be related to the fact that treatment had started lately. We assume that psychosexual problems such as dissatisfaction or shame for

an ambiguous genital may gradually develop prior to adolescence but may intensify in puberty when the body will develop into an ambiguity, visible for everybody and making the affected persons vulnerable for stigmatization. Since we could not test the impact of early treatment in childhood on psychosexual development among our patients, we have not able to assess effects of early treatment on sexual functioning and quality of life yet, but we hope we will be able to study this in the future.

Study limitations

Prior to the study, locally validated instruments were unavailable. We performed an exploratory study first by utilizing Indonesian translations of existing instruments developed in Western countries. We were well aware that application of Western measures could lead to different types of methodological problems and we found solutions to these problems so that we could reach our goal to gain insight in psychosexual problems in late treated Indonesian patients with DSD. First, we carried out a pilot study to found out the applicability of the measures. We then found out that it would be better to apply questionnaires orally to avoid misunderstandings by illiteracy or unfamiliarity with *Bahasa Indonesia*. Second, we compared data of patients with those of matched controls, and finally we applied a web based survey in a large group of healthy Indonesians to carry out reliability analyses and scale construction in the Indonesian population. Our analysis showed that the Indonesian translations had many similarities with the original measures and also had good psychometric properties. Therefore, we assumed that it was valid to apply the questionnaires in our study. However, it is true that the web-based participants differed from the patient and matched control groups by their socio-economic status; these group differences may limit the applicability of the validity and reliability measures to the experimental subjects.

Another limitation is that this study included different DSD diagnoses with a small number of patients in each diagnostic group. This hampered us to perform a more detailed comparison between patients with 46,XX karyotype and CAH or 46,XY karyotype and AIS or gonadal dysgenesis that had been raised in different gender. DSD is an umbrella term for many different anomalies in sexual development that covers a large variety in the underlying biological mechanisms leading to specific types of DSD. Part of the psychological distress is probably related to specific underlying biological mechanism of each

specific type of DSD so that in studies with small groups of patients only those psychological problems will appear that are most significant and are shared by patients in all diagnostic groups.

Our patients never had received or only had received little medical attention before they entered our hospital. We therefore were able to explore psychosocial and psychosexual problems faced by patients with DSD in whom the bodies and minds had developed without or with limited influences of medical treatment for DSD in most of their life. In the past 20 years, it has become clear that many patients with DSD experience psychosocial and psychosexual problems that need to be attended. Often early medical treatment has been pointed out as source of these psychosexual problems, and some activists groups ask for delay of all childhood treatments not necessarily needed for survival. Our findings demonstrate that psychosexual problems are also present in patients who did not receive treatment and that there are many similarities with the psychosexual and psychosocial problems faced by Indonesian untreated patients and Western treated patients. These similarities in experienced psychosexual and psychosocial problems indicate that the problems are related to DSD itself rather than initiated by early medical treatment. We think that the psychosocial problems of which Indonesian patients have to deal with are large, due to lack of understanding about DSD, particularly in the community, that complicated patients' ability to cope with body ambiguity. Improvement can be reached by early diagnosis followed by comprehensive education to the parents on the diagnosis and treatment possibilities, both hormonal and surgical, so that the patients and/or parents will be able to make informed choices that they consider will be best for their child (Warne & Raza, 2008). The child's wishes need to be taken into account as soon as the child is able to become involved in medical decision making. Medical treatment of DSD is complex and only should be performed by experienced, specialized, multidisciplinary teams.

Conclusion

Having a DSD condition, being infertile and fearing rejection caused significant distress, particularly among women. A non-exclusively heterosexual orientation in sexual attraction was more likely reported among adults with DSD than their matched controls. Late-treated patients experienced similar

problems to untreated patients. Health practitioners should be aware of the social implications of reduced infertility and sexual functioning among adults with DSD. Genetic counseling, patient education, and psychological counseling may provide support for patients and caregivers to discuss sexual problems, strategies for coping with the conditions, ultimately facilitating greater acceptance. We recommend that primary health care providers identify patients with DSD early in life and refer them to a specialized multidisciplinary team, so adequate intervention can be provided.

As the majority of our patients never had received medical attention before they entered our hospital, we had been able to study the course of development without medical treatment for the DSD and its impact on the psychosexual and psychosocial aspects of persons with DSD. By studying psychosexual functioning in untreated or late treated patients we have been able to explore the problems faced by patients with DSD in whom the bodies and minds had developed without or with limited medical intervention for their DSD for most of their life.

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Chapter 4

Gender development in Indonesian children, adolescents, and adults with disorders of sex development

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Chapter 5

Emotional and behavioral problems in Indonesian children, adolescents, and adults with disorders of sex development

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Chapter 6

Social stigmatization in Indonesian patients with disorders of sex development

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Chapter 7

Health-related quality of life in Indonesian children, adolescents, and adults with disorders of sex development

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RUMAH ADAT
BAANJUANG

Chapter 8

General discussion

General discussion

The management practice of patients with a DSD in Western countries differs greatly from those approaches applied in Asian countries[1]. Late presentation, delayed identification, lack of diagnostic facilities and treatment options, and lack of expertise have been reported as a major challenges in management of DSD in poor-resource countries[1-4]. It was argued that poverty and cultural aspects influence the management practices between Western and non-Western countries differently [1]. Poverty makes health-care facilities not only being less available but –if available- also less accessible for poor patients. Cultural background and social context influence patients' as well as health-care professionals' cognition about illness and their decision in dealing with it. In poor-resource countries of Asia, it is common that children born with ambiguous genitals grow up with their original anatomy due to unaffordable medical treatment or cultural acceptance [1,4]. As many people with disabilities in these societies remain untreated, people are accustomed to regard this as the only option feasible for them. They may seek medical advice when a problem escalates, which in the case of DSD is often in adolescence or adulthood. How do children, adolescents, and adults with DSD deal with such situation? Are they treated with respect and dignity that would allow them to grow-up with self-confidence? Are they empowered to make their own decisions on treatment, surgery, and even gender identity?

The aim of our study was to investigate gender development, emotional and behavioral functioning, social stigmatization, body image, sexual functioning and sexual orientation, as well as health-related quality of life in patients with DSD in Semarang, Indonesia who, for a long time, had been lived with limited or no medical care. DSD is not widely known; neither by medical professionals nor the general population of Indonesia. Therefore genital anomalies or other signs of DSD are not recognized; and if they are recognized, referral to a specialized medical center stays out, either because the medical professionals are unaware or the patients are uninformed to refer themselves. Consequently, they have been living in an ambiguous body and gender, without sufficient or proper information and treatment for their DSD condition. In Western countries, most of the patients with DSD were identified and treated early in life. Nevertheless, previous studies performed in Western countries have reported psychological problems despite of medical

treatment provided in early life[5-7]. As in this decade, only few Western patients with DSD are untreated or treated lately, which limits studying the course of psychosexual development and psychological well-being in these patients. In fact, the course of DSD and its associated psychological consequences by types of DSD is essentially unknown. In working within a multidisciplinary team treating patients with DSD in Semarang-Indonesia, we were confronted by many parents and patients with questions regarding gender assignment and reassignment, gender of rearing practices, infertility, and sexuality functioning. They had problems in having romantic relationships and wanted answers for emotional and behavioral problems of their children. Patients suffered from social stigmatization and had problems in accepting their DSD condition. Their questions and concerns formed the basis of this psychological study. In fact, this is the first psychological study reported among Indonesian patients with DSD.

