

Monitoring fertility (semen analysis) by cancer survivors who banked sperm prior to cancer treatment

65

A.A. Pacey^{1,*}, H. Merrick², E. Arden-Close², K. Morris¹, L.C. Barton¹,
A.J. Crook¹, M.J. Tomlinson³, E. Wright², R. Rowe², and C. Eiser²

70

¹Academic Unit of Reproductive and Developmental Medicine, Department of Human Metabolism, University of Sheffield, Level 4, The Jessop Wing, Tree Root Walk, Sheffield S10 2SF, UK ²Department of Psychology, University of Sheffield, Sheffield S10 2TP, UK ³Fertility Unit, Nottingham University Hospital, East Block, B Floor, Derby Road, Nottingham, NG7 2UH, UK

*Correspondence address. E-mail: a.pacey@sheffield.ac.uk

75

Submitted on April 3, 2012; resubmitted on June 8, 2012; accepted on June 25, 2012

20

STUDY QUESTION: What medical and psychological variables predict why men with banked sperm do not return for semen analysis after their cancer treatment has ended?

80

SUMMARY ANSWER: Men who decline the offer of semen analysis are less likely to have reported adverse side effects during cancer treatment, and have a more negative experience of banking sperm and a more negative attitude towards disposal of their stored semen than those who attend.

25

WHAT IS KNOWN ALREADY?: Previous authors have noted that male cancer survivors seem reluctant to have their fertility tested after their treatment has ended. Moreover, the utilization rates of banked sperm are very low (<10%) and the majority of samples are kept for many years without being used.

85

STUDY DESIGN, SIZE AND DURATION: A cross-sectional study of 499 cancer survivors who were sent a questionnaire about their views on sperm banking, fertility and post-treatment semen analysis between April 2008 and December 2010.

30

PARTICIPANTS AND SETTING: Men (aged 18–55 years) who had banked sperm in Sheffield and Nottingham (UK) prior to gonadotoxic treatment for cancer more than 5 years previously.

35

MAIN RESULTS AND THE ROLE OF CHANCE: Completed questionnaires were received from 193 men (38.7% response rate) whose samples had been banked for 9.18 ± 3.70 years (range = 4.94–26.21) and whose current age was 35.08 ± 7.08 years (range = 21.58–54.34; mean \pm SD). One-third (35.8%) had never attended for semen analysis. In multivariate analysis, the odds of not attending for semen analysis were significantly greater among men who did not experience adverse treatment side effects [odds ratio (OR) = 5.72, 95% confidence interval (CI) = 2.10–15.56], who reported a more negative experience of banking sperm (OR = 1.82, 95% CI = 1.17–2.82) and a more negative attitude to disposal of their stored semen (OR = 1.56, 95% CI = 1.01–2.42).

40

LIMITATIONS AND REASONS FOR CAUTION: Only 38.7% of those eligible agreed to take part. We do not know the characteristics of men who declined to take part, if they agreed to attend semen analysis without completing the questionnaire or whether they had chosen to have semen analysis performed elsewhere (e.g. private sector). Some of the measures used (e.g. experience of banking sperm) relied on men's recall of events many years previously.

45

WIDER IMPLICATIONS OF THE FINDINGS: New strategies are required to encourage these men to engage with fertility monitoring programmes if sperm banks are to be used cost-effectively and men are to be given appropriate fertility advice.

100

STUDY FUNDING AND COMPETING INTERESTS: This paper was supported by funding from Cancer Research-UK to C.W., A.A.P. and R.R. (C481/A8141). The views expressed are those of the authors. No competing interests declared.

50

Key words: cancer / semen cryopreservation / male infertility / psychology

105

110

55

115 Introduction

120 Sperm banking is now a routine procedure recommended for all post-pubertal males where there is a risk of long-term infertility following cancer treatment (European Society for Human Reproduction and Embryology, 2004; National Collaborating Centre for Women's and Children's Health, 2004; Lee et al., 2006; Royal College of Physicians, 2007). Although many thousands of men each year decide to bank sperm following a diagnosis of cancer, most of our knowledge is limited to technical descriptions of how sperm are frozen (Tomlinson and Pacey, 2003), semen quality at the time of banking (e.g. Bahadur et al., 2005), case histories of pregnancies following the use of thawed sperm many years later (Horne et al., 2004; Feldschuh et al., 2005) and reports on the rate of utilization of banked samples (reviewed in Pacey and Eiser, 2011).

