Journal of Genetic Counseling, Vol. 14, No. 6, December 2005 (© 2005)
DOI: 10.1007/s10897-005-6192-y

Psychological Adjustment and Knowledge About Hereditary Hemochromatosis in a Clinic-Based Sample: A Prospective Study

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Published Online: 29 December 2005

This study assessed psychological adjustment and quality of life relative to population-based norms and knowledge about hereditary hemochromatosis in a sample of 101 patients who attended a hemochromatosis clinic. Participants were assessed prior to their clinic visit, and two weeks and 12 months after attendance, using self-administered questionnaires. Mean Mental Health Component Scores from the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (45.3, 95% CI 43.2, 47.4) were as compromised as those found amongst stroke victims (45.9, 95% CI 42.8, 49.0) who had participated in a national health survey. Recall of the genetic testing result was less than optimal, in that only 69.3% of those with genetic testing results knew whether they carried one or two mutations. This study demonstrates that patients would benefit from routine assessment of psychological distress and referral to mental health professionals of those whose levels of distress suggest a need for clinical intervention. Results also show that patients may benefit from strategies aimed at improving recall of genetic testing results.

KEY WORDS: hereditary hemochromatosis; psychological adjustment; knowledge; screening behaviors.

INTRODUCTION

Hereditary hemochromatosis is an autosomally inherited disorder of iron metabolism, which increases susceptibility to develop iron overload and can therefore lead to hepatic cirrhosis, primary liver cancer, diabetes mellitus and other endocrinopathy, arthropathy, cardiomyopathy and reduced life expectancy (Burke *et al.*, 1998a; Powell, 2002). The carrier rate is estimated to be 1 in 10 amongst people of Western European descent, and serum iron screening studies suggest a prevalence of hereditary hemochromatosis of between 1 in 200 and 1 in 400 persons (Adams, 1995; Burke *et al.*, 1998a; McLaren *et al.*, 2003). Hereditary hemochromatosis is one of the few genetic diseases for which an effective therapy exists, namely the removal of iron through therapeutic venesection (Adams, 1995; Burke *et al.*, 1998a).

Many uncertainties continue to exist with regard to the epidemiology and genetics of hemochromatosis. In particular the penetrance of hemochromatosis genotypes is uncertain, and estimates vary widely between studies (Burke *et al.*, 1998a),

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raising issues of case definition. The identification of a hemochromatosis gene candidate, *HFE*, led to the identification of the most common pathogenic mutations, C282Y and H63D (Feder *et al.*, 1996). These mutations have been identified in many hemochromatosis populations throughout the world, and the majority of affected people show homozygosity for C282Y. Most studies indicate a penetrance rate of between 60% and 100% amongst people who are homozygous for C282Y (Burke *et al.*, 1998a; Jazwinska *et al.*, 1996). However, other population-based studies indicate lower penetrance rates (Beutler *et al.*, 2002; Olynyk *et al.*, 1999), with Beutler *et al.* reporting that only 1% homozygotes had frank disease (Beutler *et al.*, 2002). Interestingly, 77% of his subjects had raised serum ferritin (Beutler *et al.*, 2002), indicating that the criteria used to determine clinical caseness are critical to the reporting of penetrance rates.

Similar to other genetic disorders, hemochromatosis is genetically complex. For example, in addition to C282Y and H63D, other mutations in *HFE* have been described, which means that if a person clinically affected with hemochromatosis has only one identifiable hemochromatosis mutation, a distinction from heterozygote carrier status cannot be made (Burke *et al.*, 1998b).

Because people with hemochromatosis can be identified before symptoms occur and an effective therapy exists, population-based screening has been advocated (Cogswell *et al.*, 1999; McLaren *et al.*, 2003; Nisselle *et al.*, 2004), although whether or not to screen the general population continues to be subject to debate (Allen and Williamson, 1999; Bomford, 2002; Gertig *et al.*, 2002). However, it is accepted clinical practice to genotype patients with symptoms that could be caused by iron overload and relatives of previously identified index cases (cascade testing) (Bomford, 2002).