Study limitation

Development of local instruments

Our intention was to compare the findings from our study with findings from available studies, mostly performed in patients with DSD in Western countries. Prior to the study onset, no relevant measures were available in the local language. Therefore, we searched for measures that were used in comparable studies reported from Western countries which have proven satisfactory psychometric properties, and translated the measures into local language (*Bahasa Indonesia)*. For this purpose, we followed procedures for semantic and cultural adaptation of the internationally available measures and assessed the psychometric properties of the Indonesian version of measures used in the study using healthy normative groups. We also performed pilot testing prior to implementation. Unfamiliarity with self-report measures and illiteracy were barriers that we encountered as the majority of our patients are poor, came from rural area, and have limited education. We learned that it was best to apply measures orally, as a structured interview. In general, the psychometric properties of the Indonesian measures used in the study were satisfactory. Few questions that was not applicable or need improvement in the future were identified and reported.

Cross-sectional study of patients and matched controls

Our study was designed a study of patients with matched controls. We encountered serious difficulties to fulfill the matching criteria for the healthy matched control subjects. Initially we planned to enroll siblings as the matched control, however, this most often were unfeasible due to differences in gender, no sibling, or disapproval to involve sibling in the study. Subsequently, matched control subjects were piled up from healthy control subjects lived in the similar neighborhood with the patients, which were contacted through the local leaders and then invited to join the study. These practices might be uncommon or differs greatly from common practice applied in psychological research in Western countries.

Heterogeneity of DSD, patients and clinical management

The third pitfall is related to lack of uniformity in clinical management of patients with DSD in our study. Although 118 subjects seemed sufficient for comparison, different types of treatment, DSD diagnoses and clinical features, as well as differences in gender (including changes in gender role) across age group (children, adolescents, and adults), prevented us from conducting stratified analysis with a sufficient number of subjects and statistical power. It is therefore impossible to state if emotional problems, gender identity, stigmatization and quality of life differ by subgroup of patients, type of DSD and treatment status. However, our findings are highly valuable at least in descriptive terms, as the reported outcomes were obtained mostly from untreated patients, whom are rarely seen in this decade.

Major findings in Indonesian context

The birth of a baby with ambiguous genitalia can be stressful for parents because often gender assignment is delayed and parents have to cope with an awkward moment when they cannot answer to the most common question "Is your baby a boy or a girl?". In our study on social stigmatization, we found that patients born with ambiguous genitalia, particularly those who are living in a small village, most often could not avoid being identified with DSD [11]. As ambiguous genitalia is very rare and DSD is not known widely, the birth of a newborn with an ambiguous genitalia shocked neighbors and family members, spread out throughout the village, and soon, both baby and the affected family become object of social attention, even until the baby has grown up [11]. In

young children, particularly girls with 46,XX CAH, gender identity confusion and masculine gender role behavior were reported [8]. In some patients, their DSD was unknown to others, except their parents. Children may not fully be aware of the social expectations or pressures surrounding them, but at some moment, children with DSD found out that they are different from others (e.g. boys with hypospadias could not urinate by standing or could not have circumcision as other boys of similar age had; girls with CAH present themselves as tomboy girls despite parents' efforts to dress them as feminine girls). As we observed in our study on stigmatization, the adults people rarely stigmatized children with DSD, but they addressed their positive (supporting) and negative (stigmatizing) behavior to the parents, i.e. they blamed the parents for delayed help-seeking, insulted parents for having a boy with an imperfect penis, supported parents by giving information or raising funds for medical treatment. However, children who have their DSD condition known by others were often being teased by their peers as they were mistakenly perceived as transgender children. They called them *"banci" (Bahasa:* male transvestite), made them a joke, and refused to play with them. Neither the child or the parents know how to deal with this problematic situation [11]. Lack of knowledge about DSD makes patients and parents confused with the child condition and thus it is difficult for them to explain the DSD condition to others. As children spend most of their daily time, at school as well as at home, to play with peers, it is not surprising that young patients in this study reported to be less happy, conducted more aggressive behavior, and reported more problems in their social relationships (i.e. peers, parents) compared to matched control children [10,12].

It should be mentioned that not all adolescents with DSD received social stigmatization. Patients in whom their DSD features were not visible or can be hidden (i.e. under their clothes) most often reported less stressful than patients with visible DSD features because no one was aware of their DSD [11]. Therefore, this group of adolescents keeps hanging out with their peers and involved in social activities like their peers. However, during this period puberty takes place. Bodily changes, sexual attraction, and peer pressure begin to play a role in adolescent's life. Adolescent patients, whose DSD was known since childhood, were still being teased (called *'bencong'* –*banci* in Javanese language*)* [11]. In our study on gender development [9], we observed that patients who later changed their social gender role in the adulthood, developed gender dysphoria during adolescence, but they did not share their confusion to their parents until

adulthood. Two out of 24 adolescents with DSD changed their social gender role at the aged of 17. In these patients, emotional problem were evident [9]. These may explain the lack of significant differences we observed between adolescents patients and matched control adolescents in view of emotional or behavioral problem and health-related quality of life [10,12]. Adolescents experience great changes, bodily as well as emotionally and socially in their transition to adulthood. They are more aware of peer conformity but not yet fully aware of social expectation in their future life as adult.

Being unidentified of having a DSD does not imply that emotional problems are less or absent. Adult patients as well as parents of youngsters with DSD told their worries about future, mainly about marriage, infertility and reproduction, and limited finance to afford medical treatments or surgeries [11]. In Indonesian society, marriage is a precondition for becoming a fully respected member of society and parents have great responsibility to initiate their children's marriage [13]. The newly-wed couples are expected to have children soon after being married. It is common that friends, relatives, or neighbors ask them for signs of pregnancy to show their caring, whereas in Western society this practice would be considered as rude or disrespectful to one's privacy. Our study also revealed that social consequences are far more severe for infertile women than for infertile men. We assumed that it is easier for men than for women to hide their infertility from society [8]. Being unmarried, particularly for a woman, is considered bringing shame to the family [14]. Shame is a vital element in Javanese culture[14]. In adulthood, social expectations will be intensified. As Javanese people have been taught to follow social norms [13], patients who had delayed seeking medical help or who were not aware of their DSD, began to take action to solve their problem. About the onset of adolescence, they began to inform their parents about their genital or body ambiguities, seek job to fund their treatment, or visit the medical doctor for examination. In some adults with 46,XY karyotypes assigned female at birth, their body ambiguity and sexual attraction to persons of the opposite gender confused them [8,9]. Most of them have no other option deal with than confronted with the unpleasant response given by their classmate, neighbors, or relatives through verbal and behavioral stigmatization [11]. Having insufficient understanding about the changes occurring in their body and mind, these patients decided to give it a try to live in the opposite gender by moving to other regions and start living in a new identity. Testing themselves by having a real-life experience in living

in the opposite gender seemed to have helped these patients to reduce their tension and confusion in dealing with the ambiguous body and gender. From our study on adult patients who underwent a social gender role change in the past 2-25 years, we observed that they reported severe gender-related problem during period of their living as female, but they are satisfied with their gender identity and gender role behavior during their living as men [9]. We assumed that their satisfaction with male gender identity and gender-role behavior might have been influenced by the reduced stigmatization and/or the increased acceptance of the community. More men than women with DSD are married or have romantic relationships and received acceptance and emotional support from their partners and their families, whereas women with DSD tended to avoid romantic relationships, and experienced more sexual distress. One woman even received a divorced plea due to her infertility. Despite these differences, both men and women with DSD reported dissatisfaction with their sex-related body parts, have fear of rejection from potential partners, and are concerned with their infertility [8]. Being aware of the possible failure to meet social expectations in the future, might explain that emotional problems, as in anxiety, depression, and internalizing problem are more frequently seen in adult patients with DSD than matched control adults, as we observed in our study on emotional or behavioral problem and health-related quality of life [10,12].