130 In a recent review, Pacey and Eiser (2011) concluded that little is known about the decisions men make concerning their banked sperm, apart from whether or not to bank sperm at the time of cancer diagnosis. In subsequent years, men must also decide whether or not to monitor fertility through regular semen analysis. Critically, for many cancer survivors, the timescale for making these decisions can extend substantially beyond discharge from cancer care. These survivors may not have access to oncologists or reproductive medicine specialists but have to rely on their own recall of information about fertility given at banking and the more general knowledge of primary care doctors.

140 The monitoring of fertility by men with banked sperm is of interest because spermatogenesis may recommence in a substantial number of patients following completion of cancer treatment (Tomlinson and Pacey, 2003; Bahadur et al., 2005; Pacey, 2007). However, interviews with 19 men who had banked sperm at least 5 years previously suggested that they were often unaware that their fertility could recover (Eiser et al., 2011), and that they saw no point in attending for semen analysis simply to be told that their semen quality remained poor. This may contribute to observations by healthcare professionals (Wasserman et al., 1987; Tomlinson and Pacey, 2003; Van Casteren et al., 2008) that men with banked sperm seem reluctant to attend for semen analysis.

150 Suggesting men have regular semen analysis following the end of cancer treatment would seem to be good advice, since the information can facilitate their decisions about appropriate use of contraception, or where necessary referral for Assisted Conception. In addition, in countries such as the UK, fertility monitoring through semen analysis serves an important regulatory function, as men can now only keep banked samples in the longer term if 'significant or premature infertility' is demonstrated (Human Fertilisation and Embryology Authority, 2009). The implications are that if UK men decline to attend for semen analysis, then there is a genuine risk that their samples may be removed from storage and destroyed, even if they remain subfertile.

160 Given the need to better understand the decisions men make about monitoring their fertility after cancer treatment has ended, we conducted a cross-sectional study to quantify the percentage of men who did not accept invitations for semen analysis and to identify medical and psychological variables contributing to their decision.

Materials and Methods

Patients

170 Between April 2008 and December 2010 we contacted a cohort of 499 men who had banked sperm more than 5 years previously prior to

gonadotoxic treatment for cancer. Eligibility criteria included age (18–55 years), no known mental health problems, and sufficient English language ability to provide written informed consent and complete questionnaires.

Setting

175 Men were recruited from sperm banks located in Sheffield Teaching Hospitals NHS Foundation Trust (Jessop Wing, Tree Root Walk, Sheffield, UK) and Nottingham University Hospitals NHS Trust (Queen's Medical Centre, Derby Road, Nottingham, UK).

Recruitment procedures

180 In both facilities, men with banked sperm are written to regularly to invite them to attend for semen analysis, confirm or renew their consent for storage or give permission for disposal of banked samples. We included with this standard letter an information sheet and consent form, an 11-page questionnaire (see below) and a prepaid return envelope. Men were asked to return the questionnaire, regardless of whether or not they decided to attend semen analysis. The Trent Research Ethics Committee approved these procedures prior to the start of the study (Ref: 07/H0405/61).

Information from medical and sperm bank records

195 Information on diagnosis, treatment regimen, attendance at oncology follow-up appointments and late effects was obtained from medical records held in oncology. Information about banked sperm (number of samples stored and their quality) was obtained from separate notes held at each sperm bank. We also collected information about the number of prior letters/appointments sent to the patient inviting him for semen analysis and the number of times he attended. Where men had attended for semen analysis details of the results were also recorded. Only limited medical data could be collected for 26 patients (one patient's notes had been destroyed and notes were unavailable for 25 patients), but data from sperm bank records were obtained for all patients.

Questionnaire

200 The questionnaire included the following nine sections. Multiple choice responses and five-point Likert rating scales with appropriate endpoints were used.

(i) *Health and well-being* (Ware et al., 1995). The SF-12v2 is a widely used and validated 12-item measure generating two summary scores: physical component summary (PCS) and mental component summary (MCS). Higher scores indicate better quality of life.

(ii) *Current late effects and perceived vulnerability* (Absolom et al., 2006). This includes 17 cancer-related health problems, or 'late effects', known to occur after cancer treatment (e.g. infertility, fatigue and depression) to assess men's views about their 'vulnerability' to late effects (range = 1–5) with higher scores indicating greater perceived vulnerability, and total 'number of late effects' currently experienced (0–17).

(iii) *Experience of banking sperm*. This scale was developed specifically for this study and includes 11 items about men's experience of banking sperm (e.g. 'I had the right amount of support from others in making this choice' and 'I am pleased I decided to bank'). Higher scores indicated a more negative experience of banking sperm.

