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**Please cite as:**

Dyer, G., Gilroy, N., Bradford, J., Brice, L., Kabir, M., Greenwood, M., Larsen, S., Moore, J., Hertzberg, M., Kwan, J., Brown, L., Hogg, M., Huang, G., Tan, J., Ward, C. & Kerridge, I. (2015). A Survey of Fertility and Sexual Health Following Allogeneic Blood and Marrow Transplantation in New South Wales, Australia. *British Journal of Haematology*, 172 ( 4 ) pp. 592 - 601 . 2015, Dec 21, doi:10.1111/bjh.13872

## **A survey of fertility and sexual health following allogeneic haematopoietic stem cell transplantation in New South Wales, Australia**

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### **Abstract**

Four hundred and twenty-one adult allogeneic haematopoietic stem cell transplant (HSCT) survivors participated in a cross-sectional study to assess sexual dysfunction and infertility post-transplant. Survey instruments included the Sydney Post-Blood and Marrow Transplant (BMT) Survey, Functional Assessment of Cancer Treatment (FACT) – BMT, the Depression, Anxiety, Stress Scales (DASS 21), the Chronic Graft-versus-Host Disease (cGVHD) Activity Assessment- Patient Self Report (Form B), the Lee cGVHD Symptom Scale and The Post-Traumatic Growth Inventory. Most HSCT survivors reported sexual difficulties (51% of males; 66% of females). Men reported erectile dysfunction (79%) and decreased libido (616%) and women reported loss of libido (83%), painful intercourse (73%) and less enjoyment of sex (68%). Women also commonly reported vaginal dryness (73%), vaginal narrowing (34%) and vaginal irritation (26%). Woman had much higher rates of genital cGvHD than men (22% vs. 5%). Age and cGVHD were significantly associated with sexual dysfunction.

Few survivors had children following transplant (33%). However, for those of reproductive age at HSCT, 22% reported trying to conceive, with 103% reporting success. This study is the largest to date exploring sexual function in survivors of allo-HSCT. These data provides the basis for health service reform to better meet the needs of HSCT survivors, including evidence to support counselling and education both pre- and post-transplant.

**Keywords:** allogeneic HSCT, sexual dysfunction, infertility, survivors, survey, Australia.

## **Introduction**

Allogeneic haematopoietic stem cell transplantation (HSCT) is an established treatment for malignant and non-malignant diseases affecting both adults and children. Advances in patient and donor selection, management of acute toxicities and supportive care have significantly improved outcomes following transplant with 1-year survival rates now 80% or more for some conditions (Mohty & Mohty, 2011; Pasquini & Zhu, 2014). Unfortunately, many HSCT survivors experience significant morbidity following HSCT with late effects reducing the quality and duration of their life (Savani et al, 2011). Sexual dysfunction and infertility are among the most prevalent long-term sequelae (Mosher et al, 2009).

Sexual dysfunction and infertility occurs primarily because of the adverse effect of high dose chemo-radiotherapy, resulting in interruption of the sexual response cycle, decreased libido, erectile and ejaculatory dysfunction, vaginal alterations (dryness, narrowing, fibrosis), dyspareunia and infertility or sub-fertility due to primary ovarian failure and impaired spermatogenesis (Carter et al, 2006; Humphreys et al, 2007). In general, women tend to experience more sexual dysfunction than men (78% at 1 year compared to 50%), are more likely to experience long-term sexual dysfunction and are more likely to be infertile following HSCT (Marks et al, 1997; Humphreys et al, 2007; Thygesen et al, 2012). While successful pregnancies have occurred in survivors of HSCT, they are rare, 06% in the largest report on over 37 000 HSCT survivors (both allogeneic and autologous) (Salooja et al, 2001). With the exception of a limited number of registry studies, there is limited data on sexual dysfunction and infertility post-HSCT with most studies reporting small populations from single centres. There is no data describing the late effects in an Australian cohort of HSCT survivors. The aims of this cross-sectional study were to present data on the range and frequency of sexual dysfunction and infertility in survivors of HSCT, to address gaps in service provision and to provide better information to those undergoing HSCT, their families/carers and health care professionals.