Conclusions

Based on the findings derived from our studies, we conclude that a DSD condition has great impact on many psychological aspects of our patients across gender and developmental stage. Our studies demonstrate that patients with DSD who had received limited or no treatment for their DSD condition experienced gender-related problems, sexuality-related problems as well as, emotional and behavioral problems. Health-related quality of life was also impaired, particularly in children and adults with DSD. They were unhappy depressed and showed problems with social relations. Moreover, patients with visible DSD characteristics experienced social stigmatization and reported stress due to this stigmatizing experience. A large number of patients with DSD underwent female-to-male social gender role change, mostly as adults but also occurring during adolescence and childhood. Many of these patients

experienced major problems related to their gender identity development. The change of gender was felt as a great relief and reduced the gender problems. Such large percentages of patients with a wish for a social gender role change are not observed in countries and areas that offer diagnostic evaluation and treatment just after identification of an ambiguous genital or ambiguous body development.

Having a DSD condition, being infertile and fear of being rejected caused significant distress, particularly among women. Late-treated patients experienced similar problems as untreated patients. Ambiguity of genitals, body, gender, and appearance elicited stigmatization in patients with DSD. Having a visible DSD characteristic, living as a female, and living in rural areas in Indonesia made that person vulnerable for social stigmatization. Children and adults with DSD reported emotional and behavioral problems: internalizing problems were evident, particularly among untreated patients, and were not associated with specific DSD diagnoses. Early referral to a multidisciplinary team is crucial for patients to receive appropriate treatment soon after the identification of DSD. Education on DSD and its consequences is pivotal for patients as well as for laymen. For patients with DSD and their families (parents), education about DSD should also directed to improve their social skill in dealing with social problems encountered in daily lives.

As patients with DSD interact with their society, there is impact from society on patients' problem and experience. In a collective-driven society like Indonesia society exerts more power than individuals in the sense that they contribute to people's cognitions, attitudes, and behaviors [15]. Javanese, the major ethnic in Indonesia, emphasizes on social bonds, particularly in a village [13]. People know each other very well and share their concern about anything. "What people will say or do?" does matters, and DSD is no exception in that regard as the findings from our study show. Therefore it can be understood that problems with social functioning and emotions were evident among Indonesian patients with DSD across our studies. Children reported difficulties in dealing with peers or parents as is shown from the TACQOL and CBCL scores; whereas adults, particularly women, often withdrew themselves from social contacts and even refused to enter romantic relationships. Depressive mood, sadness, and unhappiness were also prominent among our patients with DSD. Living with a DSD is hard and even harder for patients who live in society which does not understand nor supports patients with a DSD.

Being a member of society is part of personal identity, and so does gender. Being neither male nor female is uncommon in Indonesian society, unless the person is known as *'waria, banci, wadam'* (Indonesian term for male transvestite) or '*bencong or wandu*' (Javanese terms for male transvestite)[16]. None of these term are respectful. Being labeled with these terms imply strong message of social exclusion, which is painful, as reported by patients who experienced different forms of social stigmatization due to their DSD condition. It is obvious that there is a lack of proper knowledge about DSD in the society. As a consequence, patients with DSD features that are visible to other people (i.e. girl with a virilized body, ambiguous genitalia in newborn) experienced social stigmatization in a way that was stressful for them, or patients with concealable DSD features anticipated such stigmatization by delayed help-seeking. However, as we learned from our study on stigmatization, there are few patients that received social support and acceptance when they received reliable information about DSD from the medical doctors. It indicates the possibility of promoting social acceptance for patients with DSD by giving a proper and reliable information about what DSD is and what it is not.

Recommendations

We recommend to provide education about DSD to three targeted groups. *First,* to health care providers involved in first line medical care to facilitate referral of patients with suspected DSD for medical treatment. *Second,* giving information about DSD and its consequences to patients and parents, or their family members, to facilitate acceptance of DSD in the family. *Third,* providing reliable information about DSD to Indonesian society.

In primary care centers in Indonesia (*'Puskesmas* or *Posyandu'*), general practitioners, midwives, and nurses play important roles in educating patients or people in their particular neighborhood. Ideally, referral should be to a type A hospital which has a multidisciplinary team providing medical care for patients with DSD. The information given should cover appropriate information about DSD, its clinical and psychological impacts and instruction on how to cope with practical social consequences. The information need to be communicated in a language that is easily understood. In the past decades, the knowledge obtained from scientific research on DSD had developed rapidly. To facilitate

early referral of persons with DSD, knowledge about DSD should be integrated in the education curriculum of the medical doctor, nurse, and psychologist. The newly graduated need to be updated with the latest advancement in science and research on DSD. Considering the geographical condition of Indonesia, it will be very helpful to participate in an online learning platform offered by the European Society for Pediatric Endocrinology (www.espe-elarning.org) that provides reliable information and update research on DSD that can be accessed freely by medical doctors and other health practitioners to support their understanding on DSD. With this online learning, a collaboration between medical centers in Indonesian can be facilitated.

For patients and their family members, particularly who come from rural area with limited educational background, giving oral information with sufficient opportunities for them to address their questions and confusion to the members of multidisciplinary team is essential. This group may also receive information about DSD from general practitioners or other health-care professionals (group one) or general society (e.g. journalists, NGO activists, teachers). At present, there is no one reliable source of information on DSD that can be accessed by publicly in Indonesian language. The availability of reliable information about DSD in Indonesian language, in an online format, can be helpful to educate the general population of Indonesia in order to promote acceptance for persons with DSD.

The results of our studies highlight the importance of psychological aspects in the management of patients with DSD. The involvement of a psychologist, as well as other medical specialties, is an essential part of the multidisciplinary approach of patients with DSD. Therefore, education about DSD and its psychological impacts on the lives of patients and the affected families is essential. There is a definite need for psychological counseling and follow-up evaluation of patients. It is important for psychologists to understand that DSD is a life-long condition that requires life-ling psychological care. Long-term psychological assessment and intervention are crucial and family counseling is often needed. In the context of Indonesian culture, working with the extended family or community leaders in giving proper information about DSD might be necessary in order to facilitate patient's adjustment in the society.

Thus results of our studies strongly suggest that follow-up evaluations should be performed not only of the patients presently in their childhood or adolescence but also of adult patients. This follow up should be integrated in a

long term treatment plan which needs to be well-communicated to all involved in order to understand the importance of long term support.