(iv) *Information about fertility*. We assessed four separate aspects of men's information about their fertility. These included how many samples they recalled banking, the quality of their banked samples ('did not have any sperm to bank', 'good enough for fertility treatment' or 'don't know'), how useful it was to know the quality of banked sperm (five-point scale from 'definitely very useful' to 'definitely not very

175

180

185

190

195

200

205

210

215

220

225

230

useful'), and current use of contraception, and if not why (rely on partner, trying for a child, not in a relationship, fertility too low).

(v) *Views about follow-up*. This specially developed scale included seven questions regarding men's attitude to returning for semen analysis (e.g. 'I don't want to know if my fertility has recovered or not', 'I am certain my fertility has already or will recover' and 'I don't think it's worth taking time off work for this'). Higher scores indicated a more positive attitude to returning for semen analysis.

(vi) *Attitude to disposal*. Eight questions were used to assess men's attitudes to disposal (e.g. 'If tests showed my fertility was recovered, I would agree to disposal', 'Knowing I still had sperm banked would make me feel more confident'). Higher scores indicate a more negative attitude to disposal.

(vii) *Children and parenting*. Five items were used to assess men's attitude to having children in future ('How much has your experience of cancer affected your wish to have children in future', 'How much do you want to have a child in future', 'I worry that children born from banked sperm will have health problems', 'I worry that my cancer treatment could cause health problems for any child born afterwards' and 'Before your cancer diagnosis, were you ever worried that you had fertility problems'). Men were also asked about the number of biological children conceived with their own sperm or with banked sperm in assisted conception, the number of adopted children or step-children they see regularly and the number of children conceived using donor sperm.

(viii) *Demographic information*. Information was collected about current age, relationship status (single/separated or partnered), age left full time education (under 18 or over 18 years of age), current employment (working or not working), ethnic group (white or other) and who they live with (partner or other). This section also recorded the first four digits of the UK postcode of their primary residence in order to calculate distance from the sperm bank.

Analysis

All data were double entered into SPSS version 16 and checked for accuracy. Nineteen cases had some missing data on continuous questionnaire variables. Little's Missing Completely At Random (MCAR) test (Little, 1988) showed the pattern of missing data were not significantly related to other predictor variables ($P = 0.48$). These missing values were replaced through imputation using the expectation maximization (EM) algorithm in SPSS missing value analysis (Tabachnick and Fidell, 2007). All continuous variables were standardized prior to analysis.

Independent samples t -tests and χ^2 analyses were used to examine any differences between the two recruitment sites. The relationship between non-attendance for semen analysis and demographic, medical/laboratory and psychological variables was examined using univariate logistic regressions. The extent to which these simple relationships were independent of each other in predicting non-attendance was determined by multivariable hierarchical logistic regression analysis.

All naturally continuous variables were entered as predictors in logistic regression models. Following Hosmer and Lemeshow (2000), we tested for significant non-linearity in the relationship of the continuous predictors with the logit of the dependent variable. We found no evidence this assumption was violated in any analysis and there was no evidence the multiple predictor models suffered from multicollinearity.

Treatment of scales

Reliability analyses were conducted for all scales and were good for health and well-being (Ware et al., 1995: the Cronbach alpha for PCS and MCS was 0.83 and 0.85, respectively); current late effects and perceived vulnerability (Absolom et al., 2006: alpha = 0.92 and for the scales experience of banking sperm (alpha = 0.64) and attitudes to disposal (alpha = 0.84).

However, initial reliability for the other scales fell below that considered acceptable and further analyses were conducted.

A principal component exploratory factor analysis with varimax rotation on the items in 'Views about follow-up' resulted in a two-factor solution explaining 56.8% of the variance. We identified a scale to measure 'Importance of fertility monitoring' that included three items; 'I don't want to know if my fertility has recovered or not', 'Information about the quality of my sperm will make no difference to my behaviour' and 'I don't think it's worth taking time off work to find out about my fertility' (Cronbach's alpha = 0.73). A second factor reflected 'Confidence in fertility recovery': 'I am certain my fertility has already or will recover' and 'I am confident my fertility is normal/as good as any other man of my age' (Cronbach's alpha = 0.93).

The same procedure was conducted for the scale children and parenting (alpha = 0.41) but no simple factor structure was identified. All five items of the 'children and parenting' scale were subsequently analysed separately.