Uncertainties about genotype-phenotype correlations in hemochromatosis indicate the need for an assessment of the psychosocial effects of genetic testing and counseling and the efficacy of patient education. Recent reports document attitudes to, and the psychosocial impact of, genetic testing for hemochromatosis (Bassett *et al.*, 2001; Hicken *et al.*, 2003; Hicken *et al.*, 2004; Power and Adams, 2001). Attitudinal surveys show that a majority of respondents report being interested in genetic testing for hemochromatosis (>80% of all participants) (Hicken *et al.*, 2003). Interest in neonatal screening is also very high, with over 90% of pregnant women and their partners reporting interest in screening (Bassett *et al.*, 2001). The most commonly perceived benefit was improved health through early detection/prevention (Hicken *et al.*, 2003; Hicken *et al.*, 2004), and the most commonly reported limitation was discrimination on genetic grounds (Hicken *et al.*, 2003). Using a prospective design, Power et al. showed that that genetic testing did not lead to any adverse effects on anxiety or mental and physical health status, and should therefore not be discouraged on the basis of potentially adverse psychosocial effects (Power and Adams, 2001).

To our knowledge, no studies are available that report quality of life data on people with, or at risk for, hemochromatosis relative to population norms. Moreover, almost no data are available on patients' understanding of the genetics of hemochromatosis and the meaning of their testing results. To fill this gap in knowledge, this study was undertaken to describe understanding of the genetics of hemochromatosis and the meaning of test results amongst people attending a hemochromatosis clinic. Secondary aims of the study were to assess psychological adjustment, quality of life and adherence to medical recommendations.

METHODS

Participants were recruited through a hemochromatosis clinic located at a major teaching hospital in Brisbane, Australia, between February 2001 and May 2003. All participants were seen by a single clinician (LWP). Most patients attending the clinic had been referred for diagnostic evaluation of symptoms, genetic testing for hereditary hemochromatosis, advice regarding early detection and preventative strategies, and/or standardized patient education tailored to individual needs, which was documented in patient charts. Participants were assessed at three time points: (i) just prior to their clinic visit; (ii) 2 weeks and (iii) 12 months after clinic attendance, using self-administered questionnaires that included standardized measures of psychological and quality of life outcome. Patients were considered ineligible for study participation if they were unable to give informed consent or had limited literacy in English, since data were collected using self-report questionnaires. The study was approved by the institutional ethics committee at the Royal Brisbane Hospital.

Clinic staff invited potential participants to be involved in the study in the waiting room and participants completed baseline questionnaires and consent forms prior to their clinic visit. Follow up questionnaires with reply paid envelopes were mailed 2

weeks and 12 months post-consultation. A replacement questionnaire was mailed if completed questionnaires were not received within 4 weeks.

Measures

Demographic Characteristics

At baseline, data were collected on age, educational level, marital status, and number of biological children were assessed.

Clinical Variables

Data on clinical variables (ferritin level, mutation status, presence of family history of hemochromatosis) were extracted from clinical records. Participants were categorized as either low or high in ferritin level based on published criteria (Leggett, 1996). Specifically men (women) younger than 30 years with ferritin levels above 250 μl/l (150 μl/l), and men (women) 30 years old and over with ferritin levels greater higher than 350 μl/l (250 μl/l) were categorized as high in ferritin levels. In addition, the clinician involved in the study categorized participants as either clinically unaffected or affected with hemochromatosis based on published criteria, which include presence of diabetes, cardiac involvement, endocrine dysfunction, stigmata of the liver and cirrhosis (Powell, 2002).

Genetics of Hemochromatosis Knowledge

This seven-item true-false measure was administered 2 weeks and 12 months post-consultation. It assesses knowledge about the genetics of hemochromatosis. Items are listed in Fig. 1 and were generated based on expert consultation and a review of the literature.

Understanding of Testing Result

Two weeks post-consultation, participants were asked whether they had been found to have one gene change, two gene changes or whether they could not remember. Participants' understanding of their testing result was assessed, because incorrect understanding of one's mutation status might lead to adoption of or continuation of inappropriate screening and preventative behaviors.

Impact of Event Scale (IES)

The seven-item Intrusion Subscale of the IES was used to measure the frequency and severity of intrusive thoughts about hemochromatosis, and was administered two-weeks post-consultation only. A previous validation study found that the subscale has good internal consistency (Cronbach's alpha $r =$ (0.88) and test-retest reliability $r = (0.75)$ (Thewes *et al.*, 2001). Cronbach's alpha in our sample was 0.89. In the current study, the particular stressor was concern about hemochromatosis. Participants were asked to rate symptoms of distress about hemochromatosis (for example, 'I had strong waves of feelings about hemochromatosis') on a scale ranging from 'Not at all' to 'Often'. A score of 20 or higher on the Intrusion Subscale of the Impact of Event scale is considered to be strongly predictive of a significant stress response syndrome (Cella *et al.*, 1990).