At the beginning of this study, we received critics that conducting such study in a non-Western country, using Western-based measures, is impossible and unfeasible. Indeed, our study encountered challenges and barriers, like most pioneer studies do. Nevertheless, we have put considerable effort to solve the problems and remove the barriers, and made this study happen. We acknowledge limitations in our study as well as recognize opportunities for improvement in future studies[8-12]. We believe that our experiences could be a useful lesson-learned for Indonesian researchers as well as international counterparts that willing to conduct a pioneer study in psychological field, particularly focusing in a rare-disease like DSD.

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Chapter 9

Summary

Samenvatting

Rangkuman

Summary

Disorders of sex development (DSD) are not widely known among general population in Indonesia, even among health practitioners. Therefore, management of patients with DSD in Indonesian, is being challenged by lack of diagnostic facilities and expertise, availability of medical and uro-surgical treatment. There also is a lack of awareness with respect to the consequences of having a DSD condition and impact of late treatment. In 1989, a multidisciplinary team was setup jointly by the Dr. Kariadi Hospital and the Faculty of Medicine, Diponegoro University Semarang, in Central Java (Indonesia) to provide care for patients with DSD. The team had been confronted with questions raised by patients and parents about gender issues such as gender assignment, confusion about one's gender identity and gender dysphoria, issues on body ambiguity and sexuality , emotional problems and psychological well-being. As the majority of research on DSD reported from Western countries were conducted on early treated patients, we often could not provide relevant information to our patients. The focus of our study was: "Do Indonesian patients with DSD suffer from similar psychological problems as Western patients do and what is the impact of DSD on psychosexual development and psychological well-being in patients who only received little medical attention? This psychological study, that was conducted in 2007-2013, is part of a clinical study on diagnostic evaluation on 286 patients with DSD in Indonesia.

Chapter 1, provides an introduction to DSD particularly on the DSD diagnoses found in our study, followed by an overview on common practice of management of patients with DSD in Western and non-Western countries, including our center in Semarang. This chapter also outlines psychological aspects of DSD particularly within the context of DSD diagnoses relevant to this study.

Chapter 2 comprises information about the methods applied in of this study. As many methodological issues are also described in chapters 3 – 7, this chapter focuses mainly on methodological aspects that had not been explained in these chapters, including scale validation and construction and methodological challenges in conducting a case-control psychological study in Indonesia.

In **chapter 3**, we report findings on sexuality among 34 adult patients with DSD. With respect to sexuality, male and female sexual functioning, body image, female sexual distress, and sexual orientation were investigated. Our data revealed that adults with DSD were dissatisfied with the sex-related body parts such as genitals, breasts, facial hair but not with body parts that are not related to gender such as eyes, hair etc. With respect to sexual functioning, the majority of women with DSD felt sexually distressed. The women withdraw themselves from romantic relationships and refused or delayed entering a partner relationship. Compared to the women, more men had experiences in romantic and partner relationships; they were more willing to seek partners and sexual relationships, and more men than women were married. The majority of adults in the study chose a partner or was sexually attracted to a partner in opposite of the gender they have been raised in. A few partners reported sexual attraction to persons of the same gender. Our findings also showed adult patients, either men or women, were concerned with infertility. Disclosure dilemmas, marriage or having a partner, and fear of rejection were more prominent in women than men. We concluded that DSD had major impact on sexuality. It impacted differently in the lives of men and women, in accordance to different social expectations for men and women.

In **chapter 4**, we report on a unique study on gender development in children, adolescents, and adult patients with DSD. We investigated gender identity and gender role behavior in 118 Indonesian patients (76 males, 41 females) with different DSD diagnoses and compared findings with 118 healthy controls matched for gender, age, and residential setting (rural, suburban, or urban). In the first part we report on methodological aspects of the measures such as translation, scale adaptation and assessment of psychometric properties of the translated measures. In the second part, we report on gender outcome in 60 children (42 boys, 18 girls), 24 adolescents (15 boys, 9 girls), and 34 adults (19 men, 15 women) with DSD. The majority of patients only had received little medical attention in the past and never had received any medical treatment prior to this study. We observed a remarkably high percentage of change of social gender role: 6.7% among children; 8.3% among adolescents; 44.1% among adults. All except one patient had changed gender from female to male. Of them, 81% had a 46,XY karyotype and suffered from undermasculinization, the remaining patients had 46 XX CAH-SV. Their bodies had undergone significant

masculinization during life. Confusion about gender identity and cross-gender behavior were more frequently observed in children with DSD raised as girls than in children raised as boys and in groups. Adolescents and adults with DSD raised as females experienced more gender-related problems. An integrated clinical and psychological follow-up on gender outcome is necessary during pre-puberty and adulthood.

In **chapter 5**, we present our findings from a study on emotional and behavioral problems in our patient group. By means of questionnaires patients from age 11 onwards evaluated their behavior. Parents filled out questionnaires too, for youngsters aged 6 – 18. Our findings demonstrated that patients with DSD more often withdraw themselves form social contacts reported more problems related to sadness and depression than the control group did. Men reported more anxiety and depression whereas women were more withdrawn. Parents reported similar problems in their young children but in adolescence no emotional or behavioral problems were noticed, neither by adolescents themselves nor by their parents.

In **chapter 6**, we report on patients' experiences with social stigmatization. For more than two decades, policy on medical treatments are under debate; particularly surgical treatments performed to correct or prevent genital and body ambiguity. Such treatments have been developed to prevent social stigmatization evoked by the odd appearance Interestingly, no scientific study has been published that investigated stigmatization in DSD patients. In fact, there is no literature that support this medical practice. In this study, we applied both quantitative and qualitative methods to obtain an overview of our patients experiences with social stigmatization. We developed rating scales that measure social stigmatization. Our findings indicated that patients with visible characteristics of DSD experienced more social stigmatization than patients in whom characteristics of DSD were not visible DSD condition or could be hidden under clothes. The more patients experienced stigmatization, the higher stress such experiences evoked., Patients with visible DSD characteristics, have to deal with these social reactions. Patients in with hidden characteristics of DSD anticipated or prevented themselves from being identified by other people.

In **chapter 7**, we tried to find out to what extent DSD impaired the patients' quality of life. Our data in children showed that DSD, affected their social functioning; patients had more difficulties to align to other children). Their parents also indicated their children were less happy .Adult patients reported depressive moods. In contrast, adolescents and their parents did not report signs of social stigmatization. So the data on HRQoL are in concordance with findings on emotional and behavioral problems and with findings on sexual distress.

In **chapter 8**, all findings in the described investigations will be discussed in a broader context. Recommendation are made for an integrated approach for medical and psychological problems. Not only the somatic problems need to be attacked, patients with DSD also have to deal with or fight with many psychosocial problems. Patients can benefit from the psychologist's knowledge en experiences on coping with disease and coping sensitive issues such as being watched and isolation. As these psychosocial problems are closely related to the medical aspects of DSD, treatment will be best when the medical doctor and the psychologist collaborate.