Differences between sperm banks

Both of the sperm banks in Sheffield and Nottingham were established in the mid-1980s and are similar in size and organization. Each is licensed by the Human Fertilisation and Embryology Authority and during the study was managed alongside specialist Andrology Laboratories that undertook diagnostic procedures according to World Health Organisation (1999) methods for local General Practitioners, Gynaecologists and Urologists as well as men who had banked sperm there. Both were members of the UK National External Quality Assurance Schemes in Andrology. While some laboratory methods (e.g. the technique used to measure semen volume) and aspects of sperm bank administration (e.g. the style and content of previous letters to patients) were different between the sperm banks, they were not considered to be relevant to the study and data from both sites were combined.

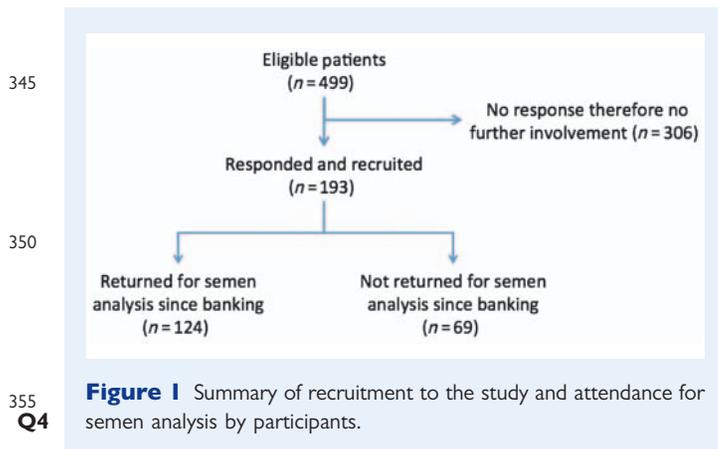
Results

Of the 499 men eligible to participate in the study, 193 (Sheffield = 114; Nottingham = 79: response rate of 38.7%) consented and returned completed questionnaires (Fig. 1). The mean age \pm standard deviation was 35.05 ± 7.08 years (range = 21.58–54.34) and their samples had been banked for 9.18 ± 3.70 years (range = 4.94–26.21). Men were on average 26.00 ± 6.45 years old (range = 14.18–42.46) at the time their samples were banked.

The most common diagnosis was Testicular cancer ($n = 85$: 44.0%), followed by Lymphoma ($n = 46$: 23.8%), Leukaemia ($n = 28$: 14.6%) and other cancers ($n = 17$: 8.8%). No diagnosis information was available for 17 men (8.8%). Thirty-seven (19.2%) experienced a relapse subsequent to the original diagnosis and underwent further cycles of treatment [time between initial treatment and treatment for relapse was $2.15 \text{ years} \pm 2.08$ (range = 0.22–9.01 years)].

Treatment information was available for 159 men, of whom 54.7% ($n = 87$) had received chemotherapy, 15.7% ($n = 25$) radiotherapy and 22.6% ($n = 36$) a combination of both. No treatment had been given to the remaining 6.9% ($n = 11$) who were maintained on a surveillance protocol: of these 10 had been diagnosed with testicular cancer and one was recorded as 'other'.

Overall, 35.8% [95% confidence interval (CI) = 28.9–42.7, $n = 69$] had never attended semen analysis, 32.6% (95% CI = 25.9–39.3, $n = 63$) had attended only once and 31.6% (95% CI = 24.7–38.5, $n = 61$) had attended twice or more. Attenders had returned between one



360 and six times (mean = 1.83 ± 1.15). Preliminary analysis revealed few differences between men who had attended once and those who had attended twice or more so these groups were combined (Fig. 1). Subsequent comparisons were made between 'non-attenders' ($n = 69$) and 'attenders' ($n = 124$). There was no significant association between non-attendance for semen analysis and oncology follow-up post-treatment ($\chi^2(1) = 2.65$; $P = 0.104$).

365 Non-attenders were significantly more likely to report being unemployed (29 versus 16.4%, respectively) and single (30.4 versus 13.0%, respectively) compared with attenders (Table I). Non-attenders were less likely to have adverse treatment side effects recorded in their oncology notes (11.9 versus 37.6%) and had been sent significantly fewer letters of invitation to attend for semen analysis (3.67 ± 1.74 versus 4.31 ± 2.06 ; Table II).

370 Non-attenders were significantly more likely to report a negative experience of sperm banking (1.94 ± 0.47 versus 1.80 ± 0.39) or knowing the quality of their banked sperm was less useful (1.84 ± 0.86 versus 1.56 ± 0.74) and a more negative attitude to disposal of their stored semen (3.56 ± 0.75 versus 3.27 ± 0.83) than men who had attended (Table III).