Uptake of Screening and Preventative Measures

At the 12-months follow up, participants were asked whether they had ever undergone a screening test (iron studies) and/or a preventative measure (venesection) and, if so, were asked to specify when.

The following measures were administered at all three time points: *State component of the State-Trait Anxiety Inventory—Short version (STAI-State):* A previously validated six-item short version of the State scale of the Spielberger State-Trait Anxiety Inventory was included as a measure of situational anxiety (Marteau and Bekker, 1992). The STAI-State was chosen as measure of generalized anxiety, because it has been used in several related studies (Michie *et al.*, 2002), and general population norms are available. The STAI-State asks respondents to indicate how they feel 'right now, at this moment' and to rate particular symptoms (for example, 'I feel worried') on a scale ranging from 'not at all' to 'very much' (Spielberger, 1983). Scores range from 20 to 80.

Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)

This measure was used to assess health-related quality of life, which has been used extensively and has well-established psychometric properties (McHorney *et al.*, 1994; McHorney *et al.*, 1993; Ware and Sherbourne, 1992). The SF-36 provides indicators across eight dimensions of health and well-being

as follows: Physical functioning, Role-physical, Bodily pain, General health, Vitality, Social functioning, Role-emotional and Mental health. Except for Physical Functioning and General health, the dimensions focus on aspects of health and well-being during the four weeks prior to interview. Scores for all dimensions range from 0 to 100, with higher scores indicating better health or well-being. The SF-36 has two summary indices, the Physical Component Summary (PCS) and the Mental Component Summary (MCS), which are derived using weighted US norm-based averages of the individual domain scores (Ware and Kosinski, 2001). Specifically, general US population averages are exactly 50 (standard deviation of 10) for both SF-36 component summaries. The standard deviation is 10 for both the PCS and the MCS.

Statistical Analysis

Data were analyzed using SPSS 11.5 (Statistical Program for the Social Sciences). Descriptive statistics were used to describe the sample in terms of sociodemographic, clinical and psychological characteristics, knowledge about the genetics of hemochromatosis and screening behaviors. To examine changes in psychological and quality of life outcomes over time, a Friedman test was conducted for quality of life scores (which were not normally distributed) and a one-way analysis of variance for anxiety scores. Bivariate associations between baseline predictor variables, on the one hand, and baseline psychological and quality of life outcomes variables, on the other, were examined, using Kendall's rank correlation or Pearson's product-moment correlation coefficient, as appropriate, for continuous outcome and predictor variables; using *t*-tests or Mann-Whitney *U* tests, as appropriate, where one variable is continuous and the other is binary; and using chi-squared tests where both outcome and predictor variable are binary. The following sociodemographic and disease-related variables were assessed as possible predictor variables or potential confounders in these analyses: age, sex, marital status, educational level, disease status and ferritin level.

RESULTS

Characteristics of Sample

All of the 101 patients who were invited to participate in the study completed the baseline questionnaire. Of these, 74 (73.3%) and 62 (61.4%) also completed the two-week and 12-months post-consultation questionnaires. There were no statistically significant differences between participants who were retained and those lost to the 12-month follow up ($n = 39$), in terms of age, sex, disease and mutation status (homozygous/compound heterozygote versus heterozygote), and Physical Component Summary scores of the SF-36. However those who were lost to follow up were more likely not to have post-school education (Pearson $\chi^2 = 5.3$; $p = 0.021$) and had significantly lower Mental Component Summary scores (Mann-Whitney $z = -2.1$; $p = 0.031$), indicating worse mental health.