## **Methods**

### **Patients and procedures**

Potential participants were identified from allogeneic transplant databases of all adult allogeneic transplant centres in New South Wales [NSW; Australia's most populous state ~7.5 million in 2013 (Australian Bureau of Statistics, 2014)]. Participants were eligible if they were ≥18 years of age and had undergone an allogeneic HSCT between 1 January 2000 and 31 December 2012, could read and write English and could provide consent. Names and phone numbers were provided to the research team. Consenting participants were given the option to self-complete the questionnaire or complete

it via a phone interview with one of the researchers. A second round of telephone calls were made to participants who had not returned the survey within a month. All authors had access to primary clinical trial data. The study protocol was approved by the Northern Sydney Local Health District Human Research Ethics Committee (NSLHD Reference:1207-217M).

## **Instruments**

The Sydney Post-BMT Study Survey (SPBS) (Appendix S1) was developed by the research team. Item construction was informed by a review of the literature and discussions with patients attending HSCT long-term follow-up clinics. It consisted of 402 questions grouped into 20 domains, including questions relating to fertility and sexual function. Other relevant domains included demographics, medical complications, specialist referrals, tests and assessments, medications and therapies, infections, vaccinations, complementary therapy use, cancer screening, close personal contacts, lifestyle, diet nutrition, occupational and relationship status following stem cell transplantation. The questionnaire used tick box responses, short answer questions and 5-step Likert scales measuring attitudes and other factors and took approximately 1 hour to complete. The questionnaire was piloted in clinic and phone interviews to assess face and content validity and comprehension.

Associations between sexual function and fertility were explored against demographics, medical complications, post-transplant medical therapies, treatments and complementary therapies, relationship status and social determinants, including income and occupational status. The relationships between sexual function and fertility were further explored against a range of validated survey instruments that measured quality of life [Functional Assessment of Cancer Therapy – Bone Marrow Transplant (FACT-BMT Version 4; Cella et al, 1993; McQuellon et al, 1997)], anxiety stress and depression [The DASS (Depression Anxiety Stress Scales) 21] (Lovibond & Lovibond, 1996; Crawford & Henry, 2003; Dahm et al, 2013), chronic graft-versus-host disease (GVHD) [The Chronic GVHD Activity Assessment – Patient Self Report (Form B) (Pavletic et al, 2006) and The Lee Chronic GVHD Symptom Scale (Lee et al, 2002b)] and an assessment of life changes in response to traumatic events (The Post Traumatic Growth Inventory score) (Tedeschi & Calhoun, 1996; Morris et al, 2013). For ease of completion all instruments were combined into one booklet.

For each participant, data was collected on dates of diagnosis and transplant, stage/remission status at transplant, conditioning, GVHD prophylaxis, stem cell source and donor type, which was completed by the research team. This information was used to compare HSCT clinical variables and the impact on sexual function and fertility in survivors.

## **Statistical analysis**

Categorical responses were summarized using frequencies and percentages. Parametric continuous variables were summarized using means and standard deviations, and non-parametric variables using medians and interquartile ranges. The Pearson  $\chi^2$  test or Fisher's Exact tests were used for comparative analysis of dichotomous categorical variables. Two sample comparisons of means and medians were determined using the independent t-test and Wilcoxon Rank Sum tests respectively; greater than two sample comparisons of means and medians were determined using one way

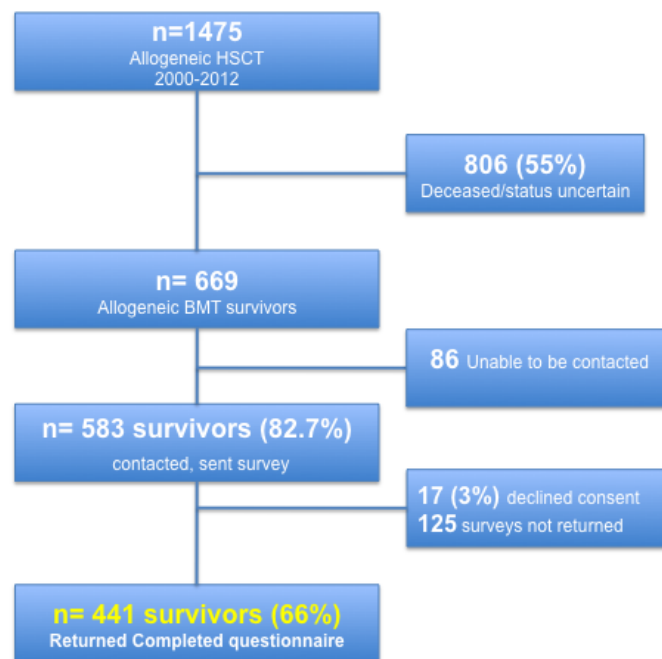
analysis of variance (ANOVA) and Kruskal–Wallis tests, respectively. A two-tailed  $P < 0.05$  was used as the level of statistical significance.