Samenvatting

Over stoornissen in de geslachtsontwikkeling (Engels: *disorders of sex disorders*, afgekort tot DSD) is in Indonesië maar weinig bekend. Niet alleen weet de Indonesische bevolking er weinig van, ook onder artsen en verpleegkundigen is er relatief weinig bekend. Diagnostiek en behandeling van DSD zijn daardoor beperkt. In 1989, werd een multidisciplinair team is opgericht in het Dr. Kariadi Ziekenhuis en de Faculteit der Geneeskunde van de Diponegoro Universiteit in Semarang, Indonesië. Het team stelde zich tot doel de zorg voor patiënten met DSD te bevorderen. In de eerste jaren van het bestaan werd het team geconfronteerd met een veelheid aan vragen van patiënten en hun ouders over gender toewijzing en verandering van gender, gedrag dat als problematisch werd ervaren omdat het niet zou passen bij de toegewezen gender, vragen over seksualiteit, emotionele problemen en het maatschappelijk stigma waarmee patiënten en ouders werden geconfronteerd. Aangezien het meeste onderzoek naar psychosociale problematiek verbonden aan DSD is uitgevoerd in westerse landen, was het vaak onmogelijk om relevante informatie te verstrekken.
Dit onderzoek richtte zich op de vraag op de psychologische problematiek zoals die bij westerse patiënten wordt gezien, ook voorkomt bij Indonesische patiënten. De meeste patiënten die zich bij het Dr. Kariadi Ziekenhuis hadden aangemeld voor hulp, hadden weinig tot geen medische behandelingen ondergaan. Een groot verschil met westerse patiënten die, zodra een afwijking in de geslachtsontwikkeling wordt vermoed, worden verwezen voor diagnostiek en behandeling. Dit onderzoek bood de mogelijkheid om uitblijven van medisch ingrijpen op de psychoseksuele en psychosociale ontwikkeling te onderzoeken. Die vraag is ook voor westerse patiënten relevant, omdat er kritiek is op het huidige behandelbeleid. Die kritiek betreft vooral het medisch ingrijpen op jonge leeftijd, waarbij kinderen zelf nog te jong zijn om hun stem te laten horen bij de beslissingen die over hen worden genomen. Deze studie werd uitgevoerd tussen 2007 en 2013, en was onderdeel van een klinisch studie over de diagnostische evaluatie van 286 Indonesische patiënten met DSD (onderzoeker: A. Zulfa Juniarto).

Hoofdstuk 1 bevat een introductie over psychologische problematiek welke voorkomt bij patiënten met DSD, waarbij wij ons hebben gericht op de diagnoses van de patiënten die aan deze studie hebben meegedaan. Het hoofdstuk bevat

tevens een overzicht op de klinische praktijk in westerse landen, niet-westerse landen en die van het Dr. Kariadi Ziekenhuis.

Hoofdstuk 2 bevat aanvullende informatie over de opzet van de studie en de research methoden die zijn toegepast. Veel van de methodologische opzet van de studie wordt beschreven in de hoofdstukken 3 t/m 7. Omdat niet alle methodologische aspecten in de artikelen konden worden opgenomen, is er voor gekozen hier een apart hoofdstuk aan te wijden in het proefschrift.

In **hoofdstuk 3** rapporteren we de bevindingen uit het onderzoek naar lichaamsbeleving en psychoseksueel functioneren. We onderzochten 34 volwassen patiënten met DSD en vergeleken hun gegevens met die van een controle groep van 34 gezonde mannen en vrouwen die met hen gematcht waren op leeftijd, geslacht en woonomgeving. Het onderzoek liet zien dat patiënten met DSD ontevreden waren over de primaire en secundaire geslachtskenmerken, zoals het genitaal, de borsten en gezichtsbeharing. Met lichaamsdelen die niet geassocieerd zijn met sekse, zoals hoofdhaar en ogen, waren patiënten in het algemeen tevreden. Op een vragenlijst over seksueel functioneren zagen we dat vrouwen bijna geen seksuele ervaringen hadden. Ook mannen hadden weinig ervaring, maar waren actiever in het aangaan van romantische en seksuele relaties dan vrouwen. Vrouwen durfden geen relaties aan te gaan uit angst dat hun aandoening bekend zou worden. Zij vreesden negatieve reacties als bekend zou worden dat zij onvruchtbaar waren. Hun terughoudendheid in de liefde leverde veel stress op, omdat van hen werd verwacht dat zij zouden trouwen en kinderen krijgen. Ook mannen maakten zich zorgen over hun onvruchtbaarheid, maar waren aanzienlijk minder bang voor negatieve reacties. We concludeerden dat DSD het aangaan van seksuele relaties negatief beïnvloedt, maar dat de impact hiervan aanzienlijk verschillend was voor mannen en vrouwen.

In **hoofdstuk 4** wordt een unieke studie over de genderidentiteit ontwikkeling bij kinderen, adolescenten en volwassen patiënten beschreven. In het hoofdstuk wordt eerst uitgebreid ingegaan op de methodologische aspecten en het onderzoek verricht naar de psychometrische eigenschappen van de gebruikte vragenlijsten. Vervolgens worden de bevindingen op de interviews en vragenlijsten gerapporteerd die verschillende aspecten van de

genderidentiteitsontwikkeling meten. Genderidentiteitsontwikkeling werd onderzocht in 60 kinderen (42 jongens, 18 meisjes), 24 adolescenten (15 jongens, 9 meisjes) en 34 volwassenen (19 mannen, 15 vrouwen) allen met DSD, en een even groot aantal gematchte controle personen. De meeste patiënten hadden nooit enige medische behandeling voorafgaand aan deze studie ondergaan. We zagen dat een opvallend hoog percentage patiënten hun sociale gender rol hadden veranderd: 6,7 % van de kinderen, 8,3 % van de adolescenten en 44,1 % onder volwassenen. Alle deze patiënten, met uitzondering van één, leefden eerst als vrouw en hadden op een gegeven moment besloten verder te willen leven als vrouw. Onder hen had 81 % een 46 XY karyogram en was er sprake van ondervirilisatie. Bij 14 % was de diagnose 46, XX CAH-SV gesteld. Alle patiënten hadden gedurende hun leven een aanzienlijke (lichamelijke) vermannelijking ondergaan. Er was verwarring over hun genderidentiteit, soms versterkt door het feit dat ook hun gedrag niet paste bij de gender waarin zij opgroeiden (kinderen die als meisjes opgroeiden maar leken in hun gedrag en interesses meer op jongetjes). Adolescente meisjes en vrouwen met DSD die wat mannelijker waren in gedrag en een stoer uiterlijk prefereerden ervoeren kritiek op hun levensstijl, hetgeen hen ongelukkig maakten. Het onderzoek toonde aan het verstandig is de medische follow-up gepaard te laten gaan met psychologische follow-up om hulp te kunnen bieden bij het omgaan met problemen op het gebied van gender identiteit en cross-gender gedrag.
In **hoofdstuk 5** presenteren we onze bevindingen betreffende emotionele en gedragsproblemen. Het onderzoek liet zien dat patiënten met DSD, in vergelijking met gezonde leeftijdsgenoten, zich vaker terugtrekken uit sociale contacten. Ook verdriet en depressieve klachten werden vaker door hen genoemd. Ernstiger vormen van depressie, waarbij behandeling moet worden overwogen, werden vaker gerapporteerd. Er was een verschil tussen mannen en vrouwen: mannen rapporteerden meer klachten op gebied van angst en depressie terwijl vrouwen zich vaker terugtrokken uit sociale contacten. Bij mannen werden de emotionele klachten vaak niet onderkend zodat er ook geen hulp werd gezocht of aangeboden. Bewust wording van het vaker voorkomen van emotionele problemen is een belangrijk om deze problemen tijdig te identificeren en hulp aan te bieden.