Table I shows sociodemographic and clinical variables of the study sample. The mean age of the sample was 45 years, ranging from 18 to 69. The sample included 61 (61.6%) male and 38 (38.4%) female participants. Forty-eight percent (47.5%) of participants had a family history of hemochromatosis, and the remainder were probands who had been referred due to clinical symptoms. Seventy-four (77.9%) participants were homozygous or compound heterozygous for C282Y and/or H63D, and 21 (22.1%) were heterozygous for C282Y or H63D. A total of 30 (31.3%) participants were categorized as being clinically affected, that is as clinically expressing hemochromatosis, and 66 (68.8%) as clinically unaffected. Amongst those categorized as clinically unaffected, 46 were homozygous or compound heterozygous for C282Y and/or H63D, and showed biochemical expression (that is elevated ferritin levels, $N = 41$, 63.1%) or did not express any symptoms ($N = 5$, 7.7%). The remaining participants ($N = 18$, 27.3%) were simple heterozygotes, who subsequently received the following diagnoses: non-alcoholic steatohepatitis (NASH) ($N = 5$), fatty liver disease ($N = 4$), alcoholic liver disease ($N = 1$), abnormal liver enzymes ($N = 2$), Gilbert's syndrome ($N = 1$), elevated serum ferritin ($N = 1$) and elevated serum ferritin following family screening ($N = 4$).

Psychological Distress Levels

Only one participant had a score greater than 20 on the Intrusion Subscale of the Impact of Event scale, which is indicative of a significant stress response syndrome (Cella *et al.*, 1990). Inspection of means did not suggest any changes across time points for the STAI-State and the PCS for both clinically unaffected and affected participants combined, and this was confirmed by statistical analyses. With

Table I. Sociodemographic and clinical variables of study sample ($N = 101$)

Variable	Level	*N*	%
Sociodemographics			
Age	<30	16	15.8
	30–39	17	16.8
	40–49	22	21.8
	50–59	37	36.6
	60+	9	8.9
Sex	Male	63	62.4
	Female	38	37.6
Marital status	Married	73	72.3
	Not married	28	27.7
Biological children	Yes	72	71.3
	No	29	28.7
Educational level	Post-school qualifications	77	65.3
	No post-school qualifications	24	23.8
Clinical variables			
Disease status	Clinically unaffected	66	68.8
	Clinically affected	30	31.3
Ferritin level[a]	Low	13	13.7
	High	82	86.3
Mutation status	Homozygous for C282Y	43	45.3
	Homozygous for H63D	11	11.6
	Compound heterozygote (C282Y & H63D)	20	21.1
	Heterozygote for C282Y	13	13.7
	Heterozygote for H63D	8	8.4
Family history of hemochromatosis[b]	Yes	48	47.5
	No	49	48.5

[a]Categorization into low and high levels of ferritin according to published criteria: men <30 years >250 μl/l; 30 years and over >350 μl/l; women <30 years >150 μl/l; and 30 years and over >250 μl/l) (Leggett, 1996).

[b]Presence of family history of hemochromatosis refers to people who were tested as a result of having a family history, as opposed to probands whose family members may have subsequently been screened and found to be carriers or homozygotes.

regard to the MCS, a statistically significant increase in the MCS score (that is better mental health) was observed at the 12-month follow up, compared to baseline.

Table II shows means and standard deviations for the STAI-State, the Intrusion Subscale of the Impact of Event Scale and the PCS and MCS of the SF-36 separately for clinically unaffected and affected participants and both combined. It also includes the results of significance tests for differences in scores between clinically unaffected and affected participants at each time point. Independent-samples *t*-tests showed no statistically significant differences between affected and unaffected participants for generalized anxiety scores, and Mann-Whitney *U* tests no differences in intrusive thoughts two weeks post-consultation. However, Mann-Whitney *U* tests demonstrated that clinically affected participants, compared to unaffected participants, had significantly lower scores on the PCS at baseline, and a trend for lower scores was observed two weeks post-consultation. Twelve months post-consultation, PCS scores were no longer significantly different. Further Mann-Whitney *U* tests showed trends for lower MCS scores amongst clinically affected compared to unaffected participants at baseline and 12 months post-consultation, but no differences two weeks post-consultation.

Figure 2 shows the mean scores for all SF-36 Subscales and the Component Summaries at baseline. For all indeces, clinically unaffected individuals had higher scores than affected individuals, and Mann-Whitney *U* tests showed that these differences were statistically significant for most subscales: Role-physical ($p < 0.001$), Bodily pain ($p = 0.039$), General health ($p = 0.01$), Vitality ($p = 0.01$), Social functioning ($p = 0.017$) and Mental health ($p = 0.02$). A trend for differences between clinically unaffected and affected participants was observed for Role-emotional ($p = 0.092$), and no statistically significant differences were found for Physical Functioning ($p = 0.20$).