Statistical analysis was performed using the STATA version 12.1 statistical package (StataCorp, College Station, TX, USA).

## Results

A total of 1475 allogeneic HSCT were performed in the study period. Of the 669 survivors known to be alive at study sampling, 583 were contactable and were sent study packs. Four hundred and forty-one (66% of total eligible, 76% of those contacted) returned the completed survey. Three per cent declined participation (Fig 1).

**Fig 1. Post-haematopoietic stem cell transplantation (HSCT) survey study flowchart.**



## Patient characteristics

Of those who completed the survey, 250 (57%) were male and 191 (43%) female. The median age of survey respondents was 54 years (range: 19–79). The median age at time of transplant was 49 years (range: 17–71). Forty per cent of survey respondents were 6 or more years post-transplant. The majority of patients resided in a major city (72%), were of middle/high income status (53%) and were in a married or defacto relationship (79%). The main indication for transplantation was acute leukaemia (62%). Matched siblings accounted for 57% of donors and a myeloablative conditioning regimen was used in 49% of transplant procedures (Table I).

**Table 1. Participant characteristics**

<b>Socio-demographic</b>	
<b>Gender (n=441)</b>	
Male n(%)	250 (56.7%)
Female n(%)	191 (43.3%)
<b>Age (years) at survey (n=441)</b>	
Median (IQR; range)	54 (44,62; 19-79)
<b>Age (years) at transplant (n=441)</b>	
Median (IQR; range)	49 (37,56; 17-71)
<b>Ethnicity (n=372)</b>	
Caucasian, European n(%)	323 (86.8%)
Other * n(%)	49 (13.2%)
<b>Educational status (n=335)</b>	
University (some/completed) n(%)	154 (46.2%)
Other n(%)	179 (53.8%)
<b>Post transplant income status (n=423)</b>	
Low income \$20,000-\$39,999 n(%)	155 (36.6%)
Middle income \$40,000-\$79,999 n(%)	123 (29.1%)
High income >=\$80,000 n(%)	145 (34.3%)
<b>Residence (n=431)</b>	
Major City n(%)	311 (72.2%)
Other (inner regional, outer regional, remote) n(%)	120 (27.8%)
<b>Relationship status (n=436)</b>	
Married-Defacto n(%)	344 (79.3%)
Other (separated, single, divorced) n(%)	90 (20.7%)
<b>Transplant -related</b>	
<b>Years since transplant (n=443)</b>	
< 2yrs n(%)	58 (13.1%)
=2 to <6 yrs n(%)	204 (46.3%)
=6 to <10 yrs n(%)	117 (26.5%)
>=10 yrs n(%)	62 (14.1%)
<b>Underlying diagnosis (n=425)</b>	
Acute Leukaemia (AML/ALL) n(%)	226 (53.4%)
Other ** n(%)	197 (46.6%)
<b>Remission status (n=405)</b>	
First/Second complete remission	271 (66.9%)
Other $\phi$	134 (33.1%)
<b>Donor type (n=439)</b>	
Sibling n(%)	250 (56.9%)
Matched Unrelated n(%)	158 (36.0%)
Haploidentical n(%)	10 (2.3%)
Mismatched Unrelated n(%)	21 (4.8%)
<b>Stem Cell source(n=441)</b>	
Bone Marrow n(%)	48 (10.9%)
Peripheral Blood n(%)	381 (86.4%)
Cord Blood n(%)	12 (2.7%)
<b>Conditioning Chemotherapy (n=439)</b>	
Myeloablative	214 (48.7%)
Reduced intensity	225 (51.2%)

**Resumption of sexual activity post-HSCT**

A total of 421 respondents provided information about sexuality, fertility and sexual activity post-HSCT; 241 (96.4%) of 250 males and 178 (93.2%) of 191 females.