375 In a subsequent multivariate hierarchical logistic regression, the demographic, medical and psychological variables identified above were entered in three steps (Table IV). Only three of these variables contributed uniquely to 'non-attendance'. The odds of being a non-attender were significantly greater for men who did not experience adverse treatment side effects [odds ratio (OR) = 5.72, 95% CI = 2.10–15.56], for men who reported a more negative experience of banking sperm (OR = 1.82, 95% CI = 1.17–2.82) and men with a more negative attitude to disposal (OR = 1.56, 95% CI = 1.01–2.42).

390 Discussion

395 The first aim of this study was to determine the proportion of men who did not return for semen analysis after banking sperm following cancer treatment. Approximately one-third (35.8%) of men in our sample had declined all invitations to attend for semen analysis over the 5–26-year period that their sperm had been banked. Previous authors (e.g. Wasserman et al., 1987; Tomlinson and Pacey, 2003) have commented that cancer survivors seem reluctant to attend for semen analysis, but this has not been examined systematically. Van Casteren et al. (2008) noted that 61% of 557 men had not returned

400 **Table 1** Univariate logistic regressions of demographic variables to identify predictors of non-attendance for semen analysis.

405

410

415

420

425

430

Variable	n (%)	OR (95% CI)	Significance
Age (years)		1.16 (0.87–1.57)	0.315
Relationship status			
Single	155 (80.7%)	2.90 (1.39–6.04)	0.005
Partner (Ref)	37 (19.3%)		
Age left full time education			
Under 18 year	108 (56.2%)	0.81 (0.45–1.47)	0.484
Over 18 years (Ref)	84 (43.8%)		
Employment			
Not working	40 (20.8%)	2.08 (1.03–4.22)	0.042
Working (Ref)	152 (79.2%)		
Ethnic group			
White	184 (95.8%)	0.55 (0.13–2.26)	0.403
Other (Ref)	8 (4.2%)		
Living status			
Other	61 (31.8%)	0.74 (0.39–1.38)	0.339
Partner (Ref)	131 (67.9%)		
Number of children		1.06 (0.79–1.42)	0.711
Current distance from sperm bank		1.29 (0.96–1.75)	0.095

On continuous variables ORs are for a one standard deviation increase.

^aDemographics missing for one patient.

Significance level $P < 0.05$ (in bold).

435 for semen analysis over an average follow-up period of 7 years (range = 2–23), considerably higher than in our study population.

440 Second, we sought to identify significant predictors of non-attendance. These included being single and unemployed (Table I), but neither of these demographic variables remained significant when taking into account medical and psychological variables. This was also true of the number of times men had been sent reminder letters to attend (Table II). How useful men considered it to know the quality of banked sperm also contributed to predicting non-attendance but again not when taking into account other variables that were measured (Table III). There was no difference between attenders and non-attenders in diagnosis or the type of treatment given.

445 Our multivariate analysis identified three variables that contributed uniquely to the decision men made to decline the offer of attending for semen analysis. A substantial effect was seen in relation to the presence or absence of treatment side effects recorded in the oncology records. The odds of non-attending were 5.72 times greater for men who did not experience side effects compared with men who experienced them (Table IV). It is possible that men not experiencing these symptoms may have felt their cancer treatment was less

450

455

Table II Univariate logistic regressions of (a) oncology and (b) andrology variables to identify predictors of non-attendance for semen analysis.

Variable	n (%)	OR (95% CI)	Significance
(a) Oncology variables			
Diagnosis			
Testicular	85 (48.3%)	1.15 (0.62–2.12)	0.665
Other (Ref)	91 (51.7%)		
Treatment			
Chemotherapy	87 (54.7%)	0.57 (0.16–2.03)	0.385
Radiotherapy	25 (15.7%)	0.94 (0.23–3.92)	0.936
Combined	36 (22.6%)	0.53 (0.13–2.10)	0.365
No treatment (Ref)	11 (16.9%)		
Treatment side effects			
Yes	54 (32.1%)	5.63 (2.35–3.45)	<0.001
No (Ref)	114 (67.9%)		
Other medical conditions			
Yes	32 (19.0%)	1.57 (0.72–3.45)	0.258
No (Ref)	136 (81.0%)		
Participation in clinical trial			
Yes	43 (74.4%)	0.64 (0.30–1.37)	0.253
No (Ref)	125 (25.6%)		
Not attendance at oncology follow-up			
Yes	39 (27.3%)	1.91 (0.89–4.08)	0.097
No (Ref)	104 (72.7%)		
Late effects recorded			
Yes	64 (37.9%)	0.61 (0.31–1.20)	0.150
No (Ref)	105 (62.1%)		
(b) Andrology variables			
Number of samples banked	–	1.30 (0.95–1.77)	0.104
Time banked (years)	–	1.06 (0.98–1.15)	0.157
Prebanking semen quality (motile concentration)	–	1.00 (0.99–1.01)	0.997
Number of invitations for semen analysis	–	0.84 (0.71–0.99)	0.033

(Ref), reference category. Significance level $P < 0.05$ (in bold).