Table II. Means and standard deviations for psychological and quality of life outcome scores ($N = 101$)

		Baseline			2-weeks post-consultation				12 months post-consultation			
Measure	*N*	Mean (*SD*)	t/z^a	p^a	*N*	Mean (*SD*)			*N*	Mean (*SD*)		
STAI-State[b]												
Unaffected	59	45.8 (7.6)	−.13	.89	38	44.6 (7.1)	.90	.37	21	43.2 (5.9)	.76	.45
Affected	26	45.5 (8.6)			18	46.5 (7.1)			16	44.6 (5.1)		
Total	89	45.8 (7.7)			58	45.1 (7.0)			37	43.8 (5.6)		
IES[c]												
Unaffected	N/A				44	4.0 (5.8)	−.70	.48	N/A			
Affected	N/A				21	5.6 (6.8)			N/A			
Total	N/A				68	4.6 (6.2)			N/A			
PCS[d]												
Unaffected	59	49.0 (7.7)	−2.4	.02*	42	47.8 (9.4)	−1.8	.06	23	45.1 (11.5)	−.70	.50
Affected	28	42.9 (10.7)			20	43.6 (10.0)			17	41.1 (14.0)		
Total	91	46.9 (9.4)			65	46.4 (9.7)			40	43.4 (12.6)		
MCS[e]												
Unaffected	59	46.7 (9.7)	−1.9	.06	42	47.2 (9.8)	−1.4	.17	23	51.0 (8.5)	−1.8	.08
Affected	28	42.3 (10.5)			20	42.5 12.0)			17	45.7 (9.6)		
Total	91	45.3 (10.0)			65	45.6 (10.6)			40	48.7 (9.3)		

[a]Statistical findings refer to comparisons of mean scores between clinically affected and unaffected participants.
[b]STAI-State: State component of the State-Trait Anxiety Inventory Short Versions.
[c]IES: Impact of Event Scale.
[d]PCS: Physical Component Score of SF-36.
[e]MCS: Mental Component Score of SF-36.
*Significant at $p < 0.05$.

At baseline, Pearson's correlations and independent-samples *t*-tests showed no statistically significant associations between generalized anxiety and age (Pearson's $r = 0.017$, $p = 0.88$), sex ($t = 1.02$, $p = 0.31$), educational level ($t = 0.56$, $p = 0.57$), marital status ($t = 0.37$, $p = 0.72$) and ferritin levels ($r = 0.032$, $p = 0.77$). Likewise, Spearman's correlations and Mann Whitney U tests demonstrated no statistically significant associations between baseline PCS scores and age (Spearman's $r = -0.08$, $p = 0.53$), sex (Mann Whitney's $z = -0.19$, $p = 0.85$), educational level ($z = -0.18$, $p = 0.86$), marital status ($z = -0.029$, $p = 0.98$) and ferritin levels ($r = -0.077$, $p = 0.54$). Nor did Spearman's correlations and Mann Whitney U tests identify any significant associations for baseline MCS scores and age ($r = 0.19$, $p = 0.12$), sex ($z = -0.03$, $p = 0.98$), educational level ($z = -0.06, p = 0.95$), marital status ($z = -1.24$, $p = 0.22$) and ferritin levels ($r = 0.087$, $p = 0.49$).

Knowledge About Genetics of Hemochromatosis and Understanding of Testing Result

Figure 1 shows the percentages of participants who responded correctly to the items assessing knowledge about the genetics of hemochromatosis. For all items, the percentages responding correctly two weeks post-consultation ranged from 45.2% to 93.2%. Most participants responded correctly to items two (87.3%) and four (76.1%), which assessed understanding of the significance of carrying two and/or one mutation for hemochromatosis respectively. Ninety-three percent knew that regular removal of blood will avoid or reduce many of the symptoms of hemochromatosis. By contrast, fewer participants (45.2%) knew that the 282Y mutation is found in most people with hemochromatosis.