One hundred and sixty-seven (69.2%) males and 122 (68.5%) females reported resumption of sexual activity posttransplant; 30 (12.4%) of males and 21 (11.8%) of females had not yet resumed sexual activity post-HSCT. The remaining 44 (18.3%) of males and 35 (19.7%) females reported being sexually inactive pre and post-transplant.

Males who had resumed sexual activity had a median age of 52 years, compared to 58 years for those who had not yet resumed sexual activity post-transplant ( $P = 0.04$ ). The median years since transplantation in males who had returned to sexual activity was 5 years, and was not significant from males who had not yet returned to sexual activity. Males who had resumed sexual activity showed no significant differences in relationship status, donor type, diagnosis, conditioning, remission status or distribution of comorbidities when compared to males who had not resumed sexual activity.

Morbidity from cGVHD was significantly higher in males who had not resumed sexual activity post-transplant. These males reported significantly higher rates of moderate and severe cGVHD symptoms ( $P = 0.003$ ), significantly higher Lee Chronic GVHD scores ( $P = 0.001$ ) and had significantly higher rates of immunosuppression ( $P = 0.001$ ) and anti-infective drug use ( $P = 0.0007$ ). Males who had not returned to sexual activity post-transplant had significantly lower scores on physical ( $P = 0.001$ ), functional ( $P = 0.0009$ ) and HSCT FACT subscales ( $P = 0.0003$ ), and had significantly lower scores on composite FACT scores ( $P = 0.001$ ). No significant difference was observed in the Post-Traumatic Growth Inventory scores for males who had resumed sexual activity (Tables II and III<sup>1</sup>).

Females who had resumed sexual activity had a median age of 49 years compared to 57 years for those who had not resumed sexual activity ( $P = 0.06$ ) and were more likely to be further out from their date of transplant than those who had not resumed sexual activity with a median duration of 6 years since transplantation, compared to 3 years ( $P = 0.0009$ ). Females returning to sexual activity were more likely to be in a married/defacto relationship, though this was not statistically significant ( $P = 0.09$ ). In contrast to male survivors of HSCT, the self-reported severity of GVHD symptoms and Lee GVHD scores were not significantly different in women who had, or had not resumed sexual activity. Females who had returned to sexual activity had significantly higher FACT BMT subscale scores, but did not have any significant differences across other FACT domains or in the post-transplant Growth Inventory scores. Females who had resumed sexual activity reported significantly higher rates of anxiety and/or depression ( $P = 0.05$ ). The use of psychotropic medications (antidepressants, anxiolytics and/or sedatives) was not significantly different between the two groups. The underlying haematological diagnosis, conditioning regimen, donor type, medical comorbidity profile and medication use was not significantly different in females who had resumed sexual activity (Tables II and III).

### **Sexual dysfunction**

Fifty-one per cent of males who had resumed sexual activity since their HSCT reported difficulties with sexual function since transplant (Table IV). The majority (77%) of sexual difficulties in males related to erectile dysfunction, and decreased libido was the second most common reported problem (62%). Pain with intercourse accounted for 9% of sexual difficulties. Of the 122 females who had resumed sexual activity since their HSCT, 81 (66%) reported having difficulties with sexual

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<sup>1</sup> Tables 2-6 are located at the end of this document.

function since transplant (Table IV). Specific issues in those who had resumed sexual activity post-transplant were compared across genders. Females had significantly less enjoyment of sex [odds ratio (OR) 43 95% confidence interval (CI) 22, 88 P < 00001], less sexual desire (OR 30 95% CI 14, 66 P = 0002) and more pain with intercourse (OR 26 95% CI 102, 713 P < 00001) when compared to their male counterparts. Sexual problems arising from partner issues were similar between the two genders.

### **Genital pathology**

The only genital pathology reported in men was penile cGVHD, which occurred in 13 (5%) of 250 respondents.