In **hoofdstuk 6** staat het onderzoek beschreven naar ervaringen van patiënten met sociale stigmatisering. Een deel van de chirurgische en hormonale

behandelingen zijn er op gericht om ambiguïteit van het lichaam te corrigeren. Dit wordt gedaan maatschappelijke stigmatisatie te voorkomen en er voor te zorgen dat patiënten optimale maatschappelijke kansen krijgen. Er zijn echter ook bezwaren: het zijn behandelingen die een grote impact hebben op het leven van het kind en het kind zelf is vaak nog te klein om te betrekken bij de beslissingen voor de behandelingen. Er is weinig onderzoek gedaan naar maatschappelijke stigmatisatie van DSD patiënten. Toch vragen bijna alle ouders van westerse patiënten om deze behandelingen.
De Indonesische patiënten van het Dr. Kariadi Ziekenhuis / Diponegoro Universiteit hadden weinig behandelingen ondergaan. Veel van hen hadden een ambigue lichaam. Daarom besloten we bij deze patiënten te onderzoeken of zij sociale stigmatisatie ervoeren en hoe stressvol dit voor hen was. We ontwikkelde een meetinstrument voor volwassenen en ouders; de Sociale Stigmatisatie Schaal voor DSD, met aparte versie voor volwassenen en ouders van kinderen en adolescenten. Daarnaast vroegen we patiënten of hun ouders hun antwoorden toe te lichten en voorbeelden te geven. Uit het onderzoek bleek dat patiënten sociale stigmatisatie ervoeren. Dat bleek zeker zo te zijn, met name patiënten die uiterlijke kenmerken van ambiguïteit hadden. Patiënten die ambigue kenmerken konden verbergen onder kleding kregen minder vaak te maken met sociale stigmatisatie. Stigmatisatie was stressvol en riepen veel emoties op. Deze patiënten werden vaak voor transgenders gehouden en ontmoetten veel hostiliteit. We hopen dat een betere bewustwording van het bestaan van DSD deze vooroordelen kan voorkomen. Daarnaast is het belangrijk de patiënt te ondersteunen en met hen copings strategieën te bespreken zodat zij vaardiger worden om voor zichzelf op te komen en een einde te maken aan de vijandigheden.

In **hoofdstuk 7** staan de bevindingen naar *health-related quality of life* (HRQoL). Op de vragenlijsten bleek dat DSD de kwaliteit van leven negatief beïnvloedde, met name bij kinderen en volwassenen. Kinderen vonden een slechtere aansluiting bij leeftijdsgenootjes en waren minder gelukkig dan controle kinderen (door de ouder en de kinderen zelf aangegeven). Volwassenen waren verdrietiger dan controle personen. Adolescenten en ouders rapporteerden geen invloed van DSD op hun kwaliteit van leven. De bevindingen op de kwaliteit van leven vragenlijsten kwamen overeen met de bevindingen op vragenlijsten voor gedrags- en emotionele problemen. Opnieuw is bewust

wording van de problematiek nodig om deze problemen tijdig te identificeren en hulp aan te bieden.

In **hoofdstuk 8**, worden de bevindingen van de verschillende onderzoeken besproken en in een bredere context geplaatst en aanbevelingen gegeven voor een geïntegreerde medische en psychologische aanpak voor behandeling zodat niet alleen de lichamelijke problematiek wordt behandeld, maar er ook oog is voor de maatschappelijke problemen die deze patiënten moeten overwinnen.

Rangkuman

Gangguan perkembangan organ reproduksi (dalam Bahasa Inggris disebut sebagai "*Disorders of sex development*" atau umumnya dan untuk selanjutnya disingkat dengan DSD) belum dikenal secara luas di masyarakat Indonesia, bahkan di kalangan praktisi kesehatan. Oleh karena itu, penanganan DSD di Indonesia menghadapi banyak rintangan disebabkan oleh kurangnya fasilitas diagnostik, pakar di bidang DSD, dan pengobatan medis, termasuk tindakan operatif. Disamping itu kesadaran masyarakat akan dampak DSD bagi penderita serta dampak yang muncul jika DSD terlambat ditangani sangatlah kurang. Pada tahun 1989, suatu tim multidisiplin untuk penanganan kasus-kasus DSD telah dibentuk, yakni Tim Penyesuaian Kelamin, yang merupakan kerjasama antara RS Dr. Kariadi dan Fakultas kedokteran Universitas Diponegoro (UNDIP) Semarang, Jawa Tengah (Indonesia) yang bertugas memberikan perawatan medis kepada pasien DSD. Tim Penyesuaian Kelamin ini seringkali dihadapkan pada pertanyaan-pertanyaan yang diajukan oleh pasien dan orangtuanya berkaitan dengan gender, antara lain mengenai penentuan jenis kelamin, kebingungan akan identitas gender, ketidakpuasan gender; persoalan dengan citra tubuh dan seksualitas; problem emosi, dan problem psikologis lainnya. Karena sebagian besar riset DSD di negara Barat dilakukan terhadap pasien yang telah ditangani sejak dini, kami seringkali mengalami kesulitan untuk memberikan informasi yang relevan dengan kondisi pasien kami.

Fokus riset kami adalah: "Apakah pasien DSD di Indonesia mengalami problem psikologis yang sama dengan pasien DSD di negara-negara Barat dan apakah dampak DSD terhadap perkembangan psikoseksual dan kesejahteraan psikologis pada pasien yang hanya sedikit mendapatkan bantuan medis?"

Penelitian psikologi yang dilakukan sejak tahun 2007 hingga 2013 ini merupakan bagian tak terpisahkan dari penelitian klinis yang mengkaji diagnosa 286 pasien DSD di Indonesia.

Bab 1 berisi pengantar mengenai DSD, terutama mengenai diagnosis DSD yang digunakan dalam penelitian ini, diikuti dengan gambaran umum mengenai pendekatan yang umumnya digunakan dalam menejemen pasien DSD di negara-negera Barat dan Timur, termasuk Indonesia (Semarang). Bab ini juga memaparkan secara garis besar aspek-aspek psikologis dari DSD, terutama dalam konteks diagnosis DSD yang dikaji dalam penelitian ini.

Bab 2 berisi informasi mengenai metode-metode yang digunakan dalam penelitian ini. Sebagian besar bahasan metodologi dipaparkan dalam bab 3-7, sehingga bab ini hanya dikhususkan pada aspek metodologi yang belum dijelaskan dalam bab-bab tersebut, termasuk antara lain konstruksi dan validasi skala serta hambatan metodologis yang dihadapi dalam melakukan suatu riset psikologi di Indonesia dengan menggunakan kelompok perlakuan dan kontrol.