‘damaging’ and therefore assumed their fertility was less likely to be affected. However, there was no difference between attenders and non-attenders in terms of any late effects men reported either now or in terms of their perception of their future vulnerability (Table II).

In addition to treatment-related side effects, men’s initial ‘experience of banking sperm’ was also associated with attendance, with those reporting a more negative experience more likely to be subsequent non-attenders. This measure included 11 items to assess experience, but it was not possible with the current data to identify exactly which aspects of the process coloured attendance. However, data from an interview study (Eiser *et al.*, 2011) suggest that men view sperm banking as just part of their oncology journey, accepting the oncologist’s advice and keeping appointments at the sperm bank in the same way that they keep appointments for other aspects of their treatment care plan, such as blood tests and scans. A negative experience recorded in this scale may therefore reflect more than what happened within the confines of the Sperm Bank, but include

other aspects of how the process was managed within the oncology team. Crawshaw *et al.* (2008) highlighted some of the other difficulties young men can experience, including practical difficulties to do with transport, or pressures from family members. If these findings are replicated, the implications are that initial negative experience of banking sperm or general oncological care may jeopardize the probability of a patient returning for semen analysis in the future.

Finally, men with more negative attitudes to disposal were less likely to attend for semen analysis. This may suggest that men are aware that one of the purposes of semen analysis is to consider the options regarding disposal. In previous work, we have found that men are often reluctant to agree to disposal even when they have no wish for children, in part because they see stored semen as a protection against future disease recurrence (Eiser *et al.*, 2011). We suggest that men’s reluctance to attend is a strategy they adopt to ensure they are put under no pressure to dispose. In fact, given the current requirements of the Human Fertilisation and Embryology Authority

Table III Univariate logistic regressions to identify psychological predictors of non-attendance for semen analysis.

Variable	OR (95% CI)	Significance
Health and well-being		
PCS	1.00 (0.96–1.03)	0.857
MCS	1.01 (0.98–1.04)	0.569
Current late effects and perceived vulnerability		
Perceived vulnerability	1.05 (0.78–1.42)	0.733
Total cancer problems	0.77 (0.55–1.08)	0.131
Experience of banking sperm	1.39 (1.03–1.88)	0.032
Information about fertility		
Quality of banked sperm ^a		
Good enough for fertility treatment	0.65 (0.34–1.22)	0.179
Do not know (Ref)		
Usefulness of knowing quality of banked sperm	1.41 (1.04–1.90)	0.025
Use of contraception ^a		
Never	0.65 (0.31–1.37)	0.254
Sometimes	0.61 (0.25–1.49)	0.280
All the time (Ref)		
Views to follow-up		
Confidence in fertility recovery	0.89 (0.67–1.20)	0.456
Importance of fertility monitoring	0.99 (0.74–1.34)	0.994
Attitude to disposal	1.47 (1.06–2.03)	0.020
Children and parenting		
Influence of cancer on wish for children in the future	1.06 (0.78–1.42)	0.726
Want for children in the future	0.91 (0.68–1.21)	0.506
Worry of health problems for future children using banked sperm	1.11 (0.82–1.49)	0.508
Worry of health problems for future children from cancer	1.10 (0.82–1.48)	0.525
Concerns about fertility before cancer	1.11 (0.83–1.48)	0.488

Predictors are standardized continuous scales unless otherwise indicated.

^aCategorical predictor variables.

Significance level $P < 0.05$ (in bold).

(2009), it is now more likely that those who do not attend, and therefore cannot demonstrate on-going infertility, may find their samples have been disposed after the initial 10 year consent period has elapsed.

It is interesting to consider those variables that were unrelated to whether or not men return for semen analysis. These include demographic variables such as age, number of biological children and level of education as well as oncology variables such as diagnosis, treatment and attendance at oncology follow-up. The fact that there was no relationship between non-attendance for semen analysis and oncology follow-up post-treatment suggests that our results do not simply reflect a general reluctance in these men to attend medical appointments.

There are considerable challenges in work of this kind, not least the difficulty of engaging men in the research process. Only 38.7% of those eligible agreed to take part. Similar reluctance of men to take part in studies concerned with fertility (Stewart et al., 2009) or post-vasectomy testing schedules (Chawla et al., 2004) has been described.