Genital problems reported by sexually active females included vaginal dryness (73%), vaginal narrowing (34%), vaginal irritation and soreness (26%), thrush (8%), cystitis (17%) and lower back pain (27%). Vaginal dryness was the only symptom that was statistically significantly different between women who were sexually active and those who were not (OR 52 95% CI 25, 11; P < 00001).

### **Menstrual irregularities**

Seventy-nine (44%) of 178 females reported having menstrual cycles prior to HSCT. Fourteen (18%) reported a return of menstrual function post-transplant, of which seven experienced a temporary cessation of up to 2 years following the transplant procedure.

### **Fertility post-HSCT**

Three hundred and ninety-three participants provided a response to questions regarding post-transplant conception. Thirty-five of 395 respondents indicated that they had tried to conceive post-HSCT: 21 (10%) males and 14 (8%) females. Of these 35 participants, 15 (43%) were successful (11 males; 4 females). Females who successfully conceived were all aged less than 30 years and males less than 41 years at the time of transplantation (P = 008).

Of the 15 successful pregnancies, 6 (40%) were the result of natural conception (two females; four males) and two were the result of natural conception that followed prior attempts at in vitro fertilization (IVF), including IVF in one male and his partner and IVF followed by implantation of a donor egg in one female. A total of seven successful pregnancies were the result of IVF; six (all males) with IVF alone and one IVF and donor egg (female). No association was found between the use of reproductive technologies by HSCT survivors with residential location (major city versus inner or outer regional) and household income.

### **Fertility preservation pre HSCT**

Forty-seven (20%) of 233 males reported banking sperm pre-HSCT with a median age (at transplant) of 31 years [inter-quartile range (IQR) 24–40; range 18–51]. There were no statistically significant socio-demographic differences (income, residence) between males who did and did not bank sperm. Donor type did have a significant effect on banking sperm with those who had a haplo/MUD or mismatched transplant being 26 times more likely to bank than those who had a matched sibling transplant (95% CI 128, 544; P = 0.004). Males who had a myeloablative HSCT had a threefold higher rate of banking sperm than those who had reduced intensity conditioning (95% CI 167, 658; P =

00004) though this was not significant when adjusting for the effect of younger age for those receiving myeloablative conditioning [adjusted odds ratio (AOR) 0.82; 95% CI 0.32, 2.08; P = 0.67].

Three hundred and sixty-one participants responded to the question of embryo banking after a cycle of IVF. A total of 6 (2%) reported using this technology (two males and four females). Three hundred and twenty-nine participants reported whether or not they had donated ovarian tissue and frozen eggs for storage. Overall, 7 (2%) had used this procedure (six females and one male HSCT recipient with his female partner).

The most common reasons for young women (aged 18–29) to have not pursued fertility preservation pre-HSCT were they had already completed a family or were too sick to have done so. For females in the 30–39 years age group, 40% declined the procedure but in a significant proportion (23%) the reproductive intervention was not offered. In females aged 40–49, the majority declined the procedure, though 15% reported that it had not been offered. Of male HSCT survivors who did not store sperm this was generally because they declined to do so (79%) or were too unwell to undergo the procedure (8%). Only 8 (5%) men, 2 of whom were under 40 years of age, were not offered sperm storage (Tables V and VI).

## **Discussion**

While sexual dysfunction has previously been documented in HSCT survivors, most reports are from single centres and/or comprise small sample sizes. This study is the largest to date exploring sexual activity in survivors of allogeneic HSCT and the largest and most comprehensive study of fertility and sexuality in an Australian context. While the high response rate (76%) and use of validated instruments makes it likely that these results represent an accurate account of the experience of survivors of HSCT, the heterogeneity and restricted ethnic diversity in our population may limit the generalizability of these results to HSCT survivors in other countries and settings. The results from this research are also limited by the fact that it relied upon self-report and because no data is available about non-responders. Further, the instruments used in this study were ones that are widely used in HSCT settings to assess quality of life, physical and psychosocial function in HSCT survivors and were not specifically targeted at sexual function.