Understanding of genetic testing results for hemochromatosis was also assessed. Genetic testing results were available for 95 participants. Amongst these, 80 participants (84.2%) had learnt their genetic testing result prior to their attendance at the clinic through another health professional, and 15 (15.8%) learnt their result at the clinic through the clinician involved in this study (LWP). Table 3 shows the numbers and percentages of participants in each mutation status group (homozygotes, simple heterozygotes, compound heterozygotes) who believed that they had either one or two gene changes or reported that they could not remember. Amongst all homozygotes, compound heterozygotes and heterozygotes combined, 69.3% correctly stated the number of mutations they carried. There were

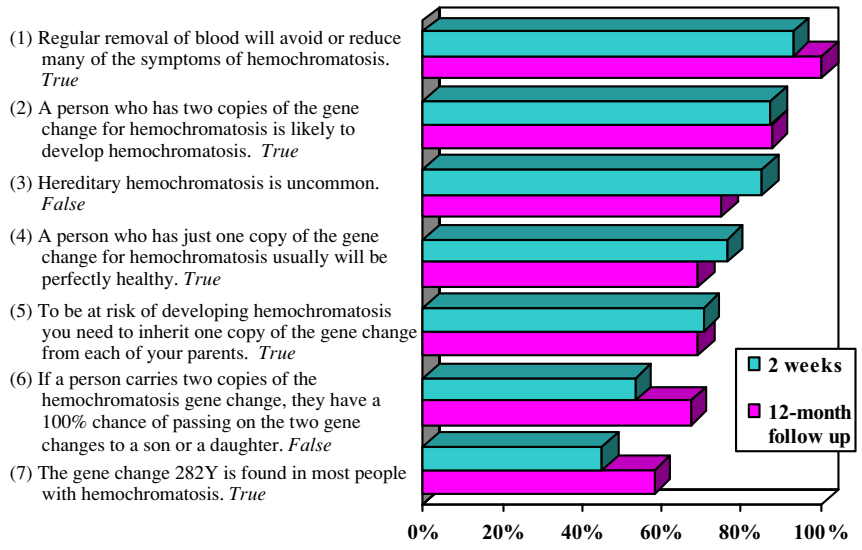

Fig. 1. Percentages responding correctly to hemochromatosis genetics knowledge items ($N = 101$).

no associations between educational level (Mann Whitney's $z = -1.06$, $p = 0.29$) and presence of a family history of hemochromatosis (Pearson's $\chi^2 = 0.40$, $p = 0.53$), on the one hand, and having an accurate understanding of the number of gene changes associated with one's particular genetic testing result, on the other.

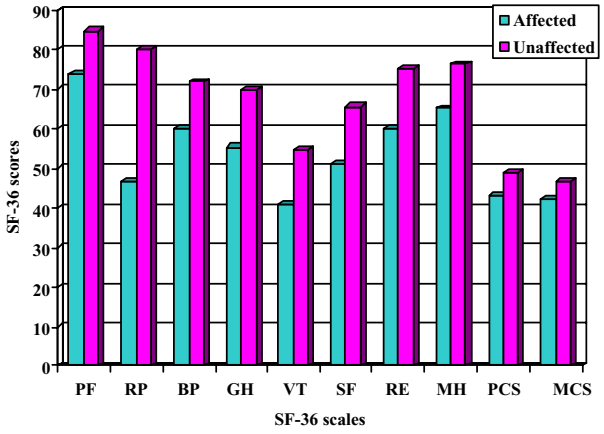

Fig. 2. Mean scores for SF-36 Subscales and the Component Summaries at baseline, separately for clinically affected and unaffected participants ($N = 101$), Health-related quality-of-life comparison between patients affected and unaffected by hereditary hemochromatosis. PF: Physical function; RP: Role-physical; BP: Bodily pain; GH: General health; VT: Vitality; SF: Social functioning; RE: Role-emotion; MH: Mental health; PCS: Physical Component Summary scores for SF1; MCS: Medical Component Summary scores for SF1).

Uptake of Iron Studies and Venesection

At the 12-month follow up, all participants for whom iron studies are recommended (that is homozygotes and compound heterozygotes) reported having ever had iron studies, and 96% reported having had iron studies in the past year. At the 12-month follow up, 62% of those participants who had increased serum ferritin at baseline as per published cut-off points (Leggett, 1996) reported ever having had a venesection, and 57% reported having undergone a venesection in the past year, which included any that may have been carried out at the actual clinic visit.