Pada **bab 3**, kami paparkan temuan kami dalam riset yang melibatkan 34 pasien dewasa yang menderita DSD. Dalam hal seksualitas, fungsi seksual laki-lai dan perempuan, citra tubuh, distres seksual pada perempuan, dan orientasi seksual dikaji dalam penelitian ini. Data yang diperoleh menunjukkan bahwa pasien dewasa merasa tidak puas dengan bagian tubuh yang berkaitan dengan seks, seperti kelamin, buah dada, bulu wajah tetapi tidak demikian dengan bagian tubuh lainnya yang tidak berkaitan dengan seks, seperti mata, rambut, dan sebagainya. Dalam hal fungsi seksual, sebagian besar pasien wanita merasa tertekan dengan seksualitasnya. Perempuan dewasa penderita DSD menarik diri dari hubungan lawan jenis dan dari menghindarkan diri dari relasi cinta lawan jenis (pacaran). Dibanding perempuan, pasien laki-laki memiliki lebih banyak pengalaman dalam hal relasi dengan lawan jenis; mereka lebih cenderung ingin memiliki pasangan dan hubungan lawan jenis (pacaran), serta lebih banyak pasien laki-laki daripada perempuan yang menikah. Sebagian besar pasien dewasa yang diteliti, memilih atau tertarik secara seksual pada pasangan yang berlawanan gender dengan dirinya. Sebagian kecil pasien mengaku tertarik secara seksual pada orang dengan gender yang sama dengan dirinya. Temuan kami juga menunjukkan bahwa pasien dewasa, baik laki-laki maupun perempuan, khawatir dengan persoalan ketidaksuburan (infertilitas). Dilema untuk terbuka kepada orang lain atau pasangan mengenai kondisi DSDnya, pernikahan atau pasangan, dan ketakutan ditinggalkan atau ditolak pasangan merupakan persoalan-persoalan yang lebih sering ditemukan pada pasien perempuan daripada laki-laki. Kami menyimpulkan bahwa DSD berdampak besar bagi seksualitas pasien. Dampak yang ditimbulkannya berbeda pada laki-laki dan perempuan seiring dengan perbedaan tuntutal sosial pada laki-laki dan perempuan.

Dalam **bab 4**, kami melaporkan studi yang unik mengenai perkembangan gender pada pasien anak-anak, remaja, dan dewasa yang menderita DSD. Kami meneliti

identitas gender dan peran jenis gender pada 118 pasien Indonesian (76 laki-laki, 41 perempuan) dengan berbagai jenis diagnosa DSD dan membandingkan hasilnya dengan 118 subjek kontrol yang dipasangkan berdasarkan gender, umur, dan area tempat tinggal (desa, kota kecil, atau kota besar). Pada bagian pertama, kami laporkan aspek metodologi pengukuran, seperti penerjemahan alat ukur, adaptasi skala, dan asesmen kualitas psikometrik dari skala yang telah diterjemahkan. Pada bagian ke dua, kami melaporkan perkembangan gender pada 60 pasien DSD anak (42 laki-laki, 18 perempuan), 24 remaja (15 laki-laki, 9 perempuan), dan 34 dewasa (19 laki-laki, 15 perempuan). Sebagian besar pasien hanya menerima sedikit perhatian medis atau belum pernah menerima pengobatan media, sebelum pengambilan data psikologis ini. Kami menemukan sejumlah pasien, dalam persentase yang sangat tinggi, yang telah berubah gender: 6.7% di kalangan pasien anak-anak, 8.3% di kalangan pasien remaja, dan 44.1% di kalangan pasien dewasa. Kecuali satu orang, semua pasien tersebut berganti gender dari perempuan menjadi laki-laki. 81% diantaranya memiliki karyotipe 46,XY dan mengalami demaskulinisasi , sedangkan sisanya (19%) memiliki diagnosis 46,XX CAH-SV (hiperplasia adrenal kongenital tipe virilisasi simpel). Tubuh mereka mengalami maskulinisasi yang sangat signifikan. Kebingungan akan identitas gender dan perilaku berlawanan gender lebih sering dijumpai pada pasien anak-anak yang dibesarkan sebagai perempuan daripada pasien DSD anak yang dibesarkan sebagai laki-laki. Pasien DSD remaja dan dewasa yang dibesarkan sebagai perempuan juga lebih sering memiliki persoalan yang berkaitan dengan gender. Pemantauan lanjutan terhadap perkembangan gender pasien perlu dilakukan secara terpadu, melibatkan pemeriksaan klinis maupun psikologis, terutama menjelang pubertas dan masa dewasa.

Di **bab 5**, kami kemukakan temuan kami dari studi tentang problem emosi dan perilakuan pada pasien yang kami teliti. Dengan menggunakan kuesioner untuk pasien usia 11 tahun ke atas, kami mengevaluasi perilaku mereka. Orangtua juga mengisi kuesioner untuk anak-anak mereka yang berusia 6-18 tahun. Hasil temuan kami menunjukkan bawah pasien DSD lebih sering menarik diri dari lingkungan pergaulannya dan lebih sering merasa sedih dan tertekan dibandingkan subjek kontrol. Dibandingkan subjek kontrol, pasien dewasa laki-laki lebih sering mengalami kecemasan dan depresi, sementara pasien dewasa perempuan lebih sering menarik diri. Orangtua anak-anak melaporkan

persoalan yang sama dengan persoalan yang dikemukakan anaknya, namun di kalangan remaja tidaklah demikian. Tidak ada persoalan yang khas yang dilaporkan oleh remaja maupun orangtuanya.

Pada **bab 6**, kami sampaikan pengalaman pasien dalam hal stigmatisasi sosial. Lebih dari dua decade, kebijakan penanganan pasien DSD telah diperdebatkan, terutama karena tindakan operatif yang dilakukan dalam rangka pencegahan kerancuan tubuh dan kelamin. Tindakan operatif tersebut dilakukan untuk mencegah terjadinya stigmatisasi sosial yang terjadi dikarenakan penampilan yang aneh atau ganjil. Menariknya, belum ada penelitian yang secara khusus mengkaji stigmatisasi pada pasien DSD. Dalam kenyataannya, tidak ada literature yang mendukung praktek medis ini. Dalam penelitian ini, kami menggunakan metode kuantitatif dan kualitatif untuk mendapatkan gambaran mengena pengalaman pasien kami dalam hal stigmatisasi sosial. Kami menyusun skala rating untuk mengukur stigmatisasi sosial. Hasil temuan kami menunjukkan bahwa pasien yang memiliki karakteristik DSD yang mudah dikenali orang awam lebih sering mengalami stigmatisasi sosial dibanding pasien yang karakteristik DSD-nya tidak tampak mata atau dapat disembunyikan dibalik pakaian yang dikenakannya. Semakin sering stigmatisasi sosial yang dialami, semakin tinggi stress yang ditimbulkan oleh pengalaman tersebut. Pasien dengan karateristik DSD yang mudah dikenali harus menghadapi reaksi sosial terhadap DSD. Pasien dengan karakteristik DSD yang dapat disembunyikan dapat mengantisipasi dan mencegah agar DSD-nya tidak diketahui oleh orang lain.