This study demonstrates that the majority of HSCT survivors experience a wide range of sexual difficulties in the years following transplantation. Although most had resumed sexual activity, a significant proportion reported sexual difficulties (51% of males; 66% of females). Common to both genders were loss of libido and less enjoyment of sexual activity while 72% of women experienced pain with intercourse. These results are broadly consistent with other reports of sexual dysfunction after HSCT (Marks et al, 1997; Lee et al, 2002a; Tierney et al, 2007). As with other studies, age and cGVHD were significantly associated with sexual dysfunction post-HSCT (Heinonen et al, 2001; Lara et al, 2010; Mueller et al, 2013; Wong et al, 2013).

While most patients generally resumed sexual activity post HSCT, consistent with other research, we found that this occurs most frequently and earlier in men than in women, and in younger HSCT survivors (Watson et al, 1999; Shanis et al, 2012). The association between cGVHD and the lack of return to sexual activity appeared to be more evident in males than females, with males who had



not resumed sexual activity following transplant reporting higher rates of immunosuppression, higher anti-infective drug use and higher self-reported cGVHD symptoms which is in keeping with previous studies (Lee et al, 2002a; Humphreys et al, 2007; Lara et al, 2010). Quality of life measures, especially those reflecting physical and functional well-being, were lower in males who had not returned to normal sexual activity and Lee cGVHD scores were significantly higher in these survivors.

Female HSCT survivors commonly report a range of genitourinary symptoms with significant vulvo-vaginal cGVHD occurring in 221% of women who develop cGVHD post transplant. Genitourinary symptoms are more often reported in women who have resumed sexual activity however it is unclear if sexual activity exacerbated the problem, or if sexual activity allowed women to identify these problems (Spinelli et al, 2003; Zantomio et al, 2006; Stratton et al, 2007).

As has been reported elsewhere, HSCT is invariably associated with premature ovarian failure and azoospermia; however, small numbers of survivors, particularly those aged under 30 years at the time of HSCT, may recover ovarian function/spermatogenesis and fertility (Sanders et al, 1988; Wang et al, 1998; Grigg et al, 2000; Salooja et al, 2001; Rovo et al, 2006; Jadoul et al, 2011; Wu et al, 2012). The majority of HSCT survivors are rendered infertile, however because the mean age at HSCT is 49 years this may not constitute a significant concern for many HSCT survivors. While few HSCT survivors attempt to conceive post-transplant, many will be successful (43%), often with assisted reproductive technologies (Lipton et al, 1997; Demeestere et al, 2006; Donnez et al, 2011). Unfortunately such technologies are expensive and are located primarily in metropolitan areas – raising questions about equity of access. The challenges involved in conception post-HSCT underlie the importance of utilizing pre-HSCT fertility preservation measures, including sperm storage, ovarian tissue and/or oocyte or embryo storage (Lee et al, 2006; Wallace, 2011; Joshi et al, 2014). In this regard it was noteworthy that, in our population, a significant number of women rather than men (23% vs. 5% respectively) were not offered reproductive interventions. While this probably reflects practical difficulties associated with fertility preservation methods in women, it also highlights continuing uncertainty regarding the availability and efficacy of techniques for females.

This study provides important insights into sexual dysfunction and infertility in an Australian cohort of HSCT survivors. Given the high prevalence of continued sexual dysfunction in the post-HSCT period (>66% for females, >50% for males), it is clear that pre-HSCT counselling and post-HSCT care needs to include full disclosure and assessment of the effects of transplant on sexual health and fertility, both for men and women, with greater attention paid to vaginal cGVHD than currently occurs. Consensus guidelines have recently been released with recommendations for regular, integrated gynaecological review both pre- and post-HSCT (Frey Tirri et al, 2015; Stratton, 2015). While such practice change seems undeniable, further work is required to establish whether other pre- and post-HSCT interventions, including education, counselling and early treatment, improves sexual function and quality of life outcomes for survivors.

### **Acknowledgements**

This research was funded by the New South Wales Agency for Clinical Innovation Blood and Marrow Transplant Network and supported by the Northern Blood Research Centre. These sponsors are public health organizations that support medical science and health care reform. They had no role in gathering, analysing, or interpreting the data.

### Author contributions

GD, NG, LB and IK designed the study. All authors contributed to study recruitment, data analysis, drafting of the publication and approval of the final version.

### Conflicts of interest

The authors declare no conflict of interest.