This may be related to the general stereotype that men seem reluctant to be involved in health care decisions (Kraemer, 2000). We do not know the characteristics of men who declined to take part and whether or not they agreed to attend semen analysis without completing the questionnaire, nor do we know if any of them chose to have semen analysis performed elsewhere (e.g. private sector). This has implications beyond the interpretation of our study, since health-care policy and advice given to patients about the prospect of recovering spermatogenesis is informed from audits which do not take into account the fact that not all men with banked sperm may have been tested (cf. Bahadur et al., 2005). We cannot conclude that men did not attend for semen analysis because they had fathered more children (and therefore knew they were fertile) because there was no difference in family size between attenders and non-attenders (Table I).

Second, some of the measures used in this study (e.g. experience of banking sperm) relied on men's recall of events many years previously. We know that cancer patients typically have a great deal of information to remember, much of which (40–80%) is forgotten immediately

Table IV Multivariate hierarchical logistic regression of demographic, medical and psychological variables predicting non-attendance for semen analysis (OR and 95% CIs are shown).

Variable	Demographic ($R^2 = 0.06$ (Nagelkerke))		Demographic + medical ($R^2 = 0.21$ (Nagelkerke))		Demographic + medical + psychological ($R^2 = 0.30$ (Nagelkerke))	
	OR (95% CI)	Significance	OR (95%CI)	Significance	OR (95% CI)	Significance
Relationship status (single) ^a	2.27 (0.97–5.34)	0.060	1.86 (0.75–4.62)	0.181	1.77 (0.68–4.59)	0.240
Employment Status (not working) ^a	1.73 (0.77–3.92)	0.186	1.74 (0.73–4.14)	0.209	1.25 (0.49–3.18)	0.641
No treatment side effects ^a			5.83 (2.27–14.96)	<0.001	5.72 (2.10–15.56)	0.001
Number of contacts (laboratory to patient)			0.81 (0.56–1.16)	0.251	0.70 (0.47–1.05)	0.083
Experience of banking sperm					1.82 (1.17–2.82)	0.007
Attitudes to disposal					1.56 (1.01–2.42)	0.048
Usefulness of knowing quality of banked sperm					1.21 (0.79–1.86)	0.373

Predictors are standardized continuous scales unless otherwise indicated.

^aCategorical predictor variables (for reference groups, see Tables I and III).

Significance level $P < 0.05$ (in bold).

and half recalled incorrectly (Kessels, 2003). If the same is true of men's recall of events that took place at the time of sperm banking, then we need to interpret these results with caution.

Although our findings suggest attendance for semen analysis was better than found in some earlier work (e.g. Van Casteren *et al.*, 2008) attendance is still considerably below optimal. Our distinction between attenders and non-attenders was based on attendance at least once, but as all those involved in this study were relatively long-term survivors it means the majority had missed some appointments. The challenge of encouraging attendance is considerable in that after a decade many men have been discharged from oncology follow-up and may recall little of the information given to them when they first banked sperm (Eiser *et al.*, 2011). In these circumstances, it is interesting to consider what men themselves gain from undergoing semen analysis.

We suggest that men may perceive there are few tangible benefits in attending for semen analysis. Attendance can bring to mind previous negative experiences around time of diagnosis, and raise questions about ongoing infertility that challenge self-esteem (Eiser *et al.*, 2011) and precipitate discussion about unwanted disposal. It is also easy to identify barriers to attendance including the need to ask for time off work.

Timely letters from the sperm bank may encourage attendance, but it is important to include clear information about possible benefits (e.g. access to assisted conception or information about changes to fertility). Framing information in terms of these benefits rather than focusing on disposal may contribute to improved attendance. Given the current UK Legislation that banked sperm can only be stored beyond 10 years if there is evidence of 'significant or premature infertility' (Human Fertilisation and Embryology Authority, 2009), it is

essential that men become better informed about the rationale underlying semen analysis. Our study suggests that this may involve correcting assumptions about the possible recovery of fertility after cancer treatment, and emphasizing the unlikely relationship between cancer treatment side effects and subsequent infertility.

Acknowledgements

The authors would like to thank Debbie Saxton (Sheffield) and Tracey Kohut (Nottingham) for their help with the recruitment procedures.

Authors' roles

A.A.P. and C.E. designed the study and were equally responsible for the conception and drafting of the paper. R.R. was responsible for the statistical analysis along with H.M. and E.W.; K.M., L.C.B., A.J.C., E.A.-C. and M.J.T. undertook patient recruitment and the collection of medical data.

Funding

This paper was supported by funding from Cancer Research-UK to C.E., A.A.P. and R.R. (C481/A8141). The views expressed are those of the authors.