Di **bab 7**, kami mengkaji sejauhmana DSD berdampak pada kualitas hidup penderitanya. Data yang kami peroleh dari subjek anak-anak menunjukkan bahwa DSD mempengaruhi fungsi sosial anak. Pasien anak mengalami kesulitan bergaul dengan anak-anak atau orang lain dalam lingkungan pergaulannya. Orangtua mereka juga melaporkan bahwa mereka kurang bahagia. Pasien dewasa menyatakan lebih sering merasa depresif atau tertekan. Sebaliknya, pasien remaja maupun orangtuanya tidak menunjukkan adanya tanda-tanda problem emosi maupun perilaku. Dengan demikian data yang kami peroleh dari studi kualitas hidup yang berkaitan dengan kesehatan (*health related quality of life* atau disingkat HRQoL) selaras dengan temuan kami dalam penelitian mengenai problem emosi dan perilaku serta temuan kami mengenai distres seksual.

Di **bab 8**, semua temuan dari studi-studi yang telah kami paparkan sebelumnya akan dibahas dalam konteks yang lebih luas. Rekomendasi disusun sebagai pendekatan terpadu terhadap persoalan klinis dan psikologis. Pasien DSD tidak hanya menghadapi persoalan somatis saja, namun ia juga harus bergelut dengan banyak persoalan psikologis. Pasien dapat mengambil manfaat dari pengetahuan dan pengalaman psikolog dalam menerima penyakitnya dan dalam menghadapi persoalan sensitif lainnya, misalnya ketika diamati atau dikucilkan. Karena persoalan psikologis ini berkaitan erat dengan aspek medis, penanganan terbaik bagi pasien DSD akan dapat dicapai melalui kolaborasi antara dokter dan psikolog.

Appendices

About the author

Annastasia Ediati was born on September 13, 1973 in Sragen, Central Java, Indonesia. She went to study psychology at the Faculty of Psychology, Gadjah Mada University (UGM), Yogyakarta between 1991 and 1997. Then she took professional program to become a psychologist at the Faculty of Psychology-UGM and graduated at 1999. Before graduated as a psychologist, she passed the selection to be a lecturer at the Faculty of Psychology, Diponegoro University (UNDIP), where she works until now. In 2001 she received STUNED scholarship to pursue a master program on the Human Resource Development at the Faculty of Educational Science and Technology, University of Twente, the Netherlands. Since 2006, apart from her main duties as lecturer at the Faculty of Psychology-UNDIP, she has been involved in a multidisciplinary team to provide care for patients with DSD that were referred to the Sexual Adjustment Team (SAT) from the Dr. Kariadi Hospital and Faculty of Medicine, Diponegoro University. Her main responsibility was to conduct psychological assessment and counseling to patients with disorders of sex development and their parents. Following her involvement in the SAT, she also involved as researcher in the Center for Biomedical Research (CEBIOR), Faculty of Medicine-UNDIP where she began to expand her interests on psychological aspect of genetic-related disease. Before leaving to Rotterdam for her Phd program, she also involved in teaching medical doctors –students of the genetic counseling master program in UNDIP- about the psychological aspect of DSD. She is married with Justinus Badiaraja Simanullang in December 27th , 2011 and will leave together in Semarang, Central Java as she will continue her work at the Diponegoro University.

PhD Portofolio

Name of PhD researcher:	: **Annastasia Ediati**
PhD period:	: September 2010 – January 2014
Promotors:	: Prof.dr. S.L.S Drop Prof.dr. S.M.H. Faradz
Co-promotors:	: Dr. A.B. Dessens Dr. E. Birnie

Description	Year
General courses	
- Basic SPSS	2011
- Biomedical English Writing and Communication	2012
Seminars and workshop	
- I-DSD workshop on e-learning	2013
- Symposium on "Disorders of Sex Development: a new paradigm?" Jakarta, Indonesia	2011
- PhD day of the Erasmus-MC	2011
Presentations	
- 4th International Symposium of DSD, Glasgow, UK (Oral)	2013
- Psychologist Research Meeting, Sophia Children Hospital (Oral)	2012, 2013
- Indonesian Student Association (PPI) Rotterdam (Oral)	2013
- Sophia Research Day – 150th anniversary of Sophia Children Hospital (Poster)	2013
- DSD symposium, Erasmus-MC (Oral)	2012
- 2nd International seminar and workshop on DSD, Semarang, Indonesia (Oral)	2012
- 1st international conference of Paediatric Psychology Network (PPN) UK & NL Oxford, UK (Poster)	2012
- 38th meeting of the International Academy of Sex Research (IASR), Lisbon, Portugal (Poster)	2012
- 37th meeting of International Academy of Sex Research (IASR) Los Angeles, USA (Poster)	2011

Other

- Applying research grants (by Erasmus MC Postdoc network) 2013
- Systematic Literature Retrieval using PubMed (by Medical Library) 2012
- Systematic Literature Retrieval using Medline/ PsycInfo (by Medical Library) 2012

Grant/reward

- Runner-up Best oral presenter at the 4th International Symposium of DSD, Glasgow, UK 2013
- Travel grant from the *Erasmus Trustfonds* to present at the 37th meeting of International Academy of Sex Research (IASR) Los Angeles, US 2011
- DIKTI scholarship from the Directorate of Higher Education, Ministry of Education and Culture, Indonesia 2010

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List of Publications

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A Ediati, AZ Juniarto, E Birnie, SLS Drop, SMH Faradz, & AB Dessens. Gender development in Indonesian children, adolescents, and adults with disorders of sex development. *Submitted*.

A Ediati, SMH Faradz, AZ Juniarto, J van der Ende, SLS Drop, & AB Dessens. Emotional and behavioral problem in Indonesian children, adolescents, and adult patients with disorders of sex development. *Submitted*.

A Ediati, SMH Faradz, GHW Verrips, AZ Juniarto, SLS Drop, & AB Dessens. Health-related quality of life in Indonesian children, adolescents, and adult patients with disorders of sex development. *Submitted*.

A Ediati, AZ Juniarto, E Birnie, J Okkerse, A de la Croix, SLS Drop, SMH Faradz, & AB Dessens. Social stigmatization in Indonesian patients with disorders of sex development. *In preparation*.

AZ Juniarto, A Ediati, YG van der Zwan, LHJ Looijenga, FH de Jong, AB Dessens, SLS Drop, & SMH Faradz. (2013). Virilization due to androgen hypersecretion in a patient with an ovarian Leydig cell tumor: diagnostic and psychosocial implications. *Acta Medica Indonesiana*, 45 (2), 130-135.

TI Winarni, FEP Mundhofir, A Ediati, W Nillesen, HG Yntema, BCJ Hamel, SMH Faradz, & RJ Hagerman. (2013). The Fragile X-associated Tremor Ataxia Syndrome (FXTAS) in rural Indonesia. *Clinical genetics*, 83 (3), 263-268.

CG Widayanti, A Ediati, M Tamam, SMH Faradz, EA Sistermans, & AMC Plass. (2011). Feasibility of Preconception Screening for Thalassemia in Indonesia: Exploring the Opinion of Javanese Mothers. *Ethnicity & Health*, 16, (4-5), 483-499.

Gunungan is a puppet (wayang) that shaped like a mountain. At the front of the mountain, there is a gate with two giants as the guardians. Gunungan also known as the three of life, with many animals or fantastic creatures are depicted: a tiger, a bison, peacocks, birds, dragons. Gunungan represents the world and its content. During the puppet performance, gunungan is used to mark the beginning or the end of the story, or to signal between the scenes.