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**Table 2. Demographic, social and clinical variables and their association with resumption of sexual activity post transplant, by Gender**

	Males			Females		
	Resumed Sexual Activity post HSCT n=167	Not resumed Sexual activity Post HSCT n=30	P value	Resumed Sexual Activity Post HSCT n=122	Not resumed Sexual activity post HSCT n=21	P value
<i>Socio-demographic factors</i>						
<b>Age in years at survey</b> (median; range)	52 (21-79)	58 (21-73)	<b>0.04</b>	49 (21-75)	57(34-69)	0.06
<b>Years since transplant</b> (median,; range)	5 (1-14)	5 (1-14)	0.32	6 (1-14)	3 (1-8)	<b>0.0009</b>
<b>Relationship status</b> Married/defacto Single,divorced, separated	137/166(82.5%) 29/168 (17.5%)	22/30(73.3%) 8/30(26.7%)	0.31	106/119 (89%) 13/119 (11%)	15/20 (75%) 5 /20(25%)	0.09
<i>Transplant factors</i>						
<b>Diagnosis</b> Acute leukaemia Other diagnoses	75 /140(53.6%) 65/140 (53.6%)	14/25 (56.0%) 11/25(44.0%)	0.82	76/102(65.5%) 40/102(35.5%)	14/18(73.7%) 4/18(26.3%)	0.60
<b>Donor type</b> Sibling Haploidentical Unrelated(matched) Unrelated (mismatched)	89/166(53.6%) 4 /166(2.4%) 63/166(38.0%) 10/166 (6.0%)	16(53.3%) 1 (3.3%) 13(43.3%) 0	0.55	74(60.7%) 3 (2.5%) 38(31.5%) 7 (5.7%)	12(57.1%) 1 (4.8%) 7 (33.3%) 1 (4.8%)	0.93
<b>Conditioning</b> Myeloablative Reduced Intensity	84 (50.9%) 81(49.1%)	11(36.7%) 19(63.3%)	0.15	77(63.1%) 45(36.9%)	10(47.6%) 11(52.4%)	0.18
<b>Remission status</b> CR1/CR2 Other	95(56.9%) 72(43.1%)	14(46.7%) 16(53.3%)	0.30	87(71.3%) 35(28.7%)	17(81.0%) 4 (19.0%)	0.36
<i>Post-transplant factors</i>						
<b>Comorbidity</b> Cardiovascular risk factors Bone disease Anxiety/depression Thyroid disease Iron overload	69(43.7%) 39(24.3%) 48(28.7%) 5(3.4%) 53(35.6%)	16(53.3%) 11(36.7%) 8(26.7%) 2(7.1%) 6(23.1%)	0.13 0.15 0.82 0.31 0.26	45(36.9%) 41(33.6%) 32(26.2%) 7(5.7%) 34(27.9%)	6(28.6%) 5(23.8%) 1(4.8%) 2(9.5%) 6(28.6%)	0.62 0.45 <b>0.05</b> 0.62 1.0
<b>Medical Therapy</b> Immunosuppression Antiinfective	65(38.9%) 67(40.1%)	19(63.3%) 20(66.7%)	<b>0.01</b> <b>0.007</b>	26(21.3%) 39(32.0%)	5(23.8%) 10(47.6%)	0.78 0.16

Psychotropic medication	37(22.2%) 12(7.2%)	5(16.7%) 0	0.63 0.22	22(18.0%) 41(33.6%)	3(14.3%) 5(23.8%)	1.00 0.45
Hormone Replacement						
<b>chronic GVHD</b>						
<b>Self-reported severity</b>						
None	20/105(19.1%) 55/105(52.4%)	1/19(5.3%) 6/19(31.6%)	<b>0.03</b>	15/77(19.5%) 41/77(53.2%)	1/12(8.3%) 6/12(50.0%)	0.66
Mild	18/105 (17.1%)	7/19(36.8%)		18/77(23.4%)	4/12(33.3%)	
Moderate	12/105 (11.4%)	5/19(26.3%)		3/77(3.9%)	1/12(8.3%)	
Severe						
<b>Lee Chronic GVHD score</b>	16 (0-77)	30(5-54)	<b>0.01</b>	15(0-61)	20(6-47)	0.40
Median (range)						