Conflict of interest

None declared.

References

- Absolom K, Greenfield D, Ross R, Horne B, Davies H, Glaser A, Simpson A, Waite H, Eiser C. Predictors of clinic satisfaction among adult survivors of childhood cancer. *Europ J Cancer* 2006;**42**:1421–1427.
- Bahadur G, Nahadur G, Ozturk O, Muneer A, Wafa R, Ashraf A, Jaman N, Patel S, Oyede AW, Ralph DJ. Semen quality before and after gonadotoxic treatment. *Hum Reprod* 2005;**20**:774–781.
- Chawla A, Bowles B, Zini A. Vasectomy follow-up: clinical significance of rare non-motile sperm in postoperative semen analysis. *Urol* 2004;**64**:1212–1215.
- Crawshaw MA, Glaser AW, Hale JP, Sloper P. Young males' experiences of sperm banking following a cancer diagnosis—a qualitative study. *Hum Fertil* 2008;**11**:238–245.
- Eiser C, Arden-Close E, Morris K, Pacey AA. The legacy of sperm banking: how fertility monitoring and disposal are linked with views of cancer treatment. *Hum Reprod* 2011;**26**:2791–2798.
- European Society for Human Reproduction and Embryology. Taskforce 7: Ethical considerations for the cryopreservation of gametes and reproductive tissues for self-use. *Human Reprod* 2004;**19**:460–462.
- Feldschuh J, Brassel J, Durso N, Levine A. Successful sperm storage for 28 years. *Fertil Steril* 2005;**84**:1017.
- Horne G, Atkinson AD, Pease EH, Logue JP, Brison DR, Lieberman BA. Live birth with sperm cryopreserved for 21 years prior to cancer treatment: case report. *Hum Reprod* 2004;**19**:1448–1449.
- Hosmer DW, Lemeshow S. *Applied Logistic Regression*, 2nd edn. New York: Wiley, 2000.
- Human Fertilisation and Embryology Authority. *Code of Practice*, 8th edn. London: HFEA, 2009.
- Kessels RPC. Patients' memory for medical information. *J R Soc Med* 2003;**96**:219–222.
- Kraemer S. The fragile male. *Br Med J* 2000;**321**:1609–1612.
- Lee SJ, Schover LR, Partridge AH, Ann H, Patrizio P, Wallace H, Hagerty K, Beck LN, Brennan LV, Oktay K. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clinical Oncol* 2006;**24**:2917–2931.
- Little RJA. A test of missing completely at random for multivariate data with missing values. *J Am Stat Assoc* 1988;**83**:1198–1202.
- National Collaborating Centre for Women's and Children's Health. *Fertility: Assessment and Treatment for People with Fertility Problems*. London: Commissioned by the National Institute for Clinical Excellence, 2004. RCOG Press ISBN 1-900364-97-2.
- Pacey AA. Fertility issues in survivors of adolescent cancers. *Cancer Treat Rev* 2007;**33**:646–655.
- Pacey AA, Eiser C. Banking sperm is only the first of many decisions for men: What healthcare professionals and men need to know? *Hum Fertil* 2011;**14**:208–217.
- Royal College of Physicians. *The Effects of Cancer Treatment on Reproductive Functions. Guidance on Management*. London: Royal College of Physicians, 2007, 72 pp.
- Stewart TM, Liu DY, Garrett C, Brown EH, Baker HWG. Recruitment bias in studies of semen and other factors affecting pregnancy rates in fertile men. *Hum Reprod* 2009;**24**:240–248.
- Tabachnick BG, Fidell LS. *Using Multivariate Statistics*, 5th edn. Boston: Allyn and Bacon, 2007.
- Tomlinson MJ, Pacey A. Practical aspects of sperm banking for cancer patients. *Hum Fertil* 2003;**6**:100–105.
- Van Casteren NJ, van Santbrink EJ, van Inzen W, Romijn JC, Dohle GR. Use rate and assisted reproduction technologies outcome of cryopreserved semen from 629 cancer patients. *Fertil Steril* 2008;**90**:2245–2250.
- Ware JE, Kosinski M, Keller SD. *How to Score the SF-12 Physical and Mental Health Summary Scales*. Lincoln: QualityMetric Inc, 1995.
- Wasserman AL, Thompson EI, Williams JA, Fairclough DL. The psychological status of survivors of childhood/adolescent Hodgkins disease. *Am J Dis Child* 1987;**141**:626–631.
- World Health Organisation. *WHO Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction*, 4th edn. Cambridge, UK: Cambridge University Press, 1999.