DISCUSSION

Psychological Adjustment and Quality Life

To our knowledge, this is the first study amongst people at risk for hemochromatosis to provide quality of life data using the SF-36, relative to general population norms. Our data show that, for both clinically unaffected and affected individuals combined, baseline means for the Physical Component Score (46.9, 95% CI 45.0, 48.8) and the Mental Health Component Score (45.3, 95% CI 43.2, 47.4) were below the mean Physical (49.7) and the Mental Health Component Scores (50.1) for a large Australian general population-based sample ($N = 18,468$) with a similar age and sex distribution

Table III. Participants' understanding of the number of gene changes involved two weeks post-consultation (N (101)[a]

	Beliefs about number of gene changes involved							
Participant's mutation status	One gene change		Two gene changes		Unable to remember		Total	
Homozygous for C282Y or H63D	No	%	**No**	**%**	No	%	No	%
	7	16.7	**28**	**66.7**	7	16.7	42	100
Heterozygote for C282Y or H63D	**No**	**%**	No	%	No	%	No	%
	12	**63.2**	3	15.8	4	21.1	19	100
Compound heterozygote (C282Y & H63D)	No	%	**No**	**%**	No	%	No	%
	4	23.5	**10**	**58.8**	2	17.6	16	100

[a]Correct responses are bolded.

(Australian Bureau of Statistics, 1997), by about one third and half a standard deviation respectively. When clinically unaffected participants were considered separately, the baseline Mental Component Score (46.7, 95% CI 44.2, 49.2) still indicated somewhat poorer mental heath compared to the general population norm, while the Physical Component Score (49.0, 95% CI 47.0, 51.0) was comparable with the Australian norm. Consistent with these findings were the high STAI-State scores, indicating increased levels of generalized anxiety, both amongst clinically unaffected and affected participants combined (45.8, 95% CI 44.2, 47.4) and unaffected participants separately (45.8, 95% CI 43.9, 47.7). No Australian general population norms are available for the STAI-State; however US norms show mean scores of 35.7 (SD 10.4) and 35.2 (SD 10.6) amongst a general population sample of 1,387 male and 451 female adults respectively with similar age and sex distributions (Spielberger, 1983).

Comparisons of the mean Physical and Mental Health Components scores in our sample with data from a large Australian National Health Survey that examined SF-36 profiles of those with and those without particular types of conditions indicate that the mean Physical Health Component score of people with cancer (44.6) and those with diabetes (44.0) were similar to those found in our sample (Australian Bureau of Statistics, 1997). Also, Mental Health Component scores were lower for all conditions examined, compared to mean scores amongst people without serious physical conditions, although the extent to which mental health was impacted on was variable, ranging from a score of 45.9 (stroke victims) to 48.3 (people with arthritis) (Australian Bureau of Statistics, 1997). These data suggest that the level of mental health in our sample is as compromised as it is amongst stroke victims, which is a cause for concern.

Two previous studies involving patients with a clinical diagnosis of hereditary hemochromatosis and/or homozygotes who had been identified through a population-based screening study provide quality of life data using the SF-36, but do not report norm-based Physical and Mental Health Component scores (Adams and Speechley, 1996; Power and Adams, 2001), and/or only report mean subscale scores for patients with and without particular symptoms, and hence comparisons with our SF-36 data are not possible. Future studies involving larger samples of people with hemochromatosis are now needed to assess quality of life and psychological distress (anxiety, depression) to substantiate the low levels of mental health found in this study. If confirmed, this would indicate that patients would benefit from routine assessment of psychological distress using standardized measures with referral for psychiatric or psychological assistance of those whose levels of distress suggest a need for clinical intervention. Additional systematic studies would also be required to study the neurophysiological basis for the observed impairments in mental health.

The Impact of Event Scale was administered to measure the frequency and severity of intrusive thoughts and hence the subjective impact as a result of a particular stressor (in this case, hemochromatosis). The mean intrusive thoughts score (4.6, $SD =$ 6.2) is higher than that found amongst people undergoing risk factor testing for bladder cancer (2.2, $SD = 0.87$) (Hornsby *et al.*, 1985), but lower than that of women at increased risk for breast/ovarian cancer (7.5, $SD = 7.1$) (Meiser *et al.*, 2003), indicating only moderately high levels of intrusive thoughts within our clinic sample.