<b>Table 3. Quality of life measures (FACT), post traumatic growth inventory measures, and resumption of sexual activity post transplant, by Gender</b>						
	<b>Males</b>			<b>Females</b>		
	Resumed Sexual Activity post HSCT	Not resumed Sexual activity Post HSCT	P value	Resumed Sexual Activity Post HSCT	Not resumed Sexual activity post HSCT	P value
<b>FACT scores (median, range)</b>	24 (0-28)	19 (5-28)	<b>0.01</b>	25(0-28)	24(12-28)	0.34
FACT- physical	21(4-28)	22(1-27)	0.92	22(7-28)	21(14-28)	0.70
FACT- social	17(1-24)	17(7-20)	0.66	16(0-20)	17(0-20)	0.77
FACT-emotional	21(4-28)	16 (0-28)	<b>0.009</b>	21(5-28)	19(8-28)	0.21
FACT-functional	30(9-40)	26(7-38)	<b>0.003</b>	29(11-40)	26(18-32)	0.02
FACT-HSCT subscale	82(22-104) 113(32-144)	70(40-95) 94(52-129)	<b>0.03</b> <b>0.01</b>	83(36-104) 111(49-141)	81(61-103) 109(80-134)	0.58 0.23
FACT -G						
<b>FACT HSCT Total</b>						
<b>Post Traumatic Growth Inventory median, range</b>	54 (0-96)	54(16-79)	0.74	63(12-103)	53(18-93)	0.35

**Table 4: Sexual dysfunction reported by males and females who had resumed sexual activity post transplant**

Type of sexual dysfunction	Sexual dysfunction following resumption sexual activity (Females) Total=81	Sexual dysfunction following resumption sexual activity (Males) Total=86	Odds ratio (95% CI)	P value
Decreased enjoyment of sex	55/81 (67.9%)	28/86(32.6%)	4.3 ( 2.2, 8.8)	<0.0001
Pain with intercourse	59/81 (72.8%)	8/86 (9.3%)	26.1(10.2, 71.3)	<0.0001
Decreased sexual desire	67/81 (82.7%)	53/86(61.6%)	3.0 (1.4, 6.6)	0.002
Difficulties with arousal/erection	47/81 (58%)	N/A	Not comparable to males	-
Difficulties with erection	N/A	66 /86 (76.7%)	Not comparable to females	-
Difficulties with partner regarding issue of sex	27/81 (33.3%)	28/86 (32.6%)	1.03 (0.5, 2.1)	0.91
Other	Other difficulties described by females included vaginal bleeding/dryness/GVHD(11) mobility/flexibility issues (1) post gynae surgery problems (1) body confidence (1) low libido (1) partner issues(1)	Other difficulties described by males included recurrent hospitalizations (1), neurological damage to penis following episode of shingles (1), reduced muscular strength & joint pains and breathing difficulties (3)		

**Table 5: Reasons given for females who did not use medically assisted reproductive methods pre-transplant by age.**

Age range (years)	18-29 n=19	30-39 n=30	40-49 n=26	50-59 n=47	60-69 n=21	>=70 n=1	All N=144
Not offered (n=19)	1 (5.3%)	7 (23%)	4 (15.4%)	2 (4.3%)	0	0	14/144 (9.7%)
Declined	1 (5.3%)	12 (40%)	18 (69.2%)	44 (93.6%)	20	0	95/144 (66%)
Too sick or other health problems	5 (26.3%)	2 (6.7%)	3 (11.5%)	1 (2.1%)	0	0	11/144 (7.6%)
Completed family	12 (63.1%)	9 (30%)	1 (3.8%)	0	1	1	24/144 (16%)



**Table 6: Reasons given for males who did not use medically assisted reproductive methods pre-transplant by age.**

Age range (years)	18-29 n=7	30-39 n=16	40-49 n=43	50-59 n=63	60-69 n=28	>=70 n=1	All N=156
Not offered (n=19)	1	1	2	3	1	0	8/156 (5.1%)
Declined	0	8	34	54	27	1	124/156 (79.5%)
Too sick or other health problems	1	4	5	2	0	0	12/156 (7.7%)
Completed family	3	3	2	4	0	0	12/156 (7.7%)