Knowledge About Genetics of Hemochromatosis and Genetic Testing Result

Our findings on knowledge about the genetics of hemochromatosis are quite consistent with those from a study involving participants in a

population-based screening program for hemochromatosis, who had participated in an educational presentation about hemochromatosis in the workplace setting (Nisselle *et al.*, 2004). Participants in this population-based screening study also showed a good understanding of the underlying cause of hereditary hemochromatosis and how it can be prevented (Nisselle *et al.*, 2004). In our sample, it is most likely that participants' understanding of these issues was acquired at the hemochromatosis clinic through which they had been ascertained for participation in this study. Also, some participants may have had repeated exposure to information about hemochromatosis, whether through communication with other family members, general practitioners and specialists or self-motivated research activities.

This study also identified gaps in knowledge. Specifically, 30% of participants did not know whether they carried one or two hemochromatosis-related mutations. This is of some concern as it suggests that screening and preventative plans amongst patients who are misconceived about their mutation status might be misdirected. This finding is consistent with other studies that showed inaccurate recall and/or misunderstandings in about one third to one fifth of people who had undergone genetic testing for cystic fibrosis, another recessively inherited disorder (Axworthy *et al.*, 1996; Bekker *et al.*, 1994). Our results underscore the importance of further efforts at patient education amongst people being tested for hemochromatosis and other recessively inherited disorders. In particular, additional patient education tools, such as visual communication aids, might be useful in assisting this group of patients to acquire and retain knowledge about their mutation status and its implications (Lipkus and Hollands, 1999).

Uptake of Iron Studies

Almost all participants for whom iron studies are recommended reported having had iron studies in the past year, suggesting that uptake of a screening test for a disorder for which an effective preventive therapy exists is excellent. Uptake of screening is considerably higher than that amongst people who have had genetic testing for susceptibility to other diseases. For example, in a study amongst carriers of BRCA1/2 breast cancer gene mutations only 68% of women had mammographic screening one year following genetic testing (Lerman *et al.*, 2000). Another study reports that 71% of carriers of mutations related to hereditary non-polyposis colorectal cancer (HNPCC) had a colonoscopy within one year of genetic testing (Collins *et al.*, Submitted). The relatively low uptake of mammography may be related to the current lack of efficacy of mammographic screening amongst high-risk women (Kerlikowske *et al.*, 1996). In HNPCC, by contrast, the efficacy of colonoscopy in reducing incidence and mortality from colorectal cancer has been demonstrated (Jarvinen *et al.*, 2000); however colonoscopy is not a convenient screening procedure to undergo. These differences suggest that screening uptake may be related to the preventability of a disorder and the ease with which a particular screening behavior can be performed; however more research (including experimental studies) is needed to conclusively demonstrate a causal relationship.

Having discussed the implications of the study's findings, its strengths and limitations should be mentioned. Validated measures of psychological and quality of life outcomes were administered at three time points over a 12-month period, which is decidedly different to measuring psychological outcomes on a single occasion in the context of a hemochromatosis-related event, such as a clinic visit (McCaul *et al.*, 1998), and allowed us to examine the stability of the variables examined. The relatively low follow up rate (61% at 12 months follow up) and the presence of differences between those lost to follow up and those retained are limitations of our study. Specifically, participants who were lost to follow up were less likely to have post-school education and had significantly lower MCS scores, indicating lower mental health. Indeed, this differential drop out might be the reason for our finding of an apparent increase in MCS scores (and hence better mental health) at the 12-month follow up. Hence caution is warranted in interpreting this apparent change in mental health. The possible impact of having a two-year time frame for patient accrual must also be considered; in particular unmeasured factors such as media events or changes in service provision have the potential to impact on study findings. Knowledge about the genetics of hemochromatosis and intrusive thoughts about hemochromatosis were only assessed at one time point, which does not allow for changes across time to be examined. It should also be noted that our measure of knowledge about hemochromatosis has not been validated and hence its reliability and validity characteristics are unknown. Finally, it is likely that provider and patient characteristics and communication behaviors, such as the way the information about their testing result is presented to patients, will impact on patient outcomes, as has been demonstrated in the context of genetic counselling

for hereditary breast/ovarian cancer (Lobb *et al.*, 2004; Lobb *et al.*, 2002). This is an important topic for future research.

ACKNOWLEDGMENTS

The authors would like to thank Valerie Shaw for assistance with patient recruitment, and Dr Anna Hackett and Ms Justine Perry for advice on the items assessing knowledge about the genetics of hemochromatosis. Bettina Meiser is supported by Public Health Australia Fellowship No. 007079 from the National Health and Medical Research Council of Australia (NHMRC